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#### EDITORS

January-June .. R. P. KNILL JONES  
 July-December .. S. CAMPBELL-SMITH

# ST. BARTHOLOMEW'S HOSPITAL JOURNAL



Vol. LXVII, No. 1

JANUARY, 1963

## Editorial

THE recent publicity given to the Postgraduate Medical School at Hammersmith about their lack of available funds for research into the transplantation of kidneys, resulted in the provision of funds by a public benefactor; although it is doubtful whether this would have ultimately been necessary, the matter has aroused public interest in Medical Research and its place in the national economy. The usual reaction in leading articles has been that since the United States spends, per head, approximately six times as much as we do on Medical Research, we should in some way try to emulate this state of affairs as if we were a backward nation, and thereby regain some of the limelight we have lost in this field. The latter statement is perhaps not entirely accurate, but may yet become true if the drain on our highly-trained scientific manpower, into which a committee of the Royal Society is now investigating, continues at its present rate. To judge from the feelings of emigrating scientists there must be some truth in the statement that a backward-looking attitude on research is prevalent in some parts of the country, and it is this that results in a penny-pinching that is frustrating and disheartening to many research workers. However greatly we may be impressed by the American achievement in this field, there exists a nagging doubt whether all this research is necessary or even valuable. The simple fact that funds are easy to obtain may result in people going into research for reasons that are not altruistic, to produce additions to the ever-increasing flood of scientific papers because they have to, and not because of the intrinsic value of their work.

In this country finance is split between the Medical Research Council, Charities and Commercial Organisations, resulting in an expenditure of 10s. per head of population. The National Health Service provides .03 per cent. of its total budget, and while it would be easy to suggest that more comes from this source, it is unlikely, due to the large number of competing interests for its money. The only other source which does not involve the State directly are the Armed Forces, which across the Atlantic provide a large number of grants for work done outside the official research establishments, and may perhaps be persuaded to do the same in this country.

It is often said that we as a nation can do miracles with the most rudimentary equipment and resources, and this is undeniably a laudable attribute; but does it arise through choice? In order to make the biological sciences more available for objective analysis, it has been found necessary to draw deductions from results obtained by using the relatively new tool of statistical analysis. The measurements required necessitate the use of elaborate and expensive apparatus; thus the simple equipment of our predecessors is replaced by complex; both are essential to research, but the latter is difficult to obtain because of the expense. For this and other reasons research is all too often regarded as an expensive luxury which can be forgotten, but if Man is to keep control of himself and his environment it becomes a necessity.

Those who believe in this are prepared to go to great lengths to surmount difficulties which are put in front of them, and are even driven to obtaining grants from America to carry out work in this country. This is an embarrassing situation which should not have been allowed to occur, but it is hardly sur-

prising if in one country there is a relative lack of research workers, and in another a frustrated excess. Economics suggest a short-term solution of solving the problem—moving funds in one direction and men in the other; this can be seen to occur at the present time. The long-term solution is for one in the field of Education, and for the other in providing an enlightened "Official" policy for research; it is to the latter that we look hopefully for the future.

#### Clinical and Research Supplement

This issue marks the start of a new venture by the Journal, and is the first time since the cessation of the Bart's Reports in 1939 that research work carried out at Bart's has been printed in a Hospital publication, with the exception of sporadic articles in the Journal. We thus join Guy's and Westminster, among London Hospitals, in having a publication of this kind, albeit a very modest one of 12

### Calendar

#### FEBRUARY

- Sat., Sun., 2, 3 Feb.: Prof. E. F. Scowen.  
Prof. G. W. Taylor.  
Mr. H. Jackson  
Burrows.  
Dr. R. A. Bowen.
- Sat., Sun., 9, 10 Feb.: Dr. R. Bodley Scott.  
Mr. Alan Hunt.  
Mr. J. N. Aston.  
Dr. G. H. Ellis.
- Mon., 11 Feb., 5.30 p.m.: "Structure of Proteins" by Dr. M. F. Perutz—Senate House.
- Sat., Sun., 16, 17 Feb.: Dr. E. R. Cullinan.  
Mr. C. Naunton  
Morgan.  
Mr. W. E. Coltart.  
Dr. R. Ballantine.
- Thurs., 21 Feb.: Abernethian Society, 5.45 p.m., Prof. Zangwill—"Problems of Cerebral Dominance".
- Sat., Sun., 23, 24 Feb.: Dr. Graham Hayward.  
Mr. A. W. Badenoch.  
Mr. J. N. Aston.  
Dr. Ian Jackson.
- Wed., 27 Feb., 5.30 p.m.: "Auto-immunity & Oral Pathology" by Dr. J. R. Anderson—Royal College of Surgeons.
- Physician Accoucheur on duty for the month of February is Mr. D. Fraser.
- 26th February**—Matter for the March Journal should be received by this date.

pages. This is not due to lack of material, but to our financial position, but we hope eventually to project a suitable "Image" for this section of Bart's activities, and to be considered as a medium for publication of papers from all departments and laboratories in both Charterhouse and the Hospital.

#### Students' Union Report

As we go to press, we hear that the use of the whole of the top floor of the new building has been granted to the Students, and that half of it will not be used for Hospital Offices. This is some compensation for the loss of Student facilities over the years and thanks are due to the Hospital for giving the space, and to the Dean and Mr. Morris for negotiating on behalf of the Union.

#### Crossword Competition

We have pleasure in sending the prize of one guinea to Dr. R. G. Birch of Sittingbourne, Kent.

### Engagements

- BALL—MADGE.**—The engagement is announced between Peter John Ball and June Madge.
- BLAKE—CUTHBERT.**—The engagement is announced between Henry Valentine Blake and Katharine Elizabeth Cuthbert.
- BLISS—BENJAMIN.**—The engagement is announced between Philip Bliss, F.R.C.S., and Joan Elizabeth Benjamin.
- BOWLES—NEWHIGGING.**—The engagement is announced between Kenneth Bowles and Anne Newhigging.
- BURTON—HARTLEY.**—The engagement is announced between Michael Francis Digby Burton and Edna Hazel Hartley.
- ERNST—COOMBES.**—The engagement is announced between Malcolm Ernst and Jennifer M. Coombes.
- FRANK—MAN.**—The engagement is announced between Alexander John Martin Frank and Anne Elizabeth Man.

### Births

- ALEXANDER.**—On 8th December, to Elizabeth (née Gillberry) and Dr. David Alexander, a son.
- CONWAY.**—On 5th December, to Dr. and Mrs. James Conway, 3247, N. Wagner Road, Ann Arbor, Michigan, U.S.A., a son (Christopher).
- GIBSON.**—On 11th December, to Dr. and Mrs. Gibbon (Ruth Alexander), a daughter (Frances Mary).
- SIMS.**—On 3rd December, to Jennifer (née Hartley) and Dr. Robin Sims, a daughter (Clare Penelope).

### Deaths

- ECCLES.**—On 3rd December, Dr. Henry Ernest Karlslake Eccles, M.C. Qualified 1924.
- HARTLEY.**—On 6th December, John Dawson Hartley, F.R.C.S., aged 85. Qualified 1899.
- STURDEE.**—On 6th December, Edwin Lawrance Sturdee, C.B.E., M.R.C.S., D.P.H., aged 76. Qualified 1910.

### Appointments

#### University of London

Mr. B. N. Brooke, reader in surgery in the University of Birmingham, has been appointed to the new chair of surgery tenable at St. George's Hospital Medical School.

#### Army Medical Post

The Army has appointed as its first honorary advisor on obstetrics and gynaecology, Mr. Arthur Bell, president of the Royal College of Obstetricians and Gynaecologists.

#### Royal College of Surgeons of England

Diplomas of fellowship were granted to the following: Philip Bliss, L. J. Chalstrey, L. N. Dowie, Brian Richards.

The following honour was awarded in the New Year's Honours List: Aubrey Gordon Leacock, M.A., F.R.C.S., L.R.C.P.—C.B.E.

### Change of Address

Miss H. M. Brown,  
100, Paddock Road, Newbury, Berks.

Dr. E. Buchler,  
20, Glenhill Road, Blackheath, London, S.E.3.

Miss M. E. Gifford,  
Mount Gold Hospital, Plymouth, Devon.

Dr. and Mrs. C. R. Hart,  
"Goldthorns", Stilton, Peterborough, Northants.  
Tel.: Yaxley 447.

Surg.-Lt. D. A. Lammiman, R.N.,  
David Bruce Military Hospital, Imtarfa, Malta,  
G.C.

Dr. L. Levy,  
516, Harley Chambers, Cor. Kruis & Jeppe  
Streets, Johannesburg, S. Africa.

Dr. M. I. M. Noble, 10, Lismore Close, Isleworth,  
Middlesex,

Dr. R. W. E. Watts, National Institute of Arthritis  
and Metabolic Diseases, National Institutes of  
Health, Bethesda, Maryland, U.S.A.

## HOUSE APPOINTMENTS

Consultant Staff	House Officers	Male	Female
DR. F. R. CULLINAN Dr. K. O. Black	P. B. Christian	Rahere	Colston
DR. A. W. SPENCE Dr. N. C. Oswald	B. T. Marsh	Dalziel	Annie Zunz
DR. R. BODLEY SCOTT Dr. W. E. Gibb	K. E. Gray	Harvey	Luke
DR. G. W. HAYWARD Dr. H. W. Balme	T. M. Coltart	Smithfield	Mary
PROFESSOR SCOWEN Dr. A. G. Spencer	T. J. Fowler	Stanmore	Garrod
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MR. A. H. HUNT Mr. J. O. Robinson	A. M. Pollock	Miss A. M. Sinclair	Waring
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MR. E. G. TUCKWELL Mr. M. A. Birnstingl	J. F. Stevens	A. K. Thomas	Harmsworth
PROFESSOR TAYLOR Mr. B. N. Catchpole	R. V. Jeffreys	J. M. Jailler	Bowby
DR. K. O. BLACK MR. J. O. ROBINSON	Miss A. M. Sinclair	H. A. Beecham	Heath Harrison
	J. E. Ind	R. J. Shearer	Rees Mogg
	A. K. Thomas	P. W. A. Mansell	Paget
	J. M. Jailler	A. P. Ross	Percival Pott
	H. A. Beecham	H. White	Lawrence
	R. J. Shearer	M. M. Orr	
	P. W. A. Mansell	J. Spivey	CASUALTY HOUSE PHYSICIAN
	A. P. Ross	Miss M. S. Johnson	CASUALTY HOUSE SURGEON
	H. White		
	M. M. Orr		
	J. Spivey		

#### CHILDREN'S DEPARTMENT

Miss J. M. Darmady Lucas  
P. A. Bacon Kenton

#### E.N.T. DEPARTMENT

J. W. Hamilton Henry Butlin  
Miss J. E. Angell James

#### EYE DEPARTMENT

R. M. Phillips Radcliffe

MR. H. B. STALLARD  
Mr. J. H. Dobree

## Gynaecology and Obstetrics Department

MR. JOHN BEATTIE	C. A. Hood	(O)	Martha
Mr. Donald Fraser	L. R. Thomas	(O)	Elizabeth
Mr. J. Howkins	K. Manchester	(G)	Sandhurst
Mr. G. L. Bourne	(Junior H/S)	(G)	Pitcairn
		(G)	Harley

## DENTAL DEPARTMENT

MR. HANKEY	P. Cove	Fleet Street	Harmsworth
Mr. Cambrook			
Mr. Cowan			
Mr. Schofield			

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Mr. W. D. Coltart	D. M. Myers		
Mr. J. N. Aston	P. W. P. Butler	Henry	
	(Fractures)		

## DEPARTMENT OF THORACIC SURGERY

MR. O. S. TUBBS	D. W. Gau	Vicary
Mr. I. M. Hill	P. J. Watkins	

## DEPARTMENT OF NEUROLOGICAL SURGERY

MR. J. E. A. O'CONNELL	R. J. M. Irvine	W. G. Grace
Mr. R. Campbell Connolly	G. G. Ellis	

## SKIN DEPARTMENT AND SPECIAL TREATMENT CENTRE

DR. R. M. B. MacKENNA	Miss M. Janosi	Smithfield	Mary
Dr. P. F. Borrie			
DR. C. S. NICOL		Rahere	Colston

## DEPARTMENTS OF NEUROLOGY AND PSYCHOLOGICAL MEDICINE

DR. J. W. ALDREN TURNER	Stanmore	Garrod
	Harvey	Luke
	Radcliffe	
	Dalziel	Annie Zunz
DR. W. L. LINFORD REES	Miss A.-M. E. Macdonald	
Dr. C. M. B. Pare		

## FILM SOCIETY PROGRAMME

## LENT 1963

## Monday, 4th February:

## "Doctor in the House"

The film of the well-known novel by Richard Gordon inquiring into the social (and academic) sides of medical student life. Freely adapted from the Bart's curriculum and relating to members of our previous generation!

This is one of Bergman's "summer" films, in which he continues his exploration of young love. Unlike "Summer with Monika" with its often bitter comment on marriage, "Summer Interlude" is an almost lyrical film and its portrait of the young lovers finds Bergman in his most tender mood.

## Monday, 18th February:

## "Summer Interlude"

Marie, a young recruit at Opera School, falls in love with a student and they spend an idyllic holiday together; but tragedy strikes and he is killed in an accident. The years pass and she is now a Prima Ballerina. Another man comes into her life: torn between her first love and her feelings for the newcomer, she strives to achieve love and lasting happiness.

## Monday, 4th March:

## "Marx Brothers at the Circus"

Another Marx Brother's comedy, probably better than the others, and directed by Edward Buzzell.

Each film will be supported by cartoons or serious shorts. The committee is hoping to show a film of the "1962 London-Brighton Stroll". The date of showing will be posted when this film is available.

FIFTY YEARS AGO  
THE EPILEPT

"THERE'S ways and ways o' gettin' a night's lodgin', but I reckon Perky Bone h'aint tried epileptic fits for many a long summer. 'Im and me was down 'op-pickin' and tramped it up 'ere together, and by the time we got 'ere we 'adn't got a farthin' between us. Well, we was standin' under the bridge at Ludgate keepin' out o' the wet, and a couple o' coppers went by with an 'and ambulance. I wasn't takin' partic'lar notice, but Perky 'e turns round and says, 'I've got it,' 'e says. 'Well, don't lose it,' I says, 'for you'll want all you've got afore mornin'.' But Perky 'e says very solemn, 'Ave you ever seed a epileptic fit, Toff,' says 'e. 'No,' I says, 'but I seed a man fall down dead in the Blue Goat.' 'Well,' 'e says, 'my aunt Amy 'ad epileptic fits all 'er life, and I'm goin' to 'ave one to-night.' 'What's that for,' says I? 'Lodgin', says 'e, 'free lodgin' and brandy to bring me round.' 'Come along,' 'e says, 'you watch me and see 'ow to do it, and then you go and 'ave a fit across the water.' 'Now,' says Perky, 'it's like this 'ere. Fust I 'ollers out, and then I falls down a champin' my teeth a good bit, and then I lies as still as the dead. Don't you forget it,' 'e says, 'cos they'll ask you what I done.' So I says it all over. Then 'e says 'Swelp me, I'd a'most forgot the blood. Aunt Amy used to froth up a bit o' blood to 'er fits.' So arter a time 'e 'greed to prick 'is finger, an' got some blood in 'is mouth. Then, soon as 'e see a slop comin' in the distance 'e lets fly an 'owl and falls over careful, and begins frothin' and champin' like all possessed. Well, up comes the peeler, and I tells 'im my mate 'as throwed a fit, and orf 'e goes to get a ambulance. Next there comes along an old party and 'e stops and says 'Pore feller, what's the matter with 'im?' 'Fits,' says I, 'e 's a wicrim to 'em.' 'Pore feller,' says 'e, and pulls out a little bottle. Perky, 'e lay like the dead, and 'e took down the stuff like milk. Then Perky 'e makes a most 'orrible noise and out comes all the stuff. 'That's better,' says the old party, 'it's luck I 'ad the wife's sal volatily.' Just then up come the peeler, so 'e and 'is mate put Perky on the stretcher, and there 'e lay

a-frothin' fit to bust 'isself. Presently in comes one o' they young doctors and looks at Perky a lym' there bitin' on to the blanket, with 'is eyes tight shut. 'Ow long 'as 'e been like this?' says 'e. 'Bout ten minutes,' says I. 'Is 'e used to 'ave fits?' says 'e. 'From a baby,' I says. 'Allers like this?' says 'e. 'Similar,' I says. 'It's peccoliar,' says 'e. 'What's peccoliar?' says another young feller. 'Why,' says the other, 'you see 'ow 'is jaw's a goin' although 'e's been in the fit ten minutes.' Then old Perky 'e sees that 'e's orf the rails, so 'e slows up 'is champin' and lies as still as 'e can. Then the doctor goes up to Perky and tries to open 'is eyes, but Perky 'e wasn't takin' any, and froze 'em down like the top of a beef tin. Last of all the doctor done it, and put 'is finger flat on Perky's optic. Perky, 'e snaps it up tight in a minute. Then they puts pinchers on 'is tongue and 'itches it out, and wipes 'is mouth out, and the young doctor 'e turns to the nuss and 'e says 'E may 'ave blood in 'is mouth' 'e says, 'but 'e haint bit 'is tongue none the more for that.' 'E's in a desp'rate situation,' says 'e, 'and I'm afraid 'e'll need very strong measures, my man.' 'It's a painful sight,' says 'e, 'p'raps you'd rather wait outside.' But I was gettin' int'rusted so I said I wouldn't leave my mate. 'Very well,' 'e says, 'fetch the batt'ry.' Then they brings along a box with wires to it, and 'andles, and sets it buzzin' with 'lectricity, and claps the 'andles on pore Perky. Well, I judge 'e never made more faces in the time. They puts it on 'is cheek, and out goes 'is mouth all to one side like my uncle Tom's arter 'e'd fell down a area in Bloomsbury.

"Well, I must say Perky kept a stiff neck, for 'e never says a syllable. Presently the doctor gives over and says 'Dear dear, it's worse 'n I expected. I'm afraid 'e'll 'ave to be took in.' 'Bad as that, is it?' says I. 'Well,' says 'e, considerin', 'I suppose we ought to make a great effort. I suppose 'e won't say no,' 'e goes on, lookin' funny at the nuss. So then they took 'im 'long to another room, and props 'im in a chair, and straps up 'is arms and legs, so 's 'e couldn't no more'n breathe by 'isself, and the young feller 'e prises open 'is

mouth agin, and swelp me if the doctor didn't start runnin' a indyrubber gaspipe down 'is throat. It was about a yard long, and it just finished Perky. 'E let fly the best 'owl 'e could for all the things in 'is mouth, and begins fightin' like a wild cat. 'E's comin' round,' says one of 'em, and then 'e poured about a quart o' water into pore Perky with a funnel. And there was the constables a-larfin' and the

## STUDENTS' UNION REPORT

This year may be one of the more important in the history of the Students' Union. Several things will be happening that concern the students and for the first time in many years the various authorities are consulting us about our requirements and every effort is being made to fulfil these. The new Dean, Mr. Cope, is very helpful and understanding towards the Students' Union.

Sad to say, it has been decided by the Hospital that the Abernethian Room must be taken over by the Out-Patients' Department and ourselves moved into a new block between the Nurses' Home and the Children's Wards. The Union cannot possibly prevent this move but it can work for the best facilities in our new accommodation.

The new building is temporary, designed to last ten to twenty years; this probably means we will be in it for fifty years! Eventually we are to be moved to a site in Cock Lane which will be our permanent residence with lounges, snooker room, etc.

The temporary building will consist of two floors. Half the top floor will be constructed as the Locker Room, Lounge and Cloakroom for the women students. All the ground floor will be a new Abernethian Room, larger than our present one, with an adjoining Card-cum-Committee Room.

At present the Students' Union and the Hospital are discussing the design of the various rooms. We think it essential to keep a club atmosphere in the new Abernethian Room and would therefore like to move the oak panelling and the fireplace, although this is more expensive than the normal interior decoration of a lounge. We must have some good prints on the wall; preferably of famous old

doctors and the nusses all fit to bust themselves. Last of all they finished and lets 'im go. 'Feelin' better?' says the doctor. 'You've 'ad a wonderful escape my man.' But this was more 'n Perky could abide. 'Escape!' says 'e, 'escape!' 'oldin' 'is 'and to 'is stomach and countin' of 'em up. But they was too many, so we slid out, and I didn't throw no fits in Southwark."

Bart's students such as W. G. Grace, and the tables and chairs must match the above ideas. The Council has decided that the students should raise money to help pay for this venture since it will be expensive to equip as we would like. We think that the powers that be may be more generous if we make some sort of effort ourselves. Therefore the Wine, View Day Ball and Athletics and General Committees have been asked to help and all three have generously offered donations. Should students have any other ideas on how to raise more money, please contact the Secretary of the Union.

Comment among the students fears that we are being driven out of the Hospital altogether. It is difficult for me—if indeed it is my duty at all—to waylay these suspicions since the evidence does show that we are slowly losing our facilities in the Hospital. The House Snooker Room used by the students has gone, although we still have its fine table. The Vicarage Bar has gone to make way, I believe, for a Cleaners' Cloakroom. Our Rifle Range, which was generously endowed by Lord Ludlow in 1908, is soon to make way for the terrifying malignancy of the Records Department, and now the Abernethian Room, where some of our grandfathers sat and meditated, is to go to allow better facilities for the stream of postmen and porters.

On the credit side we now have the use of the Nurses' Swimming pool for two lunch-times and for two, one and a half-hour sessions of, dare I mention it, *mixed* swimming on Tuesdays and Thursdays.

We are certainly on an ebb tide at present and must hope that the new attitude towards the students will prevent us from disappearing

altogether from, and I quote the Duke of Gloucester, "this, the oldest, and in the opinion of many, the finest teaching hospital in the world". What is to be done? The problem of space on the island-site is acute, but must the students' facilities be the first to go to solve this problem? We would like to make a few suggestions.

The Rifle Club can raise £1,000 for a new rifle range at Charterhouse and needs another £5,000 for the project to become feasible. We hope that someone will help us in compensation for the loss of the old Rifle Range said by The Journal in 1908 to be the property of the Students' Union. This has never been refuted, although the deeds have been lost.

Let us have *all* the temporary building on the car park so that *we* can use the rest of the top floor, planned as offices, as a Snooker Room and even, perhaps, a refreshment bar which could also be used by the House. And now that Queen Victoria is dead, how about mixed swimming for more than three hours a week!

At Charterhouse the Council have negotiated parking space for the residents because we will lose the present residents' car park for the College Hall extension. Arrangements are under way for us to park in front of College Hall, which will be very convenient. The Staff will park in a new car park being built near the Physiology Department, also convenient. The College Council has decided that a nominal fee should be paid by those using Charterhouse parking facilities to pay for the new car park. We hope it will be nominal since many

## JOURNAL COMPETITION

Dr. Geoffrey Bourne has kindly agreed to judge entries for a new Journal Literary Competition. A prize of £5 will be awarded to the outright winner, but if two entries of similar merit result in a "tie" for first place the prize will be divided between the entrants.

Essays and articles (not more than 10,000 words) should be sent to the Editor of the Journal to arrive not later than 30th April, 1963. If there are sufficient poems submitted a separate prize of £2 will be awarded to the best entry.

There is no restriction on subject matter, but entrants are advised that attention will be paid to style and originality. The best entries will be published in the Journal.

residents run cars on a shoestring and for them more than 6d. per week would be harsh.

The Wine Committee, under the Presidency of Mr. G. H. Ellis, and the Chairmanship of R. L. Powles, has made a substantial profit for their first quarter. A very successful Smoking Concert, enjoyed by students and staff, was arranged by the Wine Committee last December and during the next year they hope to have another Smoking Concert, a large Barbecue on College Hall lawn, a wine-tasting tour of Europe and several other social events. The Wine Committee is giving £50 towards the furniture for the new Hospital Abernethian Room.

The plans are going ahead for the design of the new bar in the College Hall extension which the College have generously offered to build for us. Our exact requirements for this bar have been requested and the Wine Committee have submitted a sketch plan, drawn up by Whitbread's, to the architects. Examples of such medical college-Students' Union consultation are very encouraging.

On the domestic side the Council has decided to combine the Athletics and General Committees for a trial period of three months, since last year much business overlapped the two Committees and there is no reason why they should remain separate. An Honours Colours Sub-Committee should be set up to try and keep the awards of the various clubs standard over the years.

I hope that this report will arouse some interest in the activities of the Students' Union.

T. J. Powles (Chairman).

## VIEW DAY BALL, 1963

Patrons: The Lord and Lady Mayoress, Sir Ralph and Lady Perring.

This year the View Day Ball will be held on Friday, 7th June, at the London Hilton Hotel, Park Lane, W.1.

The Ball will be in aid of the London Homes for the Elderly.

Any enquiries to:—

Richard Maw,  
Secretary, View Day Ball Committee,  
Abernethian Room,  
St. Bartholomew's Hospital, E.C.1.

## POT-POURRI, 1962

Having reached Television, satire has at last arrived at Bart's and the Pot-Pourri with the loss to the Cambridge Footlights of Graham Chapman. Since Bart's is of an age comparable to many subjects found excellent for satirical review, it is surprising that an abundance of suitable material all about us has remained unscathed—all the more to knock next year. But budding producers are not to make a "This is Bart's that was" of every show. Further, in all the shows there was an unusual lack of reference to Bart's itself which might have taken some of the audience un-awares; those who expected to grin vacantly at private jokes by most accounts enjoyed themselves.

There has been much discussion this year on the merits of productions made up from ward-shows and those designed as a whole from the start for the Cripplegate stage. The gain in polish would be offset by a loss of the spontaneity which makes it (some say) a better evening's entertainment than other hospital shows. Patients too might lose, although some performers in the less responsive wards would doubt the truth of this. Ill patients must hate the shows!

The kids show with a pathetic straight song "Kids" reminded us that any Pot-Pourri committee, this year under Trevor Robinson, must have at least two days to cut what is positively bad and then to build up a coherent show on what is good. The Outpatients? Well, at least they attempted a show this year and the Specials had some attractive girls and some not unattractive material as well as a friendly little ditty about Mr. Capps. The Finalists stepped up the pace a bit with a show that was well organised, had continuity, a strip show and was fun.

After the interval, with the exception of the Midder and Gynae. show the standards were maintained. The Dressers revue was greeted with prolonged applause, unqualified praise and many cries of encores. It might have been labelled a one-man show, but it was not. Who can forget the clever clowning of Messrs. Matheson and Garson in the Shuffle? This was a show that surprised and succeeded. The House closed the evening with a singing show, a slow show, a gay show and a long show ably produced by Mr. and Mrs. Hood. The Path. Lab. song was excellent and "I'm an Otorhinolaryngologist", sung by Mr. Thomas and Co., was most entertaining.



THE KID'S SHOW—"CHINESE CHEQUERS".

*Kim Stevens, David Hunter, Ted Able as the "Men from Ford's".*



THE FINALISTS—"WATCH THIS SPACE".

*Peter Lever as Macmillan, Nick Dudley as De Gaulle, Tony Knight as Kennedy, Chris Ruoss as Krushchev, and "Scrubbers" in the "Decontamination Scene".*



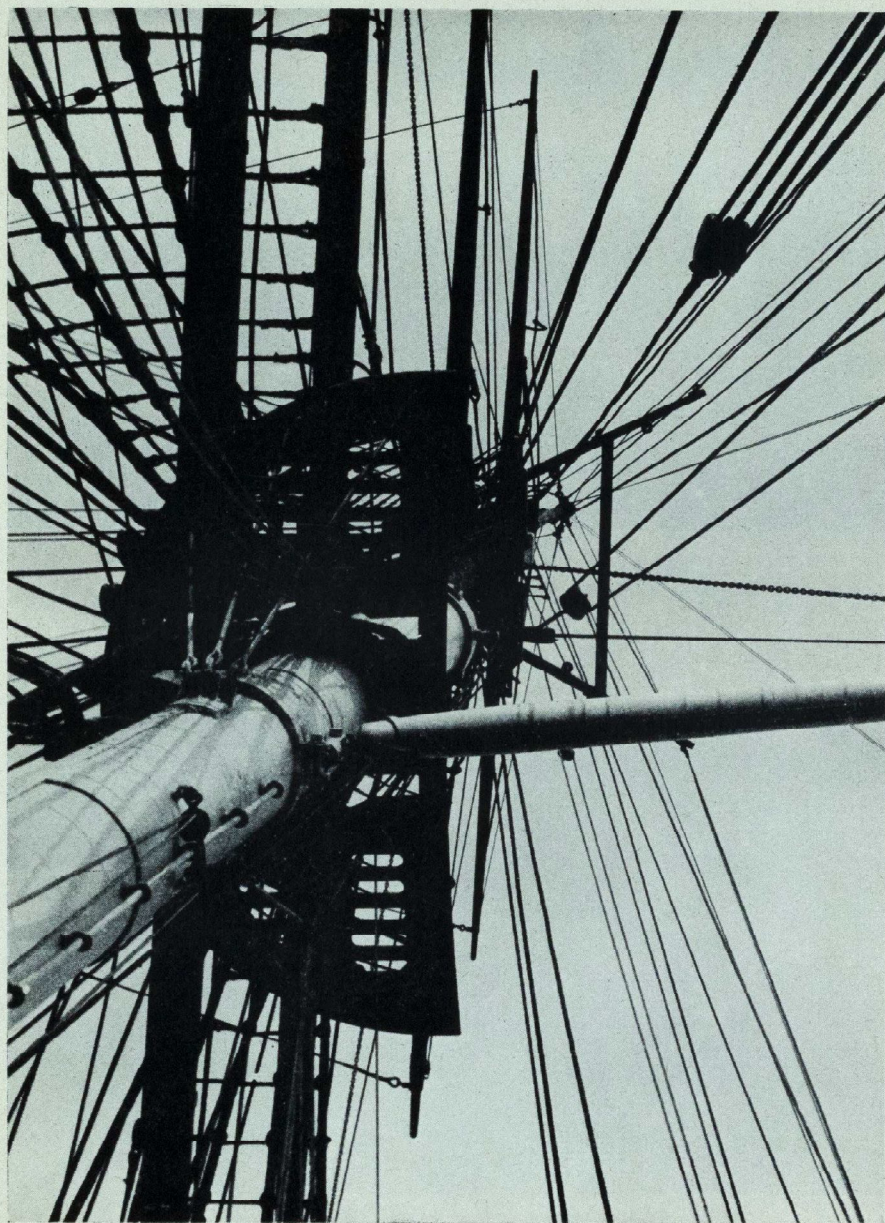
THE OUTPATIENTS—"OUR MAN IN PYJAMAS".

*Ted Carden with the double-bass, and Mike Church as "Sidel Fastro" in "Strawberry Fair".*



THE 1st TIME CLERKS—"TOO TIGHT OR HANGOVER BID".

*(a show which did not reach the Pot-Pourri.)*



Photographic Competition, 1962.  
"Cutty Sark", by D. S. Tunstall-Pedoe—Highly commended.

## THE DIABETIC IN PREGNANCY

By Ted Cantrell

**A** DIABETIC woman who becomes pregnant differs from a non-diabetic in several respects, and these all make a marked difference in the way she should be supervised. Briefly the differences are:—

### A. DIABETES. (Effect of Pregnancy.)

1. She usually develops a lowered renal threshold, and consequently a marked glycosuria, while still maintaining relatively normal blood sugar levels.
2. Her insulin requirements increase throughout pregnancy (they may even double), and drop rapidly after delivery.
3. Diabetic control becomes more difficult, and blood sugar levels may be more labile (Pedersen considers this to be sufficiently marked to adjust insulin dosage by blood sugar estimations four times daily).
4. Carbohydrate requirements are increased, partly to allow for a growing foetus, and partly to ensure adequate Glycogen stores for the time of delivery.

### B. PREGNANCY. (Effect of Diabetes.)

1. There is an increase in the incidence of complications of pregnancy, for instance pre-eclamptic toxæmia, hydramnios, hypertension and infections.
2. There is an increased incidence of Foetal abnormalities.
3. There is a greater incidence of Perinatal mortality, due to a number of factors not yet fully understood. Recent reviews suggest that these may include respiratory distress syndrome, hypoglycaemia, placental insufficiency, and disorders of fat metabolism, water content (intracellular and extracellular) and electrolytes.

It is generally felt that many of these complications can be kept to a minimum if three principles are followed. Firstly, there should

be full assessment and stabilization of the diabetes early in pregnancy; secondly, the patient must be kept under careful supervision throughout the pregnancy, and close watch maintained on accurate diabetic control and foetal growth; thirdly there must be close co-operation between patient, general practitioner, obstetrician, physician and paediatrician.

### FIRST ADMISSION

At twelve weeks (or as soon as pregnancy is diagnosed) the patient is admitted to the medical ward for preliminary assessment and stabilization. Main points to be considered are:—

1. **General Health.** This is checked, a basal blood pressure noted, a search made for any sign of diabetic complications (retinopathy, neuropathy, vascular disease or nephropathy), a chest X-ray is taken early in pregnancy, and routine examination made of urine. Haemoglobin and blood group are estimated, and investigation for abnormal antibodies if thought necessary.
2. **Diet.** The aim is to reach a daily level of 200 G. carbohydrate (allowing 60 G. daily for the mature foetus) and added to this is the amount of "Glucose-leak" estimated in the urine (see below).
3. **Insulin.** Soluble Insulin twice daily is the only satisfactory method of control, whilst additional Isophane Insulin may make for smoother control. This latter has a fairly steady release, and it is unusual to find its action lasting more than fifteen hours. The Depot and long-acting Insulins apart from Isophane (I.S.P.) have been found unsatisfactory and erratic; and even very small doses of soluble insulin are preferable to oral hypoglycaemic agents, particularly at the time of delivery. Insulin dosage is initially regulated by blood sugar estimations (twice daily, 4 hours after each injection; or as frequently as



## EVALUATION OF CANCER EDUCATION

by MALCOLM DONALDSON

Synopsis of lecture read at the International Congress of Cancer, Moscow, 1962

THERE are still some members of the Medical Profession in Great Britain who are doubtful whether Cancer Education among the Public is of value. It is hoped that this lecture will help to convince them.

The lecture is written under the following headings:

1. Lay opinion on Cancer Education.
2. Opinion of Medical Profession
3. The following seven methods of evaluation are discussed:
  - (a) As a result of Cancer Education is there increased knowledge of the disease among the Public?
  - (b) Is there any improvement in the Mortality figures?
  - (c) Is there any improvement in the "Five Year Survival Rate"?
  - (d) Is there any improvement in "Early Stage Diagnoses"?
  - (e) Is there less delay in reporting symptoms by patients suffering from Cancer?
  - (f) Is there less delay in patients reporting "suspicious symptoms" regardless of the cause of such symptoms?
  - (g) Do people who have heard a lecture remember it and act upon the advice given?

### Lay Opinion on Cancer Education

There is no doubt whatever that the vast majority of the Lay Public are anxious to know more about cancer. During the Yorkshire "Pilot" experiment carried out from 1953 to 1956, ballot papers were distributed at the end of each lecture asking if more such lectures should be given. Of 5,740 votes 99.1 per cent. were in favour, 0.2 per cent. were against and 0.7 per cent. were doubtful.

In Manchester 1,200 women were asked "Do you think there should be freer public discussion concerning the disease and its possible cure?" 76 per cent. replied yes, 9 per cent. no, and 15 per cent. were doubtful. These women had not heard a lecture which may account for the difference in the figures between Manchester and Yorkshire.

In Canada a survey showed that 88 per cent. were in favour of freer discussion.

### Opinion Among the Medical Profession

In Great Britain there is some difference of opinion among the doctors. In 1952 a questionnaire was sent to 19,000 general practitioners by the British Empire Cancer Campaign asking them if they agreed with Cancer Education. Few of these had had any experience of such education, and only 24 per cent. replied. Of these 2,680 were NOT in favour and 2,148 were in favour, but with 76 per cent. of abstentions such figures are valueless.

In Manchester 108 practitioners who had seen the results of Cancer Education were asked "Have such talks ever caused you additional work?—are patients made uneasy by such lectures and come to your surgery without observable symptoms?"

ANSWER: 105 replied NO, 3 YES.

When asked whether they approved of the campaign 97 gave entire approval, i.e. 92.7 per cent., 10 were not convinced, and one very doubtful. NONE thought it harmful.

### Methods of Evaluation

#### (a) Increase of Knowledge of the disease

As a result of Cancer Education is there any increase in knowledge among the public concerning the disease?

Two surveys were carried out in Manchester at 5-year intervals, and two similar surveys were carried out in Canada.

The results in both cases showed without doubt that knowledge had increased.

#### (b) Mortality Figures

The number of patients who die each year from all types of Cancer is on the increase, but such gross figures are of no help in evaluating Cancer Education, because there are a large number of factors such as incidence of the disease, the average age of population, etc., which affect mortality figures.

It is only among the Accessible Cancers, e.g. Breast, Uterus, Rectum, etc., that Cancer Education can be of value.

#### (c) Effect on 5-year Survival

Here again cancer education is of value in the accessible cancers, which as a rule show

symptoms "in the early stages of the disease" because the object of cancer education is to cut down the delay between noticing symptoms and seeking advice. There are, however, other factors besides "delay" which affect the five-year survival rate, e.g. the rate of growth and malignancy of the individual tumour, so that there is no direct correlation between delay and 5-year survival.

#### (d) Effect on Early Stage Diagnosis

There are few definite figures in Great Britain concerning "Early Stage Diagnosis" but in Canada there are figures which compare the percentages of "early" and "late" stage cases treated, before and after Cancer Education was introduced. For example, in British Columbia the percentage of early stage cases rose from 45 per cent. to 59 per cent. with a corresponding drop in late cases, in Saskatchewan it rose from 60 per cent. to 61 per cent., and in Ontario 51 per cent. to 58 per cent. It may be argued, however, that some of this improvement might have been due to more prompt diagnosis and treatment by the medical profession.

#### (e) Delay on the part of patients in reporting symptoms due to Cancer

This is of course the most important non-controversial proof of the value of Cancer Education.

In the case of cancer of the Breast, the average delay fell in Saskatchewan from 11.1 months to 6.9 months.

In the case of Cancer of the Cervix the improvement was not so marked, the drop being from 11.7 to 9.7 months in British Columbia, but no improvement in Saskatchewan. This is probably due to the fact that the symptom "irregular bleeding" is an abnormality of a physiological process, and is therefore much harder to teach.

#### (f) Delay in reporting suspicious symptoms regardless of the cause of such symptoms

This is another way of testing the delay in seeking advice. Cancer education does not attempt to teach people how to diagnose cancer but only what are the "suspicious symptoms" which should be reported at once.

This method of evaluation was carried out during the Yorkshire Pilot experiment.

**Result.** Although there was no dramatic increase in the percentage of patients reporting within the first month, there was definite improvement in the very long delays, e.g. Rectal Bleeding. At the beginning of the experiment (during the first six months) 32.3 per cent. of patients suffering from this symptom delayed

for two years, but during the last six months it fell to 6.1 per cent.

#### (g) Do people remember and carry out the advice given at Cancer Education Lectures?

In order to test this point the Cancer Information Association, Oxford, carried out a small experiment. As a test point the subject of "Self examination of the breast" was chosen. Cards were sent to members of the Women's Institutes and other organizations who had heard the lecture three years previously. They were asked to put an X against one of the following headings.

1. Yes I have carried it out ..... times since the lecture.
2. No. I have not carried it out.
3. I intend to in the future.

An X against (1) or (3) was taken as approval of the idea. An X against (2) was assumed to mean disapproval.

The result of this small experiment was most encouraging. Of the 374 cards returned, 306 (81.8 per cent.) stated that they were carrying out the examination. 41 (10.1 per cent.) said they would now that they had been reminded. This means that over 92 per cent. were in favour. 27 (7.2 per cent.) put an X against heading (2) and must be accepted as disapproving, and it was curious that one third of these came from the same institution.

In addition to the three headings space was left for "Any Remarks". 52 of those who approved wrote remarks all of which of course were complimentary. The following are a few examples.

"Thanks to your lecture I was made aware of my trouble in the early stage—had breast removed—radiotherapy, etc., and am now fit and back at work."

"I did find a lump but glad to say it was only a fatty tumour."

"Found the lecture allayed a lot of fears and was helpful."

"Dr. Donaldson is doing a wonderful work for Fear is a dreadful thing."

"I hope others were helped as I was by the lecture."

Six of the people who did not approve added remarks such as:

"Not interested."

"I have not carried out a regular examination, but I have not forgotten your lecture, and shall certainly seek advice if I notice any unusual symptom."

"No, but if I ever have any sign of anything wrong I would do so at once."

"Trouble comes quickly enough without searching for it. I think I should know at once if anything was wrong."

"Only two types of women could possibly remember 'every three months', i.e. the methodical and self-engrossed to a degree, or morbid and fear ridden. Busy people will only remember when hearing or reading about Cancer—do an examination and forget again."

"I have had a breast operation. It was not malignant and I have been told no cause for worry."

During 1958, 3,638 people heard this lecture and since then 5,364 more. If anything like 92 per cent. of these remember the lecture

and act upon it, can anybody doubt the value of Cancer Education?

#### Summary

Various methods of evaluation concerning Cancer Education have been discussed. There is no doubt that such education is resulting in a larger number of "Early Stage" cases being treated thus saving a great many lives.

Judging by the "Remarks" on the cards, and things said at the time of the lectures, there is no doubt that Cancer Education is of great value from a Psychological point of view and is diminishing fear of the disease.

"Knowledge is the antidote to Fear."

Emerson.

## Air for Evening

*From the breathing Church, a guilty child  
tiptoes, leaving the vase broken  
on the floor; and on the ikon, a lip-print.*

*Alone in the stadium, a ground-boy  
is practising penalties; and the pigeons  
have to wait before settling for the night.*

*The concert is over; a lady remains  
searching for her gloves; the famed  
acoustics pick up her heavy breathing.*

*On the embankment, a Doctor is asleep,  
still wearing his white coat,  
like a swan, dreaming of Pyrrhus.*

J. Davies

## COMMENT

### CLINICAL TEACHING AT BART'S

HAVING reached the revision course I thought it might be interesting to set forth my thoughts on the possibility of improvements in medical teaching.

I would make it clear at once that one learns best by experience and the majority of one's learning occurs after qualification. Therefore it is vital for a teacher to imbue in his pupils a keenness for his subject. Experience can be gained by a student in three places: the post-mortem room, the operating theatres and the wards. It is important that there should be encouragement to attend these places. Short of giving prizes the best method of giving encouragement is by providing interest. I shall summarize an order of clinical appointments giving reasons for changes and then write about each appointment suggesting a few improvements.

The Introductory Course is necessary to introduce students to the Hospital. First Time Clerking and Dressing is necessary to introduce them to ward routine. After this it would seem logical to continue by combining the two in the study of Paediatrics. The Specials course would be better following Midder and Gynae. Midwifery following Paediatrics seems logical since one must combine the two very closely when studying the neo-natal period. The Specials course deals with subjects not already covered and consequently should tie up loose ends and come last in the course of new subjects.

After learning the subjects of the Science of Medicine it follows that one should finish the course by revising the more important subjects; Medicine and Surgery second-time appointments, followed by comprehensive outpatient teaching in which the student sees for the first time patients who have *not been seen before* by a doctor. Then Out-patients would be a valuable preparation for Housemanship and the revision course a preparation for finals.

The Introductory Course beginning after 2nd M.B. serves to show students the hospital way of life. Students are advised to see all and to get to know their way around the Hospital. During this course teaching in general Pathology is emphasised while no emphasis is laid on its correlation with Medicine and Surgery. If there were a lecture on, say, Acute Inflammation in the morning, it would help if students could then be taken round the wards by the Pathology Registrars to have simple examples of this subject—even an acute appendicitis—demonstrated. This procedure would eliminate the need for introductory lectures in Medicine and Surgery about which the student knows little, although rounds at this stage could include specific instruction in clerking and examination.

In the First Time Dressing Course dressings could be changed by students who have been taught sterile procedures, and after three weeks the Second Timers could be replaced by First Timers on the Outpatient boxes. Consultant teaching should be quite general for the first month and then the student could become interested in the specialisation of his Chief while still having general Surgery taught by the Registrars. During this and the Medical Clerking, Pathology Registrars might take a weekly round, teaching the Clerks and Dressers from each floor on subjects already covered in Medicine and Surgery that week. The arrangements would be similar in the First Time Clerking Course, where blood-taking leaves little time for history-taking. The Clerks of each firm should be expected to be available during duty day and to be on call in the Abernethian Room.

Paediatrics must be most difficult to teach. Some other teaching hospitals send students away to learn it at a special hospital. It is to our credit that we have two excellent consultants in Paediatrics; however, at the end of the course one feels that one still has little clue as to what would happen if one were confronted by a mother and her baby. In this course emphasis must be laid on the ability to get on well with children since they form a large percentage of the patients seen by a G.P. I would suggest a systematic course in children's diseases; we are training to be doctors, not professional examinees.

The Specials Course demonstrates the problems of teaching many different subjects together. These problems are mostly administrative, but might be overcome by coupling subjects to be taught in one group for one month. A fourth month could be taken from Paedia-

trics so that subjects would couple logically as follows:—

E.N.T., Dentistry, V.D., Anaesthetics.  
Eyes, Chest Surgery, Neurology, E.C.G.,  
Neurosurgery

Skins, Radiotherapy, Psychiatry, E.E.G.  
Orthopaedics, Fractures, Radiology.  
Further anaesthetics could be taught during  
second-time Surgery and Medicine.

During the Obstetrics and Gynaecology  
Course there is teaching on a basis of Patho-  
logy, there is a sense of humour behind the  
teaching, and in Midwifery we at last do  
something ourselves. These facts make this  
course the most enjoyable and best taught at  
present. It might be better if the second month  
on Gynaec. Outpatients was changed for a  
third month of Midwifery or an extra one in  
the revision course. The month on anaesthetics  
could remain as it is, be put into the second-  
time course, or back into Specials leaving a  
third month for Paediatrics.

Second-time Clerking and Dressing is im-  
portant since it leads up to Part One of Finals  
and it is necessary to have lectures on at  
last three afternoons a week with teaching on  
slides interposed. I believe that in order to  
gain a better working knowledge of Medicine

## LAST MONTH

The opening of the new library was the  
main event of the end of 1962 as far as Char-  
terhouse was concerned. The library, or "El  
Charterhouse" as it has been called, is a cross  
between a modern coffee bar and an American  
airport lounge. Most of us enjoy working in  
this sub-tropical paradise, but can't I have  
somewhere to hang my jacket? There is  
nothing more pleasant on these cold, cold  
evenings than dropping into the library for a  
refreshing nap in one of those Heath Robinson  
chairs with one's feet up on the little tables.

On the second day of the new year I arrived  
to find four interesting-looking gentlemen just  
about to demolish the old tin library, so dear  
to the hearts of many. I dashed round seeking  
signatures for my "save the old library" fund,  
only to find that by lunchtime it was too late  
and the hut was beyond human aid. "Alius  
alia via" (which I freely translate: "It was  
a good hut as huts go. . .").

Broadsheet, the latest Bart's publication, is  
at the time of printing still selling well. This  
fortnightly student journal contains original

and Surgery it would be better for the student  
to spend three weeks on each firm except  
those which he attended as a first timer. Ideally  
the second timers should be prepared and able  
to answer questions from the first timers. At  
this stage each student's attendance should be  
quite voluntary.

Outpatients could be the most useful ap-  
pointment of all; Pathology lectures would still  
be available for those who needed them. Stu-  
dents could be split into small groups, each  
spending two weeks with one consultant and  
the equivalent day of each week with his reg-  
istrars. Students would be expected to clerk  
and examine one patient, make a diagnosis,  
and provisionally write out investigations and/  
or prescribe appropriate drugs. The keener  
ones might help on the accident box. During  
Outpatients students are expected to go to  
special clinics either helping or learning. The  
clinics which are not generally used are the  
Diabetic, Genito-Urinary, Cardiac and Vari-  
cose Veins, all of which complete a grounding  
in Medicine and Surgery. Finally, I repeat,  
the revision course should be regarded primarily as  
practice in examination technique.

A.C.R.

articles, film reviews, theatre (amateur and  
professional) criticisms, and, editorial policy  
tells me, almost anything students care to write  
(within reason of course). Broadsheet has  
come under fire from various people and quite  
a few have encouraged it. One of the most  
interesting things, to my mind, is the constant  
reference to apathy among the student body  
that appears in each issue. This poses the  
question: do we really know what sort of  
person the apathetic one is? As a recent cor-  
respondent hinted at in Broadsheet, a person  
with a reputation for his drinking or sexual  
prowess would never be accused of apathy.  
Is it fair to label a rugby player apathetic if  
he never goes to the Drama Society functions  
or the actor for never watching rugby  
matches?

One would not normally connect 2nd M.B.  
with the football pools, although both contain  
the element of chance. But now I see the fate  
of the pools fortune is also to be decided by a  
panel of experts. I hear rumours that the fate  
of 2nd M.B. candidates is to be decided by  
chance.

## LETTERS TO THE EDITOR

Dear Sir,

Since Christmas is approaching, the time  
of universal festivities, I thought that the fol-  
lowing authentic advertisement, from a local  
paper of a certain West Indian Island, might  
be of seasonal and professional interest to your  
readers. The light-hearted and cheerful accep-  
tance of the universal fate of mankind is a  
most admirable sentiment with which we must  
all agree!

### "DEATH! WHERE IS THY STING?"

DEATH is inevitable, for man was born to  
DIE! But the STING is greatly lessened  
when JAMES WILSON AND SONS,  
Funeral Furnishers, happen to be the  
UNDERTAKERS. Less tears are shed when  
the burden of BURIAL is shifted from the  
family circle on to the capable hands of such  
efficient UNDERTAKERS as JAMES  
WILSON AND SONS. All that is necessary  
after death, is to come, send for, or ring No.:  
86 EAGLE HALL CORNER and the family  
job is over. WILSON AND SONS have  
spared no expense to give even the poorest  
man, woman or child, a decent burial at small-  
est cost. Sorrow is therefore reduced to a  
minimum. A Buick 6-cylinder engine is  
attached to the hearse, and Buick engines  
seldom play dirty tricks on the road by stop-  
ping every now and then. Lovely Caskets and  
Face-holds at various prices. Prompt atten-  
tion paid to all orders and the EAGLE HALL  
FRINDLY SOCIETY run by the same  
Undertakers at popular Weekly Contributions  
will protect you in sickness, in DEATH, and  
at Christmas time. Become a member now  
and secure yourself and family before it is  
too late."

Sincerely yours,

Geoffrey Bourne.

\* \* \*

Dear Sir,

As a perpetual student 200 miles and 20  
years away I should like to say how much I

enjoyed my first attendance at the XIIIth  
Decennial Club.

Dinner and drinks and meeting old faces  
was suitably housed at the zoo in the evening.

The Open Day at Bart's itself in the after-  
noon was, I believe, a recent innovation and  
very well organised. The North is more civil-  
ised than some people think and G.P.'s attend  
a good many lectures and postgraduate courses  
and clinical meetings, as well as swimming  
through cascades of medical writings. But to  
be back again at Bart's with our contempor-  
aries was something special. The lecturettes  
were amusing and meaty ("potted meat"—  
more meat than potty) and with a special  
Bart's flavour which is obvious but difficult to  
define. The only criticism could be that we  
did not see a patient, nurse, or ward. But  
we did have tea in the Big Hall and we thank  
the Governors for that.

Yours sincerely,

Dr. Paul Rowntree.

\* \* \*

Dear Sir,

I was very glad to see the photograph of the  
consulting staff of the Hospital. This was  
taken in 1904 on the occasion of the laying of  
the foundation stone, by King Edward VII,  
of the new Out-patient department.

There is one curious thing about it; there  
is a gap between Hugh Walsham of the X-ray  
department and Tommy Horder, as he was  
then called, who, with Horton Smith (not then  
Hartley), was a Medical Registrar. A photo-  
grapher would never have allowed a gap of  
this kind, and comparison with the photograph  
in the Library shows that the gap was filled by  
Gordon Watson. But as he was not then a  
member of the staff, his image was deleted. I  
did not come to the Hospital until three  
months later and heard about the "incident"  
shortly afterwards.

Yours sincerely,

George Graham.

## FEBRUARY SPORTS DIARY

- 1 Feb. Soccer 1st XI v. Lincoln College (A).  
 2 Feb. Men's Hockey v. Veterinary College (H).  
 Rugby 1st XV v. O.M.T. (H); A XV v. O.M.T. (A).  
 Soccer 1st XI v. Worcester College (A).  
 5 Feb. Squash v. Kensington Close.  
 6 Feb. Soccer 1st XI v. King's College Hospital (A).  
 Men's Hockey v. Middlesex Hospital (H).  
 9 Feb. Rugby 1st XV v. London University (H).  
 Rugby A XV v. Harlequins (A).  
 Men's Hockey v. U.C.H. (H).  
 12 Feb. Squash v. Metropolitan Police.  
 13 Feb. Soccer 1st XI v. R.N. College, Greenwich (H).

SPORTS DAY will be held on Wednesday, 29th May, 1963.

## Editorial

### THE CROSS-COUNTRY CLUB

Until 1961 the Cross-Country Club was merely a sideline of the Athletics Club, but with increasing membership and successes it then became a separate entity. Although many people regard cross-country running as one of the Hospital's many minor sports, the Club has distinguished itself over the last two years.

Their first major success came in the Inter-Hospital Championships two years ago, when Bart's scored an overwhelming victory. This was repeated last year, when the victory was even more convincing. In 1961 Bart's emerged as Champions of London University League II. Last year we came second in the First Division, and this year hope to go one better.

It must be emphasised that the results were made possible not by a few stars at the top, but rather by exceptional keenness lower down. Team victories are brought about by the last two or three scoring members and not the first three or four. P. Littlewood, T. Foxton, N. Pott and D. Tunstall-Pedoe have all run for the London University first team; the first two having been awarded University Purples, whilst N. Pott has United Hospitals colours. R. Thompson, R. Pickard and R. Hale have all been running well for the U.H. first team. Littlewood and Foxton have both represented their Counties in the National Championships whilst D. Tunstall-Pedoe has clocked several 4 min. 14 secs. miles for Cambridge University in their matches.

Contrary to the belief of many, training for such a sport is not an individual business.

- 16 Feb. Rugby 1st XV v. Metropolitan Police (H); A XV v. Metropolitan Police (H).  
 Men's Hockey v. London Hospital (A).  
 Soccer 1st XI v. Guy's Hospital (H).  
 19 Feb. Squash v. Beckenham C.C.  
 20 Feb. Soccer 1st XI v. Westminster Hospital (H).  
 23 Feb. Rugby 1st XV v. K.C.S.O.B. (A); A XV v. Old Paulines (A).  
 Soccer 1st XI v. West Ham College (H).  
 Men's Hockey 1st XI v. St. Mary's Hospital (H).  
 2nd XI v. St. Mary's Hospital (A).  
 26 Feb. Squash v. Middlesex Hospital.  
 27 Feb. Soccer 1st XI v. School of Oriental and African Studies (A).

Runs "en masse" take place each Wednesday afternoon in the Autumn and Winter, regardless of the weather. The team members leave the Parliament Hill running track at 2.30 to cover an approximate nine mile circuit of Hampstead Heath. This consists of free and easy running over grassland, through woods, scrub and heath and over marshland. Many members also devote considerable time to the tougher muscle-conditioning sand back on the north side of the Heath. With the gymnasium at Charterhouse now redecorated and re-equipped, evening weight training sessions will also be held. So much for the "Loneliness of the Long Distance Runner"!

The Club organises two tours each season, one to Scotland for the "Ben Nevis Race" in early September and the other in April to Westmorland for the "Three Peaks Race". This March Bart's hope to have eight of their first team included in the U.H. Tour of Ireland. G.H.

### RUGBY CLUB REPORT

17th Nov. Bart's v. Old Alleynians. Lost 3 pts.-6. Bart's were without their captain, A. J. S. Knox, and played without cohesion and consequently lost a very uninspiring game. The heavy Alleynian centres broke through tackles and constantly menaced the Bart's line; only desperate covering prevented the deficit from being greater.

The Alleynians scored a penalty and then a scrambled try to which Bart's replied with a penalty by Gibson. The forwards lacked their usual fire and the three missed M. Philips at centre who has added a good deal of maturity to their play of late.

Team: E. D. Dorrell; D. Goodall; R. V. Jeffreys, P. Savage, E. Sidebottom, A. T. Letchworth, D. C. Pope, J. Hamilton, B. H. Gurry, O. J. A. Gilmore, B. Doran, D. Delany, C. Cripps, C. Smart, J. Gibson.

### 24th Nov. Bart's v. U.S. Chatham. Won 53 pts.-3.

With the memory of the Old Alleynian game fresh in their minds the Bart's XV began the game against a weak U.S. Chatham XV with a try from the kick-off. The 50 pts. was reached in the last minute of the game and this finally removed all thoughts of the previous Saturday. The Bart's forwards kept the ball moving well, feeding their halves with constant possession from the tight and loose. Niven and Goodall ran well at centre and constantly penetrated the Chatham defence.

A record of try scorers would be difficult for obvious reasons, but two tries by Letchworth and one by Niven stood out as being particularly fine pieces of work. A gratifying afternoon's work for the XV.

Team: E. D. Dorrell; P. Bradley-Watson; D. Goodall, P. Niven, E. Sidebottom; A. T. Letchworth; D. C. Pope; O. J. A. Gilmore, B. H. Gurry, A. J. S. Knox, D. Delany, M. M. Orr, C. McKenzie, C. Smart, J. Gibson.

### 1st Dec. Old Cranleighans v. Bart's. Won 19 pts.-6.

This was another gratifying performance by the XV against the Cranleighans, as the absence of A. T. Letchworth at outside half obviously caused a certain amount of disruption of the "three-line". The game opened with a superb run by S. Harris, ending just short of the opposition try line. McKenzie opened the scoring with a crashed try, Gibson failing to convert; then Doran scored in similar style from a line-out and this time Gibson's kick went over from the touch-line.

Just on half-time a collision between opposing wingers caused the Old Cranleighans to lose a man. From this point they fought harder and although the Hospital scored a goal, try and a penalty goal, the Cranleighans replied with two tries due mainly to negligence by the Bart's defence. This was a good win and in fact, but for handling errors on the opposition's line, the score could have been much more flattering.

Team: E. D. Dorrell, S. Harris, E. Sidebottom, M. Philips, D. Goodall; P. Savage, D. C. Pope; J. Hamilton, B. H. Gurry, A. J. S. Knox, B. Doran, M. M. Orr, C. McKenzie, C. Smart, J. Gibson.

### BOAT CLUB

#### U.C. Winter Eights Regatta: December, 1962.

Junior Division won by Bart's Junior VIII. After their success in the United Hospitals Regatta our Junior VIII stayed together, with one exception, for the Winter Eights Regatta at Chiswick. Twelve crews had entered, and in the first heat Bart's showed fine form in winning by a length from Imperial College "A" and Queen Mary College "B".

Birkbeck College were apparently our opponents in the second heat, but they showed little opposition to the casual Bart's style. Just before the finish our cox was heard to order "Paddle firm!", thus increasing our lead from "comfortable" to "easy"!

The final heat was against none other than Guy's, who had provided such uncomfortable opposition in the Hospitals Regatta. Bart's

plan was to lead right from the start, and by going off at a tremendously high rate of striking they managed to do this. By half-way, with both crews rating very high, the race was still wide open. Guy's made a strong challenge, but Bart's held their lead, and then settled to a controlled, powerful stride with which they romped ahead to win convincingly. Unfortunately, there is no floating trophy for this event—the crew certainly deserved one!

Junior VIII Crew: Bow, D. Robins; 2, R. Anderson; 3, G. Libby; 4, K. Anderson; 5, J. Winter; 6, J. Silverton; 7, W. Garson; Stroke, R. McFarlane; Cox, R. Weller.

### CROSS-COUNTRY CLUB REPORT

#### University of London Cross-Country Championships

Bart's Cross-Country team came second to University College first team in the championships held at Richmond Park over five and a half miles.

The team results were :-

1. U.C. 1st .....	32 points
2. Bart's .....	92 "
3. Imperial College 1st ...	112 "
4. King's College 1st .....	124 "
5. L.S.E. ....	214 "
6. St. Mary's Hospital .....	234 "

Last year we came third, and this year's result represents a considerable improvement as we moved up a place without the services of N. Pott, who was under Dr. Oswald's care. Individually, P. Littlewood came 6th; D. Tunstall-Pedoe 8th; T. Foxton 10th; R. Pickard 30th; and R. Thompson 38th. It was not possible to turn out a full second team because the smog had taken its toll.

The course at Richmond is flat and fast, not suiting most of the Bart's runners, but the extremely strong winds and pouring rain made up for this. Times, as a result, were slow; everyone recording at least a minute below his best performance. Afterwards the team was presented with the Minor College's Cup for the second year running. It is hoped that in the New Year at least three Bart's men will represent London in Dublin, and in the National Universities' Championships to be held at the Queen Mary College sports ground in Essex on February 9th.

#### United Hospitals v. Metropolitan Police v. Lloyd's Bank v. Stock Exchange.

This was probably the greatest achievement of the Cross Country Team during the

Michaelmas Term. They supplied the first five United Hospitals runners to finish and these did not include Nick Pott.

At the start Peter Littlewood and Terry Foxton went straight into the lead and after 2 miles they had been joined by Dan Tunstall-Pedoe and had a clear lead of over 100 yards. This they held for a further 2 miles when one of the bunch of policemen pounding after them came up very fast and managed to pass two of the Bart's trio, but not Peter Littlewood.

Results:	1. P. Littlewood, Bart's ...	31.27
	2. Anderson, M.P. ....	31.33
	3. T. Foxton, Bart's .....	31.41
	4. D. S. Tunstall-Pedoe,	
	Bart's	31.51
	13. R. Pickard, Bart's .....	33.52
	14. R. Thompson, Bart's ...	34.07
	15. and 16, U.H.	
	20. R. Hale, Bart's	

Scoring four-a-side, U.H. (i.e. Bart's) won the match, but scoring a full team, U.H. came second to the Metropolitan Police.

#### SOCCER CLUB REPORT:

##### Retrospect

Record to date:

P. 14: W. 3: D. 1: L. 10.

Goals for 31; Against 60.

This record speaks for itself, and shows that the first half of the season has brought little, if any, satisfaction to the club and its members.

Where, then, does the trouble lie? It is surely fair to say that as individuals the members themselves have done their share. However, the real truth probably lies in this statement. Firstly, the club has no outstanding player, although two or three are above average. Secondly, it does not seem possible for a collection of individuals to work together, in complete co-operation, giving themselves entirely to the club. Maybe the pressure of work and a new life retards the freshman, but even so two afternoons a week and one evening should not be too much to ask; the more senior club members appear to lose their initial enthusiasm after a season or two and play with less heart. Maybe this retrospect is too sweeping and dogmatic, but there must be some truth in it. Although our morale is low, if this article can rouse some greater support and induce a better team spirit, we might hope for a marked improvement in the second half of the season.

#### LADIES' HOCKEY CLUB

v. British Petroleum. Away. Saturday, 13th October. Draw 0-0.

This match was a good start to the season. It was both fast and equal, and we fought hard to the final whistle. We were very pleased to have several freshers, who showed great promise, plus two secretaries and a physiotherapist with us. However, the game made it obvious that we needed to integrate our players into a team.

Team: T. Tennant; J. Spring; B. Bean; M. Newbolt; J. Thoroughgood; O. A. Coates; J. Dunford; G. Steele; W. Smith; J. Young; P. Knight.

v. Royal Holloway College. Saturday, 20th October. Draw 3-3.

We again had no useful goalkeeper for our second match, so that we had to play three backs. This resulted in a one-three deficit at half-time. During the second half our forwards moved well in attack and brought the scores level. J. Spring and W. Smith shot the goals.

Team: E. Evans; G. Turner; T. Tennant; J. Thoroughgood; M. Newbolt; M. Ironside; P. Kumar; J. Dunford; W. Smith; J. Spring; P. Knight.

Saturday, 27th October.

Preliminary Round of U.H. Cup v. Charing Cross. Won 3-0.

Although we won our first Cup Match we did not play very well. This may well have been due to the somewhat small pitch we had to play on. Mary Newbolt played very well and scored a goal. Other goal scorers were S. Minns and J. Spring.

Team: C. Lloyd; T. Tennant; M. Ironside; J. Thoroughgood; M. Newbolt; O. A. Coates; G. Steele; J. Spring; W. Smith; S. Minns; P. Knight.

v. Chislehurst Beavers. Saturday, 3rd November. Won 8-1.

This was a clean, open, friendly game with some welcome support from the sideline at the beginning. As the Beavers were short of players, V. Nash played for them. Most of the game was fought out by our forwards, who all played well.

Team: T. Tennant; B. Bean; E. Evans; J. Thoroughgood; M. Newbolt; O. A. Coates; J. Spring; J. Young; W. Smith; P. Knight; J. Swallow.

Wednesday, 21st November.

1st Round University Cup v. King's College 1st XI. Lost 0-2.

This was our first match since 3rd November, due to several cancellations. Unfortunately the only date we could arrange with King's for this Cup Match was a day when we could not field our usual team. However, Bart's played well enough, and we put up a strong fight resulting in a very close match, although we eventually lost.

Team: J. Frears; T. Tennant; B. Bean; J. Thoroughgood; E. Evans; O. A. Coates; J. Spring; S. Minns; J. Young; P. Knight; J. Swallow.

#### SWIMMING CLUB

United Hospitals Water Polo League.

1st Team

So far this season the team has been playing with polish and precision and only one defeat has been suffered. This was from St. Mary's, who had the double advantage of being stronger and playing in their own pool. The new five-a-side arrangement has worked to Bart's advantage, and the difficulty experienced in the past with goalkeepers has in part been overcome by playing one of the regular first team men in goal. There are still a number of matches to be played this season but the results so far are:—

Goals					
P	W	D	L	For	Against
7	6	-	1	31	17

The team has been: B. Shorey, C. Ruoss, R. Groves (capt.), D. Shand and J. Britton. B. Lask has also played.

2nd Team

The five-a-side system has also allowed us to put out a strong second team which has done well so far, except for one defeat from a 1st team side in the 2nd division. It is a pity that there are not many keen established swimmers amongst the new entry list—one, P. Quinn, shows great promise and should be a great asset to the club.

The record so far is:—

Goals					
P	W	D	L	For	Against
4	1	1	2	7	19

The team has been from R. Hillier, B. Lark, P. Quinn, J. Shearman, D. Cooke, G. Haig. T. Foxton, T. Dutt have also played.

U.L.U. Water Polo Knock-Out Competition.

Bart's entered one team in this competition, held at the Malet Street Pool. The team successfully beat Imperial College 2nd team by

5-2 in the first round and were given a walk-over in the 2nd round against U.C.H. Having by now reached the semi-final, they met Imperial College 1st Team, who were a much more formidable foe and proved too good for the goalkeeper, so that the game was lost by five goals to one.

This was a good performance by Bart's, who might have won the game if the team would only bother to train, since their tactics and passing were undoubtedly superior to those of Imperial College. Shorey was more subdued in this latter match, but the one goal for the Hospital was scored in fine style by Shand after an efficient series of moves by Ruoss and Shorey.

The team was D. Shand, B. Shorey, C. Ruoss, R. Groves (capt.), J. Britton, B. Lask—for the 1st match, R. Hillier; 2nd match, W. Davies.

#### CHESS CLUB

The A.G.M. was held on the 1st November, Dr. Oswald presided. A new committee was appointed under the able captaincy of Mr. E. Hoare.

So far, this season has been an abysmal failure—all the more disappointing since we are the holders of the Inter-Hospital Chess Cup. Our first match in November against Chelsea's first team began the rot: we lost five boards and drew on three, one of which was due to absenteeism. The team was J. Lotfi, R. Farrow, E. Hoare, R. Brown, R. Shepherd, P. Clegg, R. Pilling.

The next match was cancelled since we were unable to supply a team. The second team then played Richmond, a match which we lost 1-5. We were represented by J. McLaughlin, P. Clegg, N. Richards, L. Houghton, J. Underwood and R. Harfitt, who scored our only point.

Against Battersea on the 23rd, our first team suffered again to win only one board thanks to Mr. Adie, and losing the match 1-8. Our team was R. Farrow, B. Hoare, R. Brown, D. Bodley-Scott, D. Hardy, J. McLaughlin and T. Adie.

Unfortunately, three of our best players have been unable to play throughout most of this season; we all look forward to their return, so that the lower members of the team may resume a position more appropriate to their skill.

If you play chess and are interested in representing the Hospital, please let us know—we need support.

## BOOK REVIEW

A **Short Textbook of Medicine** by J. C. Houston, M.D., F.R.C.P., C. L. Joiner, M.D., M.R.C.P., and J. R. Trounce, M.D., M.R.C.P. Pp. x + 564. London, The English Universities Press, Ltd., 102 Newgate St., E.C.1. Price 25s.

This is the first intrusion of the "paperback" into medical publishing and it will almost certainly be followed by many more. Mr. Selwyn Taylor writes in the Editor's foreword that "it is an entirely new text intended for the medical student during his clinical apprenticeship" and this is an adequate description. In general a textbook of medicine should serve one of two functions: either it should be a manual designed for the student starting clinical medicine and shortly to face the examiners in the qualifying examination; or it should be a work of reference in which the practitioner can find information he needs when far from "the original sources of his medical school library" which the authors of this book suggest he should consult. It seems certain that both types of book will still be required, but there is little doubt that those which are not specifically designed to meet one need or the other will fade from the scene.

This is an excellent example of the first type. It is written attractively, it concerns itself with facts, it is didactic and will almost certainly prove popular with students. It has, naturally enough, some of the faults of these qualities. It suggests

that medicine is a simple subject which can be compressed into a book half the bulk of an average American novel. Its ex cathedra pronouncements imply that there is little room for argument or alternative opinions. Although no-one would accuse these authors of holding such views they are innate characteristics of small books dealing with vast subjects. They even have their uses: the student standing before the huge inchoate corpus of knowledge which more accurately represents medicine may well feel discouraged, but the assurance of the Editor that "enough material to satisfy the examiners" is contained within this easily portable book should spur him to acquire at least sufficient information to achieve this limited objective.

If these remarks are criticisms they reflect not upon the book but upon the difficulties of compression. Of the students' manuals available this is the best south of the Border and it may be anticipated that it will drive back the Scottish invader. One of its most attractive features is its price and there cannot be better value for money in medical literature to-day. Your reviewer recalls a fellow student who commuted daily from Ipswich to Smithfield; on the train journey he read Price's Textbook of the Practice of Medicine and as he finished each page he tore it out and threw it from the railway carriage window. "The Short Textbook of Medicine" places this method of revision within the reach of all. R.B.-S.

## ST. BARTHOLOMEW'S HOSPITAL JOURNAL

# CLINICAL AND RESEARCH SUPPLEMENT

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Supplement No. 1

Vol. LXVII, JANUARY, 1963

### EDITORIAL

THIS is the first issue of a clinical supplement to the Bart's Journal and marks the beginning of an enterprising experiment by the Editorial Committee. The objective is to provide a means by which current medical information and research activities within the College and Hospital can be disseminated. In this way departmental activities will become more widely known and the increasing gulf between Charterhouse Square and the Hospital may even be narrowed. The supplement is designed to publish preliminary communications or notes on work in progress; to record the activities of Medical Societies such as the Paget Club, Abernethian Society and Harvey Society; and to provide a medium for the publication of scientific articles by undergraduate students. In this latter connection it may be remembered that important original discoveries were made by Thomas Young and James Paget during their pre-clinical studies here.

Why a supplement and not an enlargement of the Journal? This device has been necessary for economic reasons and it should be recorded that the supplement has only been made possible by generous financial support from the Medical College and Board of Governors of the Hospital. This venture deserves success; whether it flourishes or not will depend on the support of its potential contributors.

G.W.T.

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## COMPARISON OF A MICROMANOMETRIC AND OF A COLORIMETRIC TECHNIQUE FOR ESTIMATION OF SERUM PSEUDOCHOLINESTERASE

by Umberto Rossi, M.D., Milan,\*

Daphne Davies, B.Sc., London, and Hermann Lehmann, M.D., Basle, Sc.D., Cambridge.

THE "pseudocholinesterases" are a group of enzymes which hydrolyse choline esters, but differ from the "true" cholinesterase in substrate specificity, resistance to specific inhibitors and distribution in human organs and tissues (27). As far as human blood is concerned there is a sharp localization, true cholinesterase being in the erythrocytes and pseudocholinesterase in the plasma (22).

The physiological significance of plasma or serum pseudocholinesterase is still not fully understood (22, 32). Like serum albumin, it is synthesized by the liver (15, 31); its level can therefore be used as an index of liver function (9, 10, 26, 29, 30).

Further development in the study of serum pseudocholinesterase has arisen from the observation that some patients developed an unusually long apnoea after exposure to the anaesthetic suxamethonium (5, 6, 19). Suxamethonium (or succinylcholine) is hydrolysed rapidly in vivo by pseudocholinesterase, which is thus responsible for the very brief action of the drug (4). Subjects with a low level of serum pseudocholinesterase have an abnormally prolonged suxamethonium-apnoea (2, 5). These low enzyme levels are often caused by impaired liver function (3, 5, 20), due to specific hepatic disease or general debility.

Apart from liver abnormalities, an occasional cause of a low level of pseudocholinesterase is chronic or acute poisoning by organic phosphorous compounds with anticholinesterase activity (such as many insecticides used in agriculture and some materials used in aircraft and car industry (20, 32)), but the greatest interest in cases of enzyme deficiency was shown following the discovery that it was in many instances, genetically determined (6, 16, 19, 20, 23). The character "low serum pseudocholinesterase level" is inherited in a semi-dominant fashion (1, 18). The frequency of unusual homozygotes among the total population has been estimated to be 0.5 per cent. and that of heterozygotes as 3-4 per cent. (13).

In the unusual homozygotes the usual serum pseudocholinesterase is substituted by another variant, which is physically different. In heterozygotes, both types of enzymes are present together (22). This was first shown by the use of the inhibitor dibucaine which under certain conditions inhibits the usual enzyme by about 80 per cent., and the unusual enzyme only by 20 per cent. This inhibitor has been used to differentiate between three genetical types: the usual homozygote (80 per cent. inhibition), the unusual homozygote (20 per cent. inhibition), and the heterozygote (60 per cent. inhibition) (11, 12, 14). Liddell *et al* (24) have recently succeeded in physical separation of the two enzymes present in heterozygote sera using either paper electrophoresis or column chromatography on a modified cellulose powder.

The most reliable method of estimating serum pseudocholinesterase activity is the micromanometric method, using the Warburg apparatus. This measures the amount of CO<sub>2</sub> liberated from a bicarbonate buffer when pseudocholinesterase hydrolyses acetyl-choline into choline and acetic acid (26). As a "Warburg unit" one defines the amount of pseudocholinesterase which causes in one minute at 37° the evolution of 1 ml of CO<sub>2</sub>. Usual values by this method range from 55 to 125 units (22). Unusual homozygotes show lower values, under 35 units (18); heterozygotes have intermediate values, ranging from 26 to 90 units (22). One has to accept a considerable overlap between the heterozygotes and the two homozygotes respectively, and in addition usual homozygotes and heterozygotes can show values which are lower than would be expected either because of an associated impairment of liver function or because of a rare and not yet fully explained genetic mechanism (8, 18, 21, 25). The distinction between low enzyme levels due to abnormal inheritance and those due to liver disease can be made by the determination of the "Dibucaine Number" (D.N.) which expresses the sensitivity of the enzyme to inhibition by this

drug: unusual homozygotes lower than 20; heterozygotes between 50 and 70; usual homozygotes more than 80. The dibucaine number does not change with the enzyme level and will be 80 in a usual homozygote even if the enzyme is low because of liver disease. The genetic group of patients with low serum pseudocholinesterase level can by this method be properly defined (8, 12, 14).

As the Warburg method is tedious and time-consuming, it is not suitable for a screening on a wider scale or for the systematic analysis of sera of patients as a diagnostic routine in an ordinary clinical laboratory and several other methods have been devised for the estimation of serum pseudocholinesterase activity (7, 32), including a colorimetric method, based on the estimation by the Folin-Ciocalteu reagent of the amount of phenol liberated by the hydrolysis of the substrate phenylbenzoate which has been devised by Smith, Loewenthal, Lehmann and Ryan (28). A first comparison was made by these authors of results obtained with this method and with the micromanometric method of Warburg. A study was also made of the factors governing the choice of reagents and the conditions of reliability of the method.

We have examined the reproducibility of the method of Smith *et al* once more to re-define the correlation with the results of micro-

manometric method of Warburg, by studying the behaviour of different serum pseudocholinesterase variants before and after inhibition with increasing concentration of eserine.

### METHODS

Pseudocholinesterase activity was estimated by the micromanometric method of Warburg (26) and by the colorimetric method of Smith *et al* (17, 28).

The conversion of colorimetric values (colorimeter Unicam—300) into "Warburg units" (W.U.) has been calculated, according to Smith *et al* (28) by multiplying the reading  $E_{\text{test-blank}}$  standard by a factor of 150. Each result reported by the colorimetric method is the mean of a duplicate estimation (2 test tubes) on a single dilution of serum, with the blank also being the mean of a duplicate estimation (2 blank-tubes); the standard value was determined every time as the mean of the readings of 2 or 3 standard tubes. Values of serum pseudocholinesterase activity higher than 150 "W.U." have not been found.

The determination of the "dibucaine number" was performed according to Kalow and Genest (12).

### RESULTS

#### Reproducibility of results obtained with the colorimetric method.

The findings are summarised in Table I.

#### Comparison of results obtained by the colorimetric and the micromanometric method.

Distribution of the values obtained by the colorimetric and the micromanometric methods, and the

TAB. I REPRODUCIBILITY OF RESULTS OBTAINED WITH THE COLORIMETRIC METHOD

Comparison between duplicate estimations of a single dilution of serum (192 estimations on 32 sera)

	Mean difference	Standard deviation	Standard error	Extreme values of differences observed
	3.26 "W.U."	3.20 "W.U."	0.23 "W.U."	0—16.7 "W.U."
Comparison between duplicate estimations on separate dilutions of serum (239 estimations on 16 sera)				
	Mean difference	Standard deviation	Standard error	Extreme values of differences observed
Comparing mean values of duplicate estimations on each dilution of serum:	3.42 "W.U."	2.28 "W.U."	0.15 "W.U."	0—11.7 "W.U."
Comparing directly single values of each determination on different dilutions of serum:	5.07 "W.U."	4.50 "W.U."	0.29 "W.U."	0—19.3 "W.U."

Optical density and "Warburg units" (working with the colorimeter Unicam SP 300)  
0.010 O.D. = 4.05 "W.U."

Comparison between duplicate readings of blank values on a single dilution of serum (180 estimations on 32 sera)

Mean difference	Standard deviation	Extreme values of differences observed
O.D. corresponding "W.U."	2.7	0—0.029 O.D.

Comparison between readings of standard values

	Mean reading	Standard deviation		Variability	Standard error	
		O.D.	Corresponding "W.U."		O.D.	Corresponding "W.U."
Comparing mean values (18), each of them being the mean of 2 or 3 estimations.	0.370 O.D.	0.0159	6.4	4.3%	0.0037	1.5
Comparing directly single values (43 estimations)	0.370 O.D.	0.0179	7.3	4.8%	0.0027	1.1

\*Fellow of the Council of Europe and of the 184th District of the Rotary International.

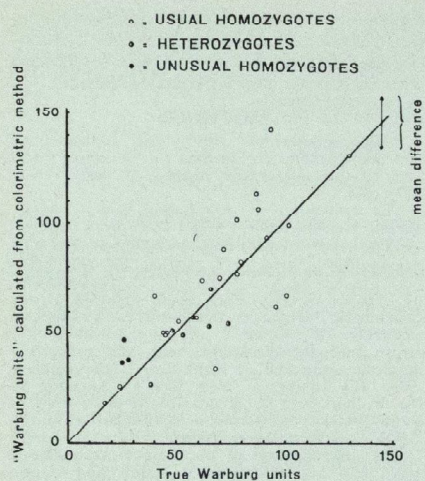


Fig. 1—Serum pseudocholinesterase values. Comparison of results obtained by the micromanometric method of Warburg (26) and the colorimetric method of Smith, Loewenthal, Lehmann and Ryan (28) with usual and unusual homozygous and heterozygous sera.

TAB. III.—Inhibition of the three serum pseudocholinesterase types by eserine salicylate.

Pseudocholinesterase	Final concentrations of eserine salicylate (mg/l)	
	30—40	50—60
USUAL HOMOZYGOTE	83 ( $\pm$ 10.6)	96 ( $\pm$ 6.4)
HETEROZYGOTE	72 ( $\pm$ 6.5)	78 ( $\pm$ 10.5)
UNUSUAL HOMOZYGOTE	48 ( $\pm$ 4.2)	53 ( $\pm$ 1.4)

relative differences, in 22 usual homozygotes, 8 heterozygous and 3 unusual homozygous subjects is shown in fig. 1. The mean difference between the values obtained with the two methods in each single case is 12.3 "W.U." (with a standard deviation of 12.5 "W.U.").

A serum from a homozygote for the "silent pseudocholinesterase gene" (25) in which no pseudocholinesterase activity at all was detectable with the micromanometric method was also examined. The determination with the colorimetric method, repeated twice, has shown values of 1.3 and 4.3 "W.U.". After incubation for 15 minutes of a mixture of this serum with a normal serum (113.6 "W.U."), the serum pseudocholinesterase activity was 109.7 "W.U.", a variation which is well within the limits of error of the method itself.

#### Serum pseudocholinesterase activity after inhibition by eserine at increasing concentrations.

The sera of 15 usual homozygotes, 6 heterozygotes and 2 unusual homozygotes were incubated for 15 minutes with eserine salicylate, in such quantities to obtain "final" concentrations (i.e. cal-

○ = USUAL HOMOZYGOTES  
◐ = HETEROZYGOTES  
● = UNUSUAL HOMOZYGOTES  
— = MEAN OF THE VALUES

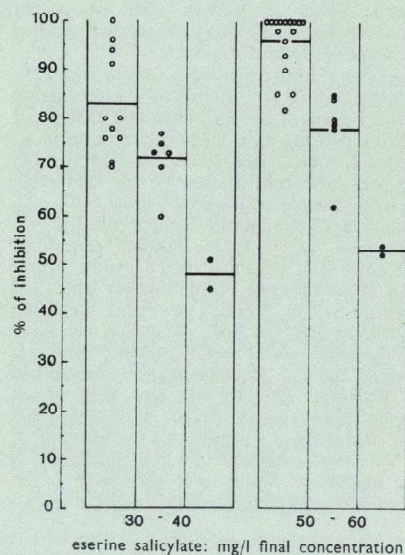


Fig. 2.—Inhibition by eserine of usual and unusual homozygous and of heterozygous sera. Values estimated by the colorimetric method.

culated on the total volume of serum diluted with NaCl 20%) of 10, 25, 30, 40, 50, 60 and 100 mg/l.

Percentages of inhibition of pseudocholinesterase activity, for the above concentrations of eserine, are reported in tab. II.

Fig. 2 shows the inhibition values for intervals of concentration from 30 to 40 mg/l (11 usual homozygotes, 6 heterozygotes and 2 unusual homozygotes) and from 50 to 60 mg/l (17 usual homozygotes, 6 heterozygotes and 2 unusual homozygotes). Mean values for these intervals of concentration (with standard deviations) are also reported in tab. III.

#### DISCUSSION

The results presented in this paper demonstrate that the colorimetric method will show rather wide variations in readings obtained not only on estimations on separate dilutions of the same serum but also on simultaneous duplicates of the same dilution, while there is also some variability of blank values in the method. Accuracy of determinations can be improved by performing duplicate estimations for both test and blank tubes. The reproducibility of the colorimetric method seems on the whole satisfactory, although the values of mean

TAB. II.—Inhibition by eserine of serum pseudocholinesterase activity of usual and unusual homozygotes and heterozygous sera. Values reported represent percentages of inhibition, as estimated by the colorimetric method.

(Figures in brackets show dibucaine numbers).

Sera	"W.U." of uninhibited sera (by colorimetric method)	Final concentration of eserine salicylate (mg/l)						
		10	25	30	40	50	60	100
<b>USUAL HOMOZYGOTES</b>								
1—V.S. ( ? )	50	71	82			96	100	
2—V.S. ( ? )	50			76			98	
3—E.T. (90)	93	42	44			82	100	
4—E.O. (79)	34	59	71			100	100	
5—E.F. (81)	67	69	75			100	100	
6—H. (84)	55			80	91	100		
7—H. (84)	56			96			100	
8—A.P. (83)	83			71	94	98		
9—A.P. (83)	82			80			90	
10—B. (80)	67		76			85	93	
11—J.M. (80)	74		65			85	100	
12—H. (86)	57			76			100	
13—H.B. (88)	49			100			100	
14—B. (79)	88			70			100	
15—L. (84)	50			78			100	
mean		60	69	81	93	94	98	100
standard deviation				10.6			3.8	
<b>HETEROZYGOTES</b>								
1—R.G. (51)	53			60			62	
2—M.P. (63)	51			75			80	
3—E.G. (56)	70			77			79	
4—K.B. (34)	18			73			79	
5—M.S. (60)	49			73			84	
6—M.G. (64)	54			70			85	
mean				72			78	
standard deviation				6.5			10.5	
<b>UNUSUAL HOMOZYGOTES</b>								
1—F.F. (25)	48			45			52	
2—A.G. (17)	37			51			54	
mean				48			53	
standard deviation				4.2			1.4	

differences we obtained are a little higher than those found by Smith *et al.* (28). The micromanometric method shows a variation of  $\pm 5$  "W.U.".

The comparison of results by the micromanometric and colorimetric methods (with conversion of OD units to "W.U." using the factor 150 proposed by Smith *et al.* (28)), shows a satisfactory degree of correlation, with a few exceptions even for values far below the normal ones. In the majority of sera where the two methods are out of agreement, higher values are given by the colorimetric method than by the micromanometric method.

The distribution of mean differences between values obtained by the two methods seems rather wide, but can be partly explained by the presence in the serum, besides the specific pseudocholinesterase, of other unspecific esterases (alisterases) which could act on the same substrate and be consequently measured by the Folin-Ciocalteu reagent (28, 32). By using specific inhibitors of serum pseudocholinesterase, one should be able to estimate by the colorimetric method any activity solely due to the presence of alisterases.

Smith *et al.* (28), using prostigmine, had observed that a final concentration of 19 mg/l gave complete inhibition of esterase activity in all cases at pH 8.6; at pH 6.3 a maximum inhibition was given by the concentration of 33 mg/l, but a variable portion of prostigmine insensitive esterase was still left in all sera; by subtracting this portion from the total esterase activity the correlation with Warburg values was improved. Using eserine at pH 8.6 with a final concentration of 50-60 mg/l the inhibition is complete in most sera (tab. III and fig. 2) and nearly complete in a few others, thus at this pH alisterases, if any, could account only for a very negligible part of the esterase activity as estimated by the colorimetric method unless alisterases themselves were inhibited by very high concentrations of eserine.

Further evidence for absence of alisterase activity is provided by the result obtained in the case of complete absence of serum pseudocholinesterase activity (homozygote for the "silent" gene): the colorimetric method could only show a

very low esterase activity, which was well within the limits of technical error.

In the normal subjects eserine inhibition is 83% at 30-40 mg/l and nearly complete (96%) at 50-60 mg/l. In the group of heterozygotes inhibitions at 30-40 and 50-60 mg/l are respectively 72% and 78%. For the three unusual homozygotes inhibition is 48% at 30-40 mg/l and only a very little higher (53%) at 50-60 mg/l. The difference between usual homozygotes, heterozygotes and unusual homozygotes is evident at 50-60 mg/l, while at 30-40 mg/l there is an overlap of borderline values of usual homozygotes and of heterozygotes.

It is suggested that the decrease in dibucaine sensitivity and the slower migration at alkaline pH in electrophoresis toward the positive pole indicate that the unusual esterase has a lesser negative charge than the usual enzyme, and it would therefore be expected also to have less power to combine with eserine.

### SUMMARY

The colorimetric methods for estimating serum pseudocholinesterase devised by Smith, Loewenthal, Lehmann and Ryan (28) has been used in the analysis of sera of homozygotes for the usual and unusual pseudocholinesterase gene and of heterozygotes, and of a case of absolute deficiency of serum pseudocholinesterase activity (homozygote for "silent" gene).

The errors and reproducibility of the method have been evaluated. The necessity for performing each test and each blank in duplicate is stressed.

Comparison with results obtained by the micromanometric method of Warburg shows a satisfactory correlation (mean difference of 12.3 "W.U.") although the distribution of differences appears to be rather wide (standard deviation of 12.5 "W.U."). The colorimetric method usually gave higher results than the manometric method.

The possibility of an important contribution of unspecific aliesterases to the total esterase activity at pH 8.6, could be excluded, for eserine was shown to inhibit completely serum pseudocholinesterase activity in most of the cases at a final concentration of 50-60 mg/l, and also the colorimetric estimation showed no significant enzyme activity in a case in which the micromanometric method had demonstrated the absence of pseudocholinesterase (homozygous for "silent" gene).

By inhibiting sera with increasing concentration of eserine, a different behaviour could be observed in sera of usual and unusual homozygotes.

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## RESEARCH IN THE DEPARTMENT OF ZOOLOGY

THE DEPARTMENT OF BIOLOGY, to use its original name, was formed with the prime purpose of teaching a special course of Biology to Medical Students. Research was hardly possible, for up to ten years ago the only tangible piece of research equipment was part of an old light microscope. Nevertheless, long range plans were in operation to remedy this state of affairs and now the situation is very different.

About three years ago a new Department of Zoology was designed with the basic concept that modern biological methods could make valuable contributions to medical research. Incorporated in the design was an air-conditioned section for electron microscopy; laboratories for tissue culture and virology; a large laboratory for analytical work and histochemistry; a small operating theatre; balance room and some office laboratories. It even included a small aquarium for studying the effect of radioactive waste on fish, a problem of both medical and economic significance. To-day these plans have come to fruition in the new building recently completed in the Medical College. Concomitant with these changes and the increasing awareness of the value of applying modern biological methods to medical research, much essential and valuable apparatus has been obtained. This has made it possible to investigate problems by means of, for example, fluorescent microscopy, ultracentrifugation, chromatographic analysis and electron microscopy.

The cost of modern research is high and it has become almost inevitable to turn to special Grant-giving bodies, both in this country and abroad, for funds. However, funds for research are limited and each request must be for a particular project and be considered strictly on a competitive basis. The competition, particularly in the International field, is fierce and underlying each success are numerous pilot experiments followed by a detailed application. During the past four years, research in the Department of Zoology has been supported by grants from seven different organisations: The Wellcome Trust; Nuffield Foundation; National Institute of Health, U.S.A.; Lalor Foundation, Inc., Delaware; Agricultural Research Council and the Department of Scientific and Industrial Research.

The thread which links together most of the research work is the need to know more about both normal and abnormal factors influencing gametogenesis. The reason for this is, of course, that such factors have an effect on future populations. On the one hand it is important to safeguard future populations by knowing how the germ cells can be adversely affected (e.g. by ionising radiation) and on the other to be able to control population size for economic and health reasons. It is interesting here to quote from the Annual Report of the Advisory Council on Scientific Policy which has just appeared (16th January, 1963). "... the two major scientific problems with which mankind is faced—the control of human fertility and the pro-

vision (including storage without wastage) of an adequate supply of human foodstuffs—are both biological problems which still call for intense research efforts over a very wide field."

*Research on reproduction related to birth and population control*, with special reference to the male, is being carried out by Dr. D. Lacy and Dr. B. Lofts. The essential part of this work is first to determine how the sperm are formed and then to see how to block this process. The above workers have obtained information which suggests that in various mammals (including Man) the formation of sperm is governed by a feedback mechanism operating within the seminiferous tubules between the germ cells and Sertoli cells. Thus it appears that as the germ cells attain maturity they send a "signal" to the Sertoli cells which release a substance which initiates the next wave of spermatogenesis.

*The effect of injurious agents on the testis*, is being studied by several members of the Department. Dr. Lacy and Dr. Lofts, in collaboration with Professor J. Rotblat (Department of Physics), are investigating damage due to ionising radiation. Dr. Lacy and Dr. Lofts have just completed a detailed study of the action of oestrogenic hormone which completely prevents sperm formation and which can be remedied by the application of follicle stimulating hormone. Dr. Lacy and Dr. K. Bowler are investigating the effect of local heat and hypothermia on the testis. It is interesting to note that after only 20 minutes at 44°C, male rats become temporarily sterile after 10 days. Dr. Lofts and Dr. Bowler are examining the action of minute traces of cadmium; one dose of only 0.04mM. causes permanent sterility in mammals.

*A study on the genetics of infertility* is one of the problems being investigated by Dr. M. Hollingsworth. Studies of this kind cannot be carried out easily on mammals because of their comparatively slow rate of breeding. Dr. Hollingsworth therefore is using the fruit fly, *Drosophila*, the insect originally used by the American worker, T. H. Morgan, and on which much of our knowledge of human genetics is based. Dr. Hollingsworth has found that after close inbreeding for as few as six generations, fertility is lowered by about 80 per cent., due mainly to chromosomal aberrations occurring during meiosis in the development of sperm.

*An investigation into the effects of malaria on infant and child mortality rates in Ghana*, is also being carried out by Dr. Hollingsworth, whose interest in this particular topic stems from the five years he spent at the University of Ghana prior to his appointment at Bart's. Dr. Hollingsworth has found that in certain regions of Ghana the infant mortality rate due to malignant tertian malaria in the first year of life is as high as 25 per cent. The

need to eradicate malaria has, of course, long been evident and a scheme is now being planned by the Government of Ghana and the World Health Organisation.

While the above represents a significant part of the research work being carried out in the Department of Zoology, several other problems are also being studied. Miss D. Ashhurst, a post-graduate worker in the department and holder of a Senior N.A.T.O. Fellowship, is engaged upon a histochemical investigation of connective tissue. Mrs. A. Nahar, a post-graduate student from the University of Dacca, is studying the mammalian uterus in an attempt to learn more about organ control of mitosis. The approach to this problem arises from the work on spermatogenesis referred to above and has obvious implications in the field of cancer research. Finally, collaborative work is being carried

out by members of the Department of Zoology with other people in the College and Hospital and also in other Institutions. For example, Dr. Lucy is helping Mr. G. Bourne, Department of Gynaecology and Obstetrics, in a detailed study of the human amnion and chorion. Mr. Bourne was able to incorporate some of the results obtained by electron microscopy in a monograph which he has published recently. Further afield, Dr. Lofts is collaborating with Dr. G. W. J. van Oordt of the Zoologisch Laboratorium der Hyksuniversiteit, Utrecht, Holland, on work designed to provide further information on the control of the adenohypophysis by the hypothalamus.

There is no doubt that considerable advances have taken place in the Department of Zoology of St. Bartholomew's Hospital Medical College in the past few years.

## A CASE OF AN ISCHAEMIC LIMB IN A PATIENT WITH PAGET'S DISEASE OF THE BONE

by R. L. Rothwell-Jackson, M.B., F.R.C.S., and C. A. Hood, M.B., B.S.

**PAGET'S DISEASE OF BONE**, or osteitis deformans, is one of the osteodystrophies which is relatively common and though rarely seen in the classical form as originally described by Paget (1877), it is often diagnosed incidentally during a radiological examination.

It is now not sufficient to consider Paget's disease purely from the point of view of the local bone pathology, i.e. absorption of the normal dense cortical bone and its replacement by spongy bone and fibrous tissue, as described in the older standard textbooks of pathology. In the last 15 years, the vascular changes both generalised and local which are associated with the disease, have come into prominence together with the resulting complications.

The patient whose case history is described below, was admitted to the Surgical Unit for treatment of an ischaemic limb, the bones of which were the site of Paget's disease. The possible bearing of this latter on the vascular pathology is discussed.

### CASE HISTORY

A 66-year-old man previously quite well, eight years ago developed intermittent claudication in his right thigh, while riding a bicycle. He gave up cycling and had no further trouble until October, 1960, when he dropped an oxygen cylinder on his right foot, injuring the small toe. This became swollen and blue and in December of the same year he developed a burning pain in and around this toe. The pain was worse at rest and relieved slightly by walking about. He had no calf pain.

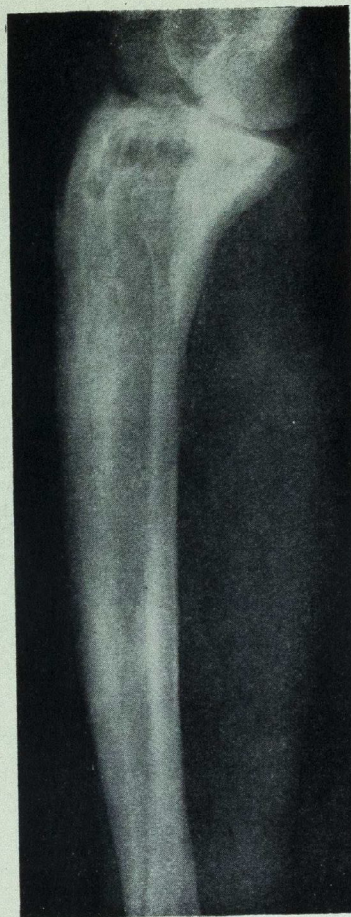
He was seen at the Connaught Hospital where examination revealed a swollen cyanotic right 5th toe and absence of pulsation in the right posterior

tibial artery. A right femoral arteriogram was performed which showed a normal femoral artery and some dilatation and tortuosity of the popliteal artery with no filling of either tibial arteries. The X-ray also showed extensive Paget's disease of the femur and tibia. He was treated with "Hexopal" and was followed in Out Patients at that hospital.

In January, 1961, he developed claudication in the right buttock and thigh after walking 50 yards. In March that year the right 2nd toe was found to be cyanosed and painful. He was then treated with tri-iodo thyronine and reserpine. Later that month he developed severe oedema and discolouration of the right 3rd toe and was re-admitted to the Connaught Hospital. Examination then showed pitting oedema of the right leg to the knee, cyanosis of the 3rd and 5th toes, and absence of foot pulses on the right. Clinical examination of the heart was normal. He was treated with bed rest and analgesics, but failed to respond and was referred to this hospital in May of that year. Physical examination here revealed signs of severe Paget's disease of the right tibia and X-ray showed extensive Paget's disease involving the pelvis, spine, both femora and both tibiae. There was pitting oedema of the right ankle and cyanosis of the 3rd and 5th toes, the 3rd being tender to touch. No foot pulses were felt on the right and bruits were heard in the right popliteal region and over the abdominal aorta. There was moderate postural colour change in the right foot.

He was admitted to this hospital in June, 1961. A right lumbar sympathectomy was performed after which the foot became warm and the rest pain disappeared.

He was followed in Out Patients and the toes improved considerably; rest pain remained absent although he still had thigh and buttock claudication at 50 to 100 yards. This improvement was maintained until August, 1962, when he experienced a gradual onset of claudication in his right calf



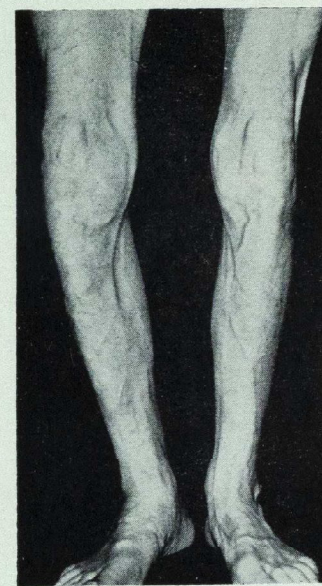
Lateral X-ray of patient's right tibia.

and severe rest pain in the right hallux and foot. He was seen in Out Patients in October with a blue, ischaemic right hallux with early necrosis on its dorsum. The foot was warm. The popliteal pulse was now absent on the right and a loud bruit was heard over the abdominal aorta, both iliacs and femorals.

He was re-admitted. Physical examination now showed signs of Paget's disease affecting the skull as well as increased thickening and pitting of the right tibia and a marked limp on walking. Examination of the heart revealed signs of left ventricular hypertrophy and a systolic ejection murmur was heard. The pulses in both feet were now absent

and the right hallux was gangrenous at its tip. Investigations were—serum calcium 9.6 mg.%, inorganic phosphate 3.5 mg.%, alkaline phosphatase 144 K—A units, 24 hour urinary phosphorus 470 mg., 24 hour urinary calcium 174 mg., F.C.G. showed left ventricular hypertrophy and slight ischaemic changes. Chest X-ray showed the aorta to be dilated and Paget's disease of the clavicles was noted. Trans-lumbar aortogram showed a filling defect in the commencement of the right common iliac and, to a lesser extent, in the left common iliac; the right common iliac was very narrow. There were no filling defects in both popliteal arteries.

An aorto-iliac disobliteration was performed and both organised and relatively recent clot was found to be obstructing both common iliacs. The right great toe was amputated. Post-operatively he did well and good femoral, popliteal and posterior tibial pulses were present bilaterally.



Photograph of the patient's legs showing the appearance due to Paget's disease of bone.

### COMMENT

The term Paget's disease of bone was coined after the two classical papers by Sir James Paget in 1877 and 1882. The first case he described in considerable detail, showed the classical deformity of the disease affecting the spine and lower limbs and the skull which becoming larger "the helmet he

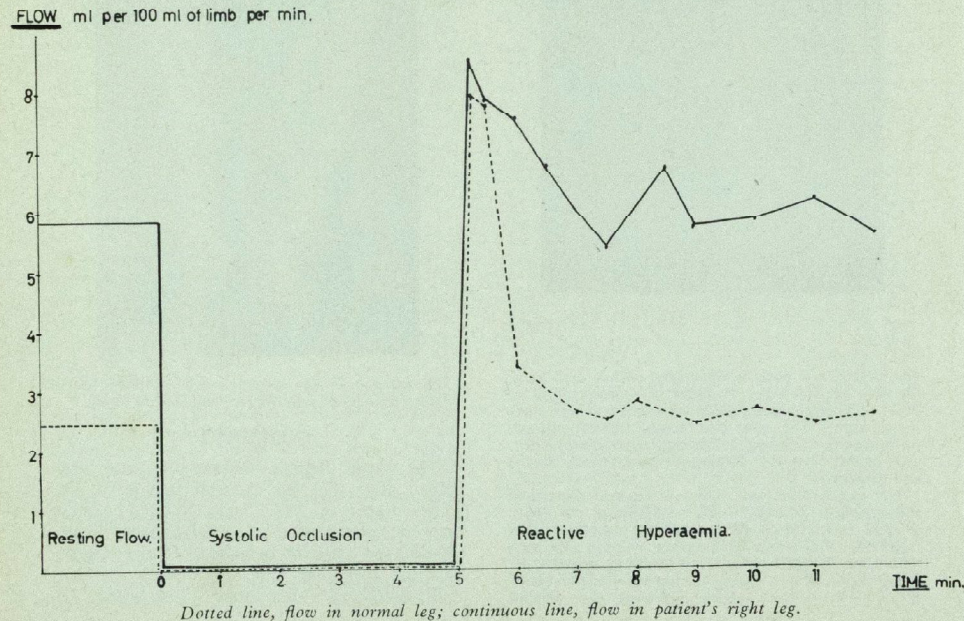
wore as a member of the Yeomanry Corps, needed to be enlarged". This patient died of multiple metastases from an osteogenic sarcoma, now well recognized as a complication of Paget's disease of bone. The description of the post mortem is also interesting, as in it, Paget noticed the markedly increased vascularity of the bone and cardiac enlargement. (The original pathology specimens can be seen in the Hospital museum.)

It is now recognised that there is marked vascularity of the bone in Paget's disease simulating an arteriovenous shunt with pooling of the blood in large venous lakes and an associated high cardiac output which may lead to high output congestive cardiac failure. In addition to this local vascular disorder, there is a high incidence of generalised arteriosclerosis in these patients, and 40 per cent. show calcification in the arteries on plain X-ray (Hunter, 1948). It has been suggested that the increased blood flow may in fact be the underlying cause of the bone pathology resulting in increased bone absorption followed by the deposition of new spongy bone and fibrous tissue. A further result of the rapid

bone absorption is a raised urinary calcium (serum calcium remains at normal levels) and this may encourage renal stone formation. As has been mentioned, there may be marked calcification in the arteries and calcification has also been described in the interventricular septum of the heart. (Harrison and Lennox, 1948.)

The patient described in this case history was admitted to hospital because of ischaemic symptoms in his right leg and gangrene of the terminal phalanx of the right hallux. Arteriography confirmed the presence of a block in the common iliac artery and this was treated by disobliteration. The plethysmography readings (Fig. 1) done preoperatively were interesting. The principle of plethysmography is well established, flow being measured indirectly by applying a cuff to occlude venous return and recording the increase in volume of the leg during a period of arterial inflow only. The ability of the vessels to dilate is measured by occluding all blood flow to the part for 5 minutes, then relaxing the cuff and taking a rapid series of flow measurements as before. (Phase of Reactive Hyperaemia.)

FIG. 1



In the graph, the blood flow of the patient's right leg is compared to that of a "normal" leg in a patient of similar age. It will be noted that the resting flow in the ischaemic leg is twice that of the normal but in reactive hyperaemia the peak flow is only  $1\frac{1}{2}$  times the resting flow in the ischaemic leg but 3 times the resting flow in the normal leg. The high resting flow in the ischaemic leg (with marked Paget's deformity of the tibia) is doubly interesting. Firstly it is surprising that a leg should be ischaemic in the presence of such a high flow. Presumably the high arterial block and good collateral circulation allowed a large volume of blood to reach the calf region where, instead of going on to the foot, it was shunted into the vascular spaces associated with the bone disease. Secondly, if this is so, it is surprising that it has shown up so well on plethysmography. Shaw (Paper S.R.S., Nov., 1962), showed that even normal bone has quite a high blood flow and it is difficult to see how plethysmography, which depends on an increase of volume in the limb as the venous return is occluded, can show any increase of volume in bone, a non-expanding tissue. Presumably the vascular abnormality associated with Paget's disease must involve the adjacent soft tissues as well to some extent.

The gangrenous terminal phalanx of the right hallux can probably be explained by a digital artery embolus from the thrombus at the site of the common iliac block, which would also explain the previous ischaemic episodes involving his other toes.

As mentioned, the arteriovenous shunting of blood through the bone vascular spaces in patients with advanced Paget's disease, will

be associated with a high cardiac output and heart failure. The cardiac output of this patient measured by a dye dilution method (by Dr. Chamberlain) was at the upper level of normal. The urinary calcium excretion, however, was within normal limits.

A further interesting point was that his brother also had Paget's disease of bone if anything even more marked. Though not usually a familial disease, such instances have been reported, e.g., 7 of 90 cases reported by Elmslie (1908).

#### SUMMARY

A case is described of a man with an ischaemic limb also the site of Paget's disease of bone, and the possible association of the two conditions discussed.

We would like to thank Professor Taylor for permission to publish this case, and the hospital photographic department for the illustrations.

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# ST. BARTHOLOMEW'S HOSPITAL JOURNAL

## CLINICAL AND RESEARCH SUPPLEMENT

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## LESIONS OF THE NERVOUS SYSTEM IN THE "MALE TURNER'S SYNDROME"

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Department of Neurology

### INTRODUCTION

FEW descriptions of Turner's Syndrome or of the "Status Bonnevie-Ullrich" include any mention of lesions in the neuraxis. The case about to be described concerns the so-called "Male Turner's Syndrome". There are interesting relationships with multiple congenital defects outside the nervous system. Slight alterations in phenotypical sex in a genotypical male prompt discussion of relationships with female Turner's Syndrome and of the advances made in recent years in the studies of chromatin and chromosomes in these conditions.

### CASE HISTORY

He is a single man, aged 22 years. He weighed 8½ lb. at birth. His parents were unrelated. The father was born in 1909 and the mother in 1919. Pregnancy was normal. There are normal, single, male and female twin siblings who were born in 1941. Another pregnancy resulted in a miscarriage in 1937 at about the third month of gestation. There were no remarkable features in his intellectual development.

At a very early age it was noticed that he had drooping eye lids and high arched feet. At the age

of five, he had an operation to raise the left eye lid. At the age of fourteen years his physical development was thought to be retarded. Sexual development appeared to be normal: pubic hair was present at the age of fourteen, and his voice broke at the age of fifteen-and-a-half. Axillary hair appeared at sixteen years. Shaving began at seventeen and is now required once every two to three days. His psychosexual outlook was male. He thinks that all his life he has been a bit unsteady on his legs. He had to be careful when walking along narrow paths.

At about the age of seventeen years he began to get occasional stabbing pains in the neck, and about the same time he noticed dysphagia and nasal regurgitation of fluids.

At the age of eighteen there was occasional blurring of vision, relieved by blinking. He ignored the pains in the neck until July 1960, when they became severe, being worse on the right side and spreading into the ears. These pains occurred at rest and were not aggravated by movement.

In February 1961, he was operated on for acute appendicitis, and in March 1961, he fell rather heavily on his buttocks. On May 15th 1961, after energetically trying his skill at a coconut shy, the neck pain became more persistent. Coughing and sneezing caused radiation of the pain to the right ear and temple. By May 25th, the pain had diminished, but there was a sudden development of pins and needles in the right leg. The limb felt

numb and heavy and dragged when he walked. It was quite severe for one week. On May 27th, the left leg ached and the skin became numb in an elongated patch on the front of the leg. His gait became unsteady.

On June 1st he was found to have nystagmus, anisocoria, weakness of ocular movements, pyramidal, sensory and cerebellar signs. He was admitted to St. Bartholomew's Hospital on August 15th, 1961.

#### PHYSICAL EXAMINATION (Figs 1, 2, 3)

The following **Congenital Abnormalities** were present:— webbing of the neck; scoliosis; high arched palate and crowded teeth; low-placed ears of abnormal shape; low hair-line; long spindly fingers; bilateral increased carrying angles; pes cavus and a number of pigmented moles.

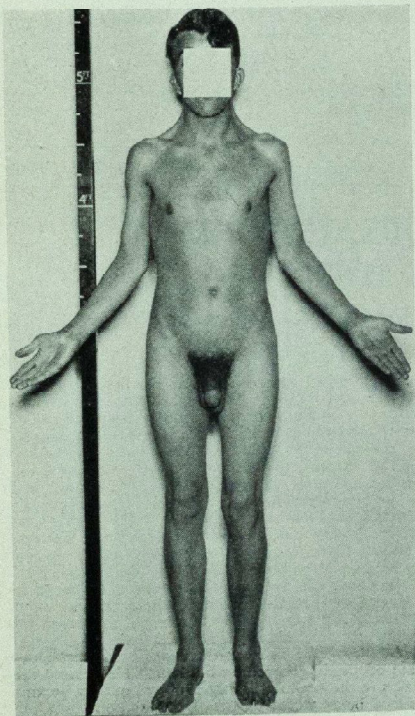


Fig. 1.  
Showing web neck, cubitus valgus, female distribution of pubic hair and normal genitalia.

The **Neurological Abnormalities** were bilateral ptosis; nystagmus; poor convergence; defective lateral movements of the eyes; poor upward gaze, slight bilateral facial weakness, and diminished palatal movement. There was loss of power in the right leg with some increase in tone.

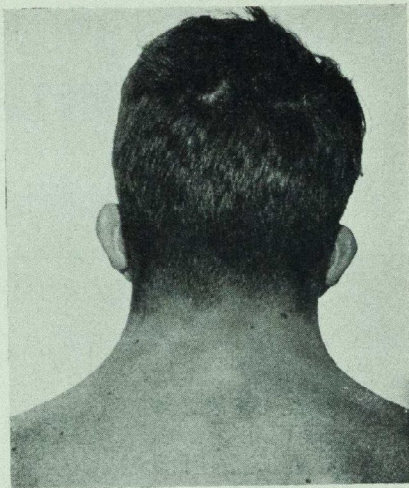


Fig. 2.  
Showing web neck, low "square" hairline, low-set ears and pigmented spots.

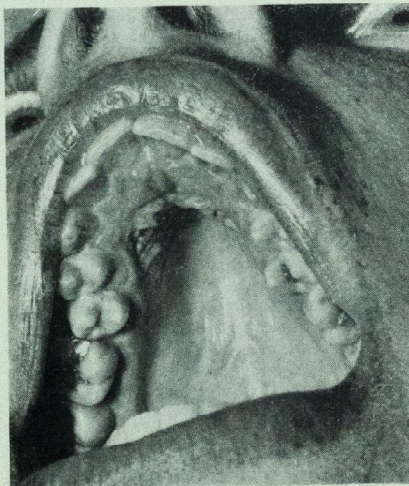


Fig. 3.  
Showing crowded teeth and high arched palate.

Sensations to pin prick, heat and cold were diminished on the front of the left leg below the knee; position sense was defective in the right foot, and vibration sense was diminished in the right leg. There was marked ataxia of the right leg and right arm. The left biceps jerk was absent, and the

supinator jerk inverted. The plantar responses were extensor. The abdominal reflexes were sluggish.

#### GENERAL EXAMINATION

Height 5 ft. 6 in. Weight 9 st. 9 lb.

Examination of the genitalia showed normal organs; penis 15 cm. long, testes—left 7½-8 cm long, right 6 cm. long, normal consistency; there was no enlargement of the breasts; pubic hair was of female distribution; blood pressure 130/60.

#### INVESTIGATIONS

Investigations showed the following results:—

**Haemoglobin**—102%; white count—6,400

**C.S.F.** —pressure and dynamics normal. The C.S.F. contained 2 lymphocytes per cu. mm., and 50 mgms. protein per 100 ml.  
—Lange O.  
—WR., R.P.C.F.T. negative.

**Urine** —17-ketosteroids = 14.8 mgms. per day, which is within normal limits. Gonadotrophin output less than 10 mouse units in 24 hours. (Normal range 5 - 20 units.)

Examination of the polymorphs in the blood showed a male chromatin pattern. Examination of the **seminal fluid** showed a slight deficit in the production of sperms.

**E.C.G.**—showed a slightly abnormal electrical axis but no signs of any other abnormality.

**X-rays.** Skull—normal. Chest—normal heart and lungs.

**Cervical Spine**—showed that the posterior arch of C.1 was incomplete (spina bifida). There was a cervical scoliosis.

**Bones**—showed that the epiphyses of the hands, wrists, and iliac crests, were fused. There was no evidence of retardation of bone age.

**Myelogram**—the contrast medium ran rather sluggishly through the cervical region. Almost the whole length of the cervical cord was widened (Fig. 4).

#### Chromatin and Chromosomes

Examination of blood and oral smears by Professor P. E. Polani showed that the patient was chromatin negative and that he had an XY chromosome constitution.

#### Operation

Early in December 1961, the neck pains became worse and the legs showed obvious signs of spasticity, and ataxia. The sensory changes were more marked and he could not walk unaided. Because of the deterioration in his condition a cervical laminectomy from C<sub>2</sub>-C<sub>5</sub> was performed by Mr. J. E. A. O'Connell on January 1st, 1962. The cervical cord was enlarged and appeared to be fluctuant at C<sub>3</sub>-5 vertebral body level. A needle inserted into the mid-line of the spinal cord did not reveal any fluid. There was some degree of tonsillar herniation and, with difficulty, because of basilar impression, a small sub-occipital craniectomy, with removal of the atlas, was performed. A catheter was passed into the IV and III ventricles. No tumour was found and there was no evidence of raised pressure in the posterior fossa.

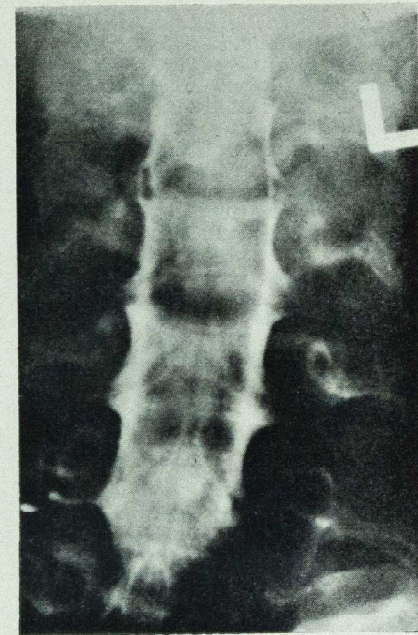


Fig. 4.  
Showing enlarged cervical spinal cord (lumbar myelogram).

#### Progress

Rapid improvement began shortly after operation. When he was last seen in February 1963, he was back at work. He could walk unaided though the legs still showed signs of spastic-ataxia. The neurological abnormalities were all less marked than previously.

#### DISCUSSION

An historical approach to the present case gives the best perspective of the conditions and syndromes concerned. In 1883 Kobylinski described webbing of the neck, a very striking feature in this patient. The author found that the "web" would hold 45 c.c. of water when his patient was lying on his back. It was Funke, in 1902, who first applied the name pterygium colli. He observed it as an isolated phenomenon in males and in association with absent secondary sexual characters in a female, aged 15 years. Bussiere described a patient with web neck in 1902. It appeared that the mother of his Hindu patient was frightened, during pregnancy, by a cobra with expanded lateral head folds.

Klippel and Feil in 1912 described a man of 46 who had no neck. There was an appearance which simulated pterygium colli. He had torticollis, a very low hair-line and scoliosis of the dorsal lumbar regions. In 1925 Frawley described two sisters aged 12 and 16, a woman of 68, and a girl of 7, with webbing of the neck. In 1930 Ullrich described various somatic abnormalities in a girl, which included pterygium colli, and reviewed male and female cases reported in the literature. He did not observe lack of pubertal development. Bonnevie, in 1932, began his studies of congenital anomalies which culminated in a theory of wandering meningocephalic blebs to explain lesions in a strain of mice which could be compared with web neck in the human. His name is usually associated with that of Ullrich who, in 1936, 1937, 1944 and 1949, expanded his original descriptions and observations. The term, status-Bonnevie-Ullrich, has since been used, especially in German literature, as a convenient diagnosis in children with multiple defects of developmental origin. Some such cases are now included in Turner's Syndrome. Mme. Nageotte-Wilbouchewitch in 1934 described that web neck was only part of a syndrome including short stature, large ears, obesity, infantilism, and defective growth of sexual hair. She suggested that web neck in man was an atavistic phenomenon to be compared with the webbing of the neck of the chimpanzee. The structure of the web neck, namely skin only with no muscle or fibrous tissue, was described in boys by Chandler in 1937, who operated on the deformity. Turner's patients were all female in appearance. In 1938 he described the triad of increased carrying angle (cubitus valgus), web neck and sexual infantilism. He thought that the cause of the infantilism was pituitary insufficiency like that of the Lovain-Levi syndrome. His patients had normal cervical spines. They were mentally normal. The neuraxis was not involved though two patients had strabismus. The term Turner's Syndrome may be used when this triad exists. It is doubtful whether it should be used if sexual development is normal.

In 1941 Sharpey-Schafer showed that ovarian agenesis was the cause of sexual infantilism, not pituitary deficiency as Turner thought. His patient had kyphoscoliosis.

In 1942 Albright *et al.* described women with ovarian deficiency and decreased stature. One had web neck and cubitus valgus, another had squint and cubitus valgus, and one had

epilepsy.

The first patient described as "Male Turner's Syndrome" was reported by Flavell in 1943. It is worth recording the main features for comparison with the present patient. These were web neck, tight facial skin, low hairline, kyphoscoliosis, cubitus valgus, third degree claw feet, wide hips, scanty beard, lack of axillary and chest hair, female pubic hair and hypoplastic testes. The penis was normal. Erections and emissions were also normal. These features are strikingly similar to those in the present patient. In addition, the patient of Flavell showed failure of union of the 5th cervical neural arch in the mid-line. However, there were no abnormal neurological signs.

Wilkins and Fleischmann, 1944, first used the term "ovarian agenesis" as an alternative to "Turner's Syndrome". One of three patients (all females) had web neck, spina bifida of several cervical vertebrae, and bilateral ptosis. The second report of "Male Turner's Syndrome" was by Dorfl, Appleman and Liveson, 1948, in a three-years-old boy who had ptosis, slight proptosis, lordosis, web neck, and a spina bifida at L5-S1.

There are reports of facial palsy (McCullough, 1948) and cervical spine anomalies (Sohval, 1951) in Turner's Syndrome. The seven-year-old male of Cunningham and Harley, 1951, can be compared with our patient. The notable features were web neck, short stature, relatively large head, flat feet, hypoplastic mandible, slight bilateral ptosis, low hair-line, cubitus valgus, under-developed penis, undescended testes (until gonadotrophins were given) and a small spina bifida occulta at L5-S1. The neuraxis appeared clinically intact. A thirteen-year-old boy described by Printy, McSwiney *et al.*, 1953, had strabismus, epicanthic folds, cubitus valgus, web neck, dextro aorta and impaired spermatogenesis.

A new phase in the knowledge of Turner's Syndrome was opened by the observations of Polani, Hunter and Lennox in 1954. They found male type sex chromatin in phenotypical female cases of Turner's Syndrome with coarctation of the aorta.

In the years before further work on this aspect of the syndrome was published there was a report by Bassoe, 1956, of members of a Norwegian family with congenital muscular dystrophy, cataracts and gonadal agenesis.

Avin, 1956, made the observation that no case of "Male Turner's Syndrome" had been shown to have complete lack of testicular tissue. All reported cases had male sex chroma-

tin. Some had raised urinary gonadotrophin output. Grumbach, 1957, also pointed out that there is a group of boys and girls with the congenital abnormalities described by Turner and by Ullrich, often with web neck, in whom testes or ovaries are present. They do not have gonadal agenesis and the chromosomal sex (chromatin) is the same as the somatic sex.

Becker, 1957, described a Male Turner's Syndrome aged 16 years, with cubitus valgus, hypoplastic genitalia, L5 spina bifida and male sex chromatin. By this time he could find 200 cases of Turner's Syndrome reported since 1939.

Hoffenberg and Jackson, 1957, stressed that gonadal agenesis could occur in females without other congenital abnormalities.

By examination of chromosomes rather than chromatin, Ford, Polani *et al.*, 1959, revealed that "females" with Turner's Syndrome were deficient of an X chromosome—they had XO karyotype instead of XX. This finding is now established in phenotypical females with the syndrome.

Unusual cases occur such as the female of Spence and Havard, 1959. She had female sex characteristics, but did not have ovarian agenesis. There was maturation arrest of ovarian follicles. In addition to web neck there was kyphoscoliosis and some features of a muscular dystrophy.

A curious chromosome constitution of XXXY was found in two male aments with small testes by Ferguson-Smith *et al.*, 1960. One had slight webbing of the neck but otherwise they bore little outward resemblance to Turner's Syndrome.

Observations which confirm the ideas of Avin, 1956, and Grumbach, 1957, were made by Court-Brown, Jacobs and Doll, 1960, who found normal chromosomes in the so-called Male Turner's Syndrome. It was clear that the somatic abnormalities were not caused by an XO karyotype.

Some somatic features not already mentioned can be culled from a review by Bush, 1960, and include osteoporosis, syndactyly, cutis laxa, moles and keloid, intestinal telangiectasis (see Haddad and Wilkins, 1959) and renal abnormalities.

In 1961 Steiker *et al.*, and Ghu *et al.*, confirmed that the chromosomal constitution in "Male" Turner's Syndrome was normal male XY. Steiker *et al.* reviewed 16 cases of Male Turner's Syndrome in the literature, and added 5 more. Some additional features which

they include are low-set ears, ear lobe anomalies, shield-like chest, hypoplastic nipples, wide nasion, high palate and others, perhaps coincidental and less frequent. Mental retardation is recorded in 6 of 16 cases. 9 testicular biopsies showed tubular hypoplasia. 2 of 9 had delay in bone age. Of 8 post-pubertal males, none showed infantilism.

The comprehensive review of the genetic aspects of Turner's Syndrome and allied conditions by Polani, 1961, should be studied for further information. In addition to the somatic abnormalities to which we have already referred, he mentions Madelung's deformity of the wrist, changes in the medial tibial condyle, camptodactyly, syndactyly, brachymetacarpalism and spinal osteoporosis. He did not describe any lesions in the central nervous system.

The present case may be considered under four headings:—

1. Multiple congenital abnormalities.
2. Chromatin, and chromosomal characteristics.
3. Changes in sexual pattern and function.
4. The lesions in the neuraxis and spine.

The first needs little comment. It will be obvious from the descriptions and photographs that he fits into the general pattern of the "Male Turner's Syndrome". The chromatin pattern was male, chromosomes normal XY. The changes in endocrine function are interesting but not new. Hypofunction of the testes has been frequently recorded in the syndrome. He had female pubic hair distribution, poor growth of beard and relatively low sperm counts. The urinary gonadotrophic output was normal. The exact relationship of this mild gonadal dysfunction to the rest of the male syndrome is not clear. There was a degree of spina bifida of C1 and a cervical scoliosis.

Clinically it seemed that the lesions in the nervous system were in the brain stem and spinal cord. One could deduce that abnormalities were present in the mid-brain which had caused long-standing ptosis, mild ophthalmoplegia, nystagmus and blurred vision; in the pons to cause bilateral facial weakness and in the medulla to cause dysphagia and nasal regurgitation of fluids. The only evidence of internal ophthalmoparesis was inequality of pupils on one occasion. The cause of ptosis and strabismus has never been ascertained in cases of Turner's Syndrome, though frequently recorded without any other neurological signs.

The cervical cord lesion was more certain though its nature was not proven. The site

of the lesion was indicated by neck pains, loss of biceps and inversion of supinator reflex in left arm.

The bilateral pyramidal lesions might be placed in the cervical cord, but could well have been higher up the neuraxis, at least in part. The jaw jerk was brisk. The lesions which produced limb ataxia, defective position and vibration senses, could have been placed at various levels. The whole picture suggested patchy lesions. Myelography and operation proved the cervical cord lesion to be a diffuse enlargement resembling the appearance of syringomyelia, but there were no crossing pain fibre lesions or trophic changes in hands or joints. Syringomyelia can be associated with many congenital abnormalities including kyphoscoliosis, pes cavus, anomalies of ears and spina bifida (Brain, 1951). It has not been described in association with Turner's Syndrome.

There are many reasons for thinking that the neural lesions in this case were a form of myelodysplasia. These include the association with a C.1 spina bifida, multiple congenital abnormalities and scoliosis. The lesions were long-standing and slow to change. Myelodysplasia may be progressive and is sometimes disturbed by trauma. Though most frequent in the lumbo-sacral region other parts can be affected. Lesions can occur at more than one level. This is a prominent feature in the present case which showed brain stem, cervical cord, and possibly lumbar localisations (there was a large patch of dissociated sensory loss at about L.4-5 on the left leg). Dissociated sensory loss of syringomyelic character in the legs is observed in myelodysplasia (Brain, 1951, p. 685). If the cervical cord lesion were syringomyelic it would be most unusual not to see "suspended" dissociated sensory loss in the arms. The fact that there was no sign of a lesion in the crossing pain fibres of the cervical cord is in favour of myelodysplasia and much against syringomyelia. Pes cavus is a frequent association with myelodysplasia.

Previous reports on "Turner's Syndrome" in the female or male have not included any cases with florid neural lesions. Minor changes such as ptosis, strabismus, mental retardation and epilepsy are recorded in the historical review.

#### NOMENCLATURE

The term Male Turner's Syndrome has been used to describe patients with web neck, wide carrying angle and other congenital abnormalities, who are distinctly male in appear-

ance and who have, in most cases, normal male sexual function. They are quite different from the true Turner's Syndrome in the female when there is gonadal agenesis and an abnormal chromosomal pattern.

The term Ullrich's Syndrome is used by Polani to describe male and female patients who have the somatic abnormalities without gonadal dysgenesis.

#### SUMMARY

A patient with Male Turner's Syndrome is described. Multiple lesions in the neuraxis, including a diffuse enlargement of the cervical spinal cord, were thought to be caused by a myelodysplasia. Such lesions have not previously been described in Turner's Syndrome. The history of Turner's Syndrome is reviewed, with particular reference to congenital anomalies, neural changes and the results of chromosomal studies.

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## PAGET CLUB REPORTS

### THE NATURE OF CARDIAC MYXOMAS

Delivered to the Paget Club on 27th March, 1963, by Dr. A. G. Stansfeld and Dr. R. Finlayson.

It is still debated whether cardiac myxomas are merely organised thrombi or true neoplasms. Evidence was presented for their neoplastic character emphasising points of distinction from cardiac thrombi in respect of their site of origin, their structure and the behaviour of emboli which break away from the main tumour.

The origin of atrial myxomas was then discussed and a fresh hypothesis was put forward; that cardiac myxomas are epithelial neoplasms derived from primitive endodermal cells which become entrapped in the developing heart at the time of closure of the foregut very early in embryonic life. A case was cited in which glandular epithelial structures were found at the base of the stalk of an otherwise typical right atrial myxoma.

### MEDICAL SURVEY OF THE TRISTAN DA CUNHA POPULATION

Delivered to the Paget Club on 27th February, 1963, by Dr. A. K. Thould.

The island has been continuously inhabited

since the military settlement of 1816, when Napoleon was imprisoned on St. Helena. From William Glass and fourteen others are descended the present population of 259. This survey was undertaken on behalf of the Medical Research Council.

The islanders were healthy in appearance, cheerful and looked young for their age. About one-third had marked dental caries and many had gingivitis. Nearly two-thirds of the men smoked, but none of the women, and all in moderation only. They were very susceptible as a whole to respiratory infection, and nearly half suffered from asthma. Chronic bronchitis affected 60 per cent. Evidence of ischaemic heart disease was remarkable by its absence, and three post-mortems confirmed how little atherosclerosis there was amongst them. There were two examples of congenital heart disease, and many more had a variety of congenital defects, including hypospadias, abnormalities of the pinna, gothic palate, retinitis pigmentosa and polydactyly. The blood-pressure distribution was similar to that found in other European populations. The menarche and puberty were delayed, but the menopause occurred at the normal time. The children were normal apart from an increased incidence of prematurity at birth.

## SOME EXPERIMENTS ON THE PRIMARY CULTURE OF NEOPLASMS IN VIVO AND IN VITRO

by A. P. Wyatt, M.B., B.S., F.R.C.S.

Research Assistant, Surgical Unit, St. Bartholomew's Hospital

OVER the last fifty years an immense amount of work has been done on the transplantation and culture of tumours from man and animals. This work was largely directed towards the study of the origin and nature of malignancy. In the last few years another factor has been stimulating research in this area; this is the development of the numerous drugs which are of some value in cancer chemotherapy.

Surgeons have become particularly interested in chemotherapy of solid tumours since the advent of the techniques of arterial infusion and isolated limb perfusion. Using these methods high concentrations of the drug can be delivered to the tumours while the rest of the body is relatively protected.

Unfortunately, the effect of these drugs is somewhat unpredictable and even tumours of similar histological appearance may respond very differently to a particular drug. As these drugs are by no means without dangerous and unpleasant side effects it would be useful if some assessment of the response of a biopsy of the tumour to the drugs could be made and thus the most suitable drug chosen for treatment.

One problem must be solved before this can be done. We must learn how to maintain living tumour tissues under experimental conditions with a considerable degree of success. At the suggestion of Professor Taylor some preliminary investigations into this problem have been carried out using both *in vivo* and *in vitro* techniques.

### IN VIVO METHODS

The heterotransplantation of human tumours into animals is a well-worked field but the degree of success has always been small. Some human tumours have become serially transmissible in animals. This is, however, the exception. The reason is that the host produces antibodies and a cellular response which rapidly destroy the tumour and also, perhaps, that certain nutrients and hormones are not available.

Some animals and certain sites in these animals have been found more tolerant of transplants. The anterior chamber of the rabbit or guinea pig eye has been used with some success. The mouse brain has also been used. A good review of the heterotransplantation of human tumours has been given by Chesterman (1959).

### 1. Diffusion Chamber Technique

Algire (1954) described the use of the diffusion chamber technique for the study of immunological problems. In principle, this consists of a chamber with porous membrane walls. The pores are of such a size that the diffusion of nutrients is possible, but there is no cellular contact between transplant and host. He showed that such a circumstance profoundly modified the graft rejection response.

The application of this technique to attempt the transplantation of human thyroid to guinea pigs was reported by Stone (1960). He found histological survival at 101 and 137 days. We hoped that using this method we would be able to maintain portions of human tumours in a living state for short periods.

Chambers were fashioned from perspex rings and Millipore filter papers as described by Curran (1958). These papers have a pore size of  $0.45 \mu$ . Tissue implants of about 1 cu. mm. in size were placed in the chambers with full sterile precautions and the chambers were sealed. Guinea pigs were used as hosts. They were anaesthetised and the chambers were implanted between the deep fascia and the dorsal trunk muscles. After varying intervals of time the animals were killed, the chambers were removed and their contents examined histologically.

Specimens of suprarenal, spleen, liver, kidney, lung, pancreas, testis and seminal vesicle from a sacrificed guinea pig were implanted in this way and removed for histology at weekly intervals for five weeks. Many cells survive in the implanted portions of testis, lung, spleen, seminal vesicle and kidney at the end of one week, but all look somewhat degenerate. The outstanding feature is that in all the chambers there is marked fibroblastic outgrowth resembling that seen in the plasma clot technique of tissue culture.

It is certain that these fibroblasts originate from the implant rather than from host invasion through fractures of the chamber as in some sections they can only be found on the membrane near the implant, and in many of the sections the thickness of the layer of fibroblasts tails off as one moves away from the implant. This is also supported

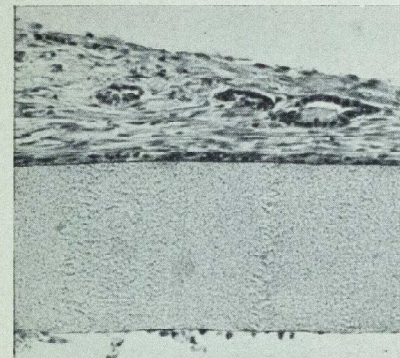


Fig. 1

This shows the fibroblastic outgrowth from an implant of homologous guinea pig lung in a diffusion chamber. The implant is to the left of the view. Note the tubule formation within the outgrowth. The implant had been growing for four weeks. H + E  $\times 135$ .

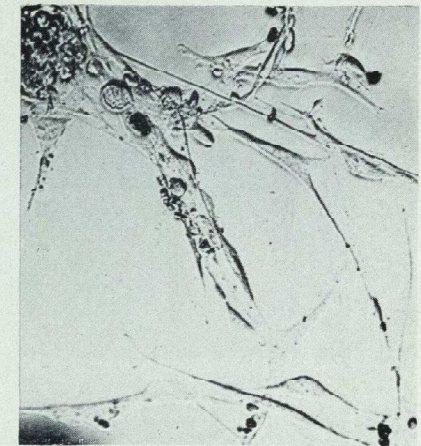


Fig. 2.

Unstained fibroblastic-type cells derived from a bronchial carcinoma growing in tissue culture. Endoxan 275  $\mu$ g. ml. was added to the medium one week prior to fixation, but as is well known this drug even in high dosage has little effect *in vitro* and this culture closely resembles control culture.  $\times 145$ .

by an unintentional series of control experiments where lines of tissue cultured cells were introduced into twelve chambers. These cells did very badly. Histology shows the chambers are empty and there is in no case any evidence of invasion by host fibroblasts.

Some interesting points are noted. In the specimens of seminal vesicle, spermatozoa are seen to be still surviving at three weeks. Some tubule formation is seen in the fibroblastic outgrowth from the lung implant; this appears to be a new formation, not something surviving from the original implant. (Fig. 1.) In the chambers containing spleen, round cells resembling lymphocytes and plasma cells are seen among the fibroblastic cells at four weeks. In all chambers healthy fibroblasts are present in the last specimens removed, i.e. up to five weeks.

Presumably the reason that the more differentiated epithelial structures do not survive is in part due to damage during implantation but mostly due to poor nutritional conditions. Brooks *et al.* (1960) in their experiments on homotransplantation of endocrine tissues in diffusion chambers also found much fibrosis. After two and a half to three months the pores of their filters became filled with calcium phosphate deposits and survival of thyroid homografts could not be demonstrated after 30 weeks; Gough (1962).

We also implanted specimens of human tumours of stomach, bronchus, colon and thyroid. The only evidence of epithelial survival was in an implant of thyroid adenoma after one week. The typical fibroblastic outgrowth was, however, again seen from bronchial, colonic and thyroid implants. The latest of these specimens was removed eight weeks after implantation.

Although this was a disappointing result as far as growing human tumours is concerned the technique is undoubtedly useful for study of the homograft reaction in such tissues as can be maintained

within the chambers, as the relative importance of cellular and humoral components in this reaction can be assessed.

### 2. The Hamster Cheek Pouch

The hamster has recently become a very popular laboratory animal. One reason for this is its possession of a cheek pouch. This is a paired structure lined with mucus membrane which reaches from the buccal cavity back almost as far as the shoulder. When the animal is anaesthetised the pouch can be everted with a pair of blunt forceps. Small pieces of tumour can then be implanted submucosally with a trocar and cannula. The animal is said to be peculiarly tolerant of hetero-grafts and may be further conditioned by the administration of cortisone. It may then be examined under anaesthesia at regular intervals to assess the size of the implant. Table I shows some results obtained. The tumours appeared to grow for two to four weeks and then to regress steadily but slowly. The animals were killed at intervals and the tumours were examined histologically. In most experiments the tumour cells did not look very healthy but exceptions were seen in one of the malignant melanoma experiments and with a squamous cell carcinoma. With the latter tumour, obtained from secondary neck glands, a distinct pattern could be traced. In the early sections the tumour cells looked rather degenerate, then nodules of healthy tumour tissue could be seen which appeared to be growing well. After eight weeks, however, the cells once more appeared to be degenerating. (Figs. 4 and 5.)

This technique has been used to assess the re-

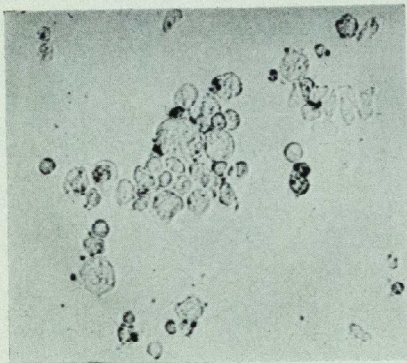


Fig. 3.

Cells from the same culture as in the previous figure but with the addition of actinomycin 0.04  $\mu$ g. ml. to the medium one week before fixation.  $\times 145$ .

sponse of serially transplantable tumours to drugs as an attempt to screen possible drugs for anti-cancer properties (Handler, 1958). The primary implantation of human tumours, however, does not achieve a large percentage of healthy nodules and histological preparation of the nodules is time-consuming and difficult. Mortality rate in this series of 80 hamsters was 12 per cent, and added to this must be the effect of any chemotherapeutic drug administered. One hamster with a melanoma implant was treated with nitrogen mustard. The animal became wasted, weak, and ill, but the tumour flourished; yet in vivo the melanoma is usually sensitive to nitrogen mustard. Another difficulty encountered is that of selecting a suitable piece of tumour macroscopically for implantation. This is particularly so with breast tumours and others having a high proportion of stroma when in a large number of experiments the implant appeared histologically to be composed of stroma only.

#### IN VITRO METHODS

##### 1. Monolayer Cultures.

An attempt was next made to examine possible in vitro methods of maintaining tumour tissue. Wright *et al.* (1962) have reported on the use of plasma clot techniques and have purported to show that there is correlation between their experimental results and the clinical response of the patient to a particular drug. Initially we used the plasma clot technique a few times. A small piece of breast carcinoma was placed on the side of a test tube, a little plasma was run in and this was then made to clot with a drop of chick extract. Medium was added and the tube placed in a rack and incubated. Progress was then observed using the low power microscope objective. Cellular outgrowth occurred from the tumour but the cells which grew out were indistinguishable from fibroblasts. This we discovered is also one of the snares in attempting to culture tumours. Tumour cells tends to be swamped by fibroblasts derived from the stroma.

Trypsin is used regularly in routine histological work to disaggregate monkey kidney and other tissues in order to obtain monolayer cell cultures.

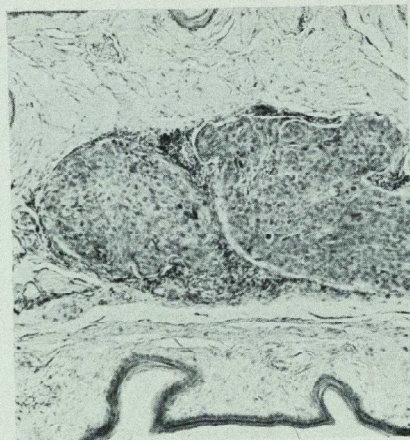


Fig. 4.

Between the two layers of mucous membrane of the hamster cheek pouch is seen an implant of healthy human tumour. This squamous celled carcinoma was obtained from a neck gland and was implanted one month prior to killing the animal.  $H + E \times 75$ .

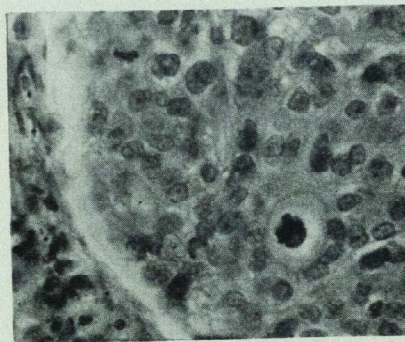


Fig. 5.

A high power view of the implant seen in Fig. 4. Note the mitosis.  $H + E \times 400$ .

Ambrose (1962) has adopted this method to obtain cultures of tumour cells for a sensitivity test but in his preliminary communication he only mentions success with malignant melanoma and astrocytoma. We used this method in an attempt to obtain cultures from twenty-three tumours. These were grown in Glaxo 199 medium with 20 per cent. human serum. Results are shown in Table II. The only case in which we could be certain that tumour cells rather than stromal cells produced cultures suitable for a sensitivity test was one of secondary malignant melanoma from a neck gland.

TABLE I  
TABLE OF RESULTS OF HAMSTER CHEEK POUCH EXPERIMENTS

Type of Neoplasm	Maximum size reached by Implant mm. diam.	Longest Experiment Weeks	Total number of pouches used	Premature deaths (no. of pouches)	Tumour found on histology	Remarks
Carcinoma of Breast	1.	1—2	6	—	5	In one slide the implant was largely stroma and in two the tumour cells appeared very degenerate.
	2.	2—4	6	4	6	In all sections of the implant the stroma had survived but very few tumour cells were seen*.
	3.	—	2	—	4	
Carcinoma of Stomach	3	9	6	—	2	Many mast cells seen in one pouch.
Fibrosarcoma	3	8	2	—	2†	
Melanoma	—	12	4	—	2	Centre of tumour necrotic but many viable cells at periphery? host ? implant.
Malignant	1.	—	6	—	3	Very healthy tumour in these sections. Pigment containing cells seen at some distance from implant.
	2.	—	8	2	3	
Squamous cell Carcinoma from neck gland	3—4	8	24	4	7	Healthy tumour nodules.

\*This experiment was intended to form the control in a chemotherapy experiment but many of the drug treated implants contained more tumour cells than these.

†The number of pouches used is recorded as sometimes both sides and sometimes only one was used in an animal.

Breast tumours gave a rather poor yield of cells which failed to flatten out on the glass or multiply. A profuse growth of fibroblastic cells resembling those obtained from foetal lung with probably a few tumour cells amongst them were cultured from four primary bronchial carcinomas. (Figs. 2, 3, 6.) However, when secondary bronchial carcinoma from a mediastinal gland was cultured in this way there was no definite evidence that the numerous round cells obtained were viable.

Usually if a growth of cells was obtained in culture they flattened out on the glass in the first two to four days. Occasionally active multiplication was obvious but after six to eight weeks this stopped, the cells became granular and dropped off the glass.

Of the twenty-eight cultures attempted either by trypsin disaggregation or using malignant effusions only those obtained from malignant melanoma and carcinoma of the kidney (Fig. 7) showed any promise of suitability for a sensitivity test. Others have reported that astrocytoma and ovarian carcinomas may give satisfactory cultures for testing.

##### 2. Organ Cultures

One other suggestion presented itself, this was the use of a modified organ culture technique. In this method the structure of the tissue is maintained and it seemed possible that tumour cells might do better while remaining in their stroma. Small pieces of tumour tissue of a few cubic mm. were simply placed in tissue culture medium and incubated for a period of time. Histological sections of the material were then prepared.

Some interesting results have been obtained by this method. Once again there is proliferation of fibrous tissue which tends to form a capsule around the specimen. Only patchy survival of tumour cells is usually seen, the majority of cells presumably dying. One of the better results is illustrated (Fig. 8.) The surviving cells look remarkably viable and from this point of view the technique is encouraging but the overall survival rate and great variability between individual specimens from the same tumour do not make the designing of a sensitivity test around this method sufficiently worthwhile.

TABLE II  
MONOLAYER CULTURES

Tumour	Type of cells obtained in the culture	Length of life of culture and termination	Growth Rate	Metabolic Rate	Effect of Drugs	Remarks
Ca Breast	1. Tumour cells only	7 months Discarded	±	+	No effect from female sex hormones seen	The cells remained round and settled at the lower ends of tubes. They did appear to survive and were stainable even after seven months. Similar to above.
	2. Tumour cells + Fibros ±	4 months Discarded	±	±	"	Although occasional cells did flatten out these did not survive.
	3. A few tumour cells	2 weeks unsatisfactory culture	—	—	"	—
	4. A few tumour cells	2 weeks unsatisfactory culture	—	—	"	—
Malignant pleural effusion from Ca breast	Tumour cells	8 weeks	±	±	"	—
Fibroadenoma of breast.	—	—	—	—	—	No culture obtained.
Malignant melanoma.	1. Tumour cells ++	10 days contaminated	++	++	—	—
	2. Tumour cells +++	—	++	++	3 µg HN <sub>2</sub> /ml produced damage to culture	Profuse growth of melanin containing cells suitable for sensitivity test.
	3. Tumour cells ++	3 weeks	—	—	—	Melanin +++ in cells but there was no evidence of growth.
Ca Colon	1. Tumour cells ++	14 weeks discarded	±	+ initially	—	Cells remained rounded up in lower end of tube. Some appeared to clump together and some "giant cells" formed. Poor culture obtained.
	2. A very few, fibroblasts and tumour cells	4 weeks degenerate	—	±	—	—
	3. A very few tumour cells	4 weeks degenerate	—	±	—	Poor culture.
Ca Bronchus (Primary tumour)	1. Tumour cells ++ Fibroblasts ++	10 months still growing	++	++	Damaged by HN <sub>2</sub> 3 µg/ml. Not by Thiotepe 10µg/ml.	Fibroblasts rapidly dominated the culture at first but after 9 weeks "epithelial" cells reappeared and finally replaced all the fibroblasts.
	2. Fibroblasts ++ Tumour cells ++	3 months degenerate	+	+	Damaged by Actinomycin but not by HN <sub>2</sub> Methotrexate Thiotepe Endoxan	A good culture and result to test—but test was conducted on fibroblastic cells from stroma rather than tumour cells.
	3. "	"	+	+	"	"

TABLE II (continued)  
MONOLAYER CULTURES

Tumour	Type of cells obtained in the culture	Length of life of culture and termination	Growth Rate	Metabolic Rate	Effect of Drugs	Remarks
(Mediastinal gland deposit)	4. No Fibroblasts Tumour cells ++	—	—	—	—	Although many cells settled on the flask they remained rounded and there was no evidence of growth or metabolism. Poor culture.
(Malignant pleural effusion)	5. A few tumour cells	4 weeks discarded	±	±	—	—
(Malignant Ascites)	6. Probable tumour cells +++	6 weeks degenerate	+	+	Damaged by HN <sub>2</sub> and Antinomycin	This was a good culture but there is some doubt if the cells were tumour cells or mesothelial in origin.
Ca Stomach	? tumour cells ++	4 months degenerate	++	++	Culture destroyed by HN <sub>2</sub> 300 µg/ml.	Good culture obtained but cell type in doubt.
Ca Ovary	—	—	—	—	—	No culture obtained.
1. Pleural Effusion	Tumour cells + Fibroblasts	4 weeks degenerate	—	±	—	Poor culture
2. Malignant Ascites	A few spindle cells	2 weeks degenerate	—	—	—	The gland was a recurrence in an irradiated area. Very poor culture obtained.
Reticulum cell sarcoma from neck gland	Tumour cells ++	3 months degenerate	++	+	—	Grew well in itself but insufficient obtained for chemotherapy test.
Ca Kidney from ascitic fluid	Tumour cells +	6 weeks degenerate	—	—	—	Many round cells settled at bottom of tubes. Doubtful if any were viable.
Ca Tongue	Many round and fibroblastic cells	4 months degenerate	+	+	Actinomycin HN <sub>2</sub> Methotrexate Endoxan Thiotepe. All ineffective	A good culture obtained but contained many different types of cells.
Ca Testis	Some round and spindle shaped cells	3 weeks degenerate	—	—	—	Poor culture of pleomorphic cells.
Hodgkins (gland)	Lymphocytes +++	3 weeks discarded	?	+	—	Numerous lymphocytes obscured any others.
Hodgkins Paragranuloma (gland)	Some fibroblastic cells	4 weeks discarded	—	+	—	—
Follicular Reticulosis (gland)	Fibroblastic cells +	—	—	+	—	—

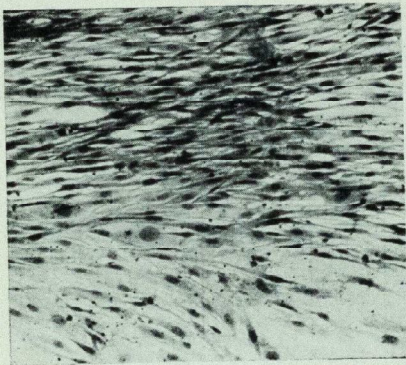


Fig. 6.  
Culture obtained from a bronchial carcinoma of squamous type by disaggregation with trypsin. Note the predominantly fibroblastic type of cell but occasional larger cells with large nuclei interspersed.  
H + E  $\times$  85.

#### DISCUSSION

It is not possible, with present methods, to keep many tumours in a viable state in tissue culture. One can predict a fair degree of success with certain neoplasms such as melanomata, astrocytoma, thyroid, renal and ovarian carcinomas. Presumably the difficulty is one of providing an environment suitable for the cells from a nutritional, respiratory, hormonal and possibly immunological aspect, bearing in mind that differing tumour types are likely to have differing needs. As experience grows it will no doubt be possible to culture successfully a much larger percentage of tumours so that routine sensitivity tests to cytotoxic drugs may become part of the accepted work of the pathological laboratory.

The difficulty of separating tumour cells from stroma, especially in scirrhous growths, presents a problem which is not easily solved, while the recognition of malignant as opposed to stromal or other benign cells in a monolayer culture may tax the powers of the most experienced cytologist. This difficulty is not so great when histological sections are studied although the tendency of malignant cells to take on a benign appearance when in culture has often been remarked upon. On the other hand histological sections take time to prepare, while a glance at a monolayer culture down the low power of a microscope is often sufficient to assess the state of a culture and its control.

Animal experiments are time-consuming and they introduce extra variables and hazards. If suitable culture conditions can be developed there is little doubt that the test tube will replace the hamster or any other animal in this type of investigation just as the Lowenstein Jensen culture has largely replaced the guinea pig in the isolation of tubercle bacilli.

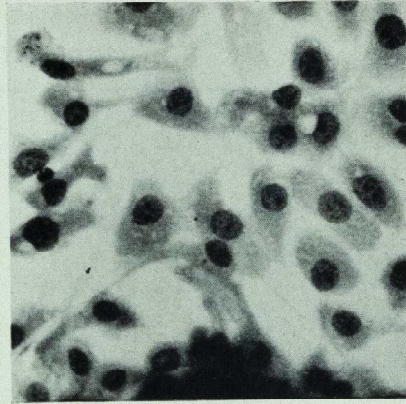


Fig. 7.  
Hypernephroma cells from a malignant ascites growing in tissue culture. Pap.  $\times$  400.

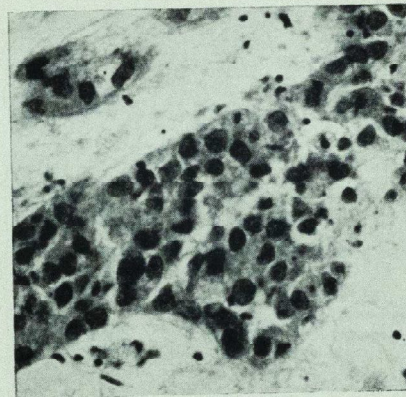


Fig. 8.  
Bronchial carcinoma cells which have survived two weeks as an organ culture. H + E  $\times$  250.

#### SUMMARY

Two in vivo and two in vitro techniques are described by which attempts have been made to maintain living human tumour material. They have been briefly examined from the point of view of developing a sensitivity test to available cancer chemotherapy agents.

I would like to thank Professor G. W. Taylor for the original stimulus to start these studies, Dr.

R. Heath for advice about tissue culture methods and free use of the virology laboratory, Misses D. Aikden and J. Faver for help with the animal work, Miss L. Tyrrell for the histological preparations and Mr. P. Crocker for the photomicrographs.

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# ST. BARTHOLOMEW'S HOSPITAL JOURNAL

## CLINICAL AND RESEARCH SUPPLEMENT

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Supplement No. 3

Vol. LXVII, JULY, 1963

### Editorial

This issue of the Clinical Supplement is attractive because it carries papers describing two creditable pieces of research performed under circumstances which would leave most of us unwilling and unable to spare the time and effort needed.

Abercrombie's investigations into the effect of laparotomy on the activity of the small intestine were carried out whilst he was a member of the staff of the Department of Physiology and working (successfully) for his primary Fellowship examination. Carter and Petty found time during their final clinical year for a careful look at *Mycobacterium smegmatis*.

Postoperative ileus is at first sight an attractive problem for the research-minded surgeon. Anybody who could establish just why it happens and how to stop it happening would be virtually assured of professional fame and fortune. Unfortunately, those who set out to enquire into intestinal motility receive an early and sharp reminder of the biological research worker's greatest handicap—which is that the act of investigation alters the thing investigated. The mere opening of the abdomen

tends to drive the gut of the experimental animal into a state of surly and prolonged silence. The radio-pill is one method of attack which avoids this dilemma but the apparatus is expensive and new knowledge gained from its use has not added much to understanding.

Abercrombie has copied Green in making use of a coloured substance whose progress down the gut at various intervals after ingestion can be determined by simple examination. His findings are negative, but not therefore useless. He has cleared away some of the undergrowth. If the cause of ileus is yet to be determined, recent reports from America suggest that electronic pacemakers (the stimulating electrode is swallowed) may prove an effective form of treatment.

Carter and Petty have made a painstaking study of the degree to which *Mycobacterium smegmatis* may confuse the issue when urine is being examined microscopically for the tubercle bacillus.

They have refocused attention upon the old problem, have shown how widely it exists, and seem to have disproved the comfortable assumption that it is really no problem at all.

## THE EFFECT OF LAPAROTOMY ON THE ACTIVITY OF THE SMALL INTESTINE

by G. F. Abercrombie, M.A., M.B., B.Ch.

### INTRODUCTION

It is clinically known and has been experimentally demonstrated by Auer (1907) and Wakim and Mann (1943) that simple laparotomy interferes with gastric and intestinal peristalsis. The condition so produced is known as postoperative ileus. In order to investigate the physiological basis of this ileus, it is necessary to adopt an experimental technique which will reliably reproduce the condition. Any method of recording intestinal activity which involves direct interference with the abdominal cavity or with the intestine itself is better avoided when the aim of the study is to record the inhibitory effects of such interference.

An attempt has therefore been made to demonstrate postoperative ileus in experimental animals using a Carmine Marker technique.

### METHODS

The method was essentially similar to the Charcoal Meal Test described by Green (1959), except that Carmine was used instead of Charcoal and the animals were allowed to feed normally without the disturbance of intubation.

Albino Wistar rats of both sexes weighing 100-200 gm. were used. They were starved for 24 hours before the experiment, during which time they were allowed free access to water. After starvation, each experimental animal was presented with its customary food mixed with Carmine powder. The food was made up by mixing wet powdered 41 B Rat Cubes with Carmine (B.P.C.) in the ratio 20:1 by weight, and allowing the mixture to dry. Two minutes after the animal started to eat, the food was taken away and the rat was left undisturbed in its cage.

The animals were then killed by a blow on the head 35 secs.-90 mins. after they had started to eat, and the stomach, small intestine and colon removed at once. The gastro-intestinal tract was laid out in a straight line, care being taken that all parts of it were subjected to an even tension, and the length of the small intestine from the pylorus to the ileo-colic junction was measured. The furthest distance

from the pylorus at which carmine could be seen within the intestine was also measured, and this distance was expressed as a percentage of the length of the small intestine. Although the endpoint was usually quite clear and sharp, measurements were made to the nearest centimetre and percentages expressed to the nearest whole number.

The technique of allowing the animal to feed for only two minutes was chosen so that there could be a true comparison with animals which were subjected to anaesthesia. These animals were taken from the cage two minutes after they started to eat and anaesthetised with ether under a glass funnel. Only freshly-opened bottles of peroxide-free ether were used, and the anaesthetic pad was changed for each animal. Anaesthesia was maintained at a level just sufficient to abolish the corneal reflex. Since induction took 1-1½ mins., all subsequent procedures were done four minutes after the animal started to feed. The animals were later killed by a blow on the head in the same way as the other rats.

In some of these anaesthetised animals anaesthesia was maintained until they were killed. Others were subjected, in addition, to laparotomy through a midline lower abdominal incision, the length of the peritoneal incision being 1.5-3.0 cm. Care was taken to avoid direct stimulation of the visceral peritoneum. The wound was immediately closed with clips so that the abdomen was open for a minimal time and no peritoneal irritant in the form of a stitch was left.

Sympatholytic and parasympathomimetic drugs were used in some experiments as follows: Guanethidine Hemisulphate (Ciba. Lab. Ltd.) (20 mg/kg) subcutaneously 24 hours before experiment; Carbachol (Savory and Moore) subcutaneously (0.01 mg/kg) or intraperitoneally (0.005 mg/kg); Neostigmine methylsulphate (Prostigmin, Roche) subcutaneously (0.04 mg/kg) or intraperitoneally (0.02 mg/kg). The latter two drugs were either given subcutaneously 2 minutes after the animal started to feed, or intraperitoneally at laparotomy 4 minutes after the animal started to feed.

### RESULTS

In a series of 100 rats the length of the small intestine varied from 72 to 110 cm., the mean value being 87.5 cm. It was found that there was no hold-up of the carmine in the stomach for it was always present in the duodenum in animals killed 35 secs. or more after starting to eat.

The possibility that the results might have been confused by vigorous intestinal activity occurring post mortem due to local ischaemia is offset by the fact that no such movements were ever observed when the abdomen was opened immediately after the animal was killed. Furthermore, killing the animals with excess ether or ethyl chloride rather than with a blow on the head made no difference to the results.

#### Unanaesthetised rats

These results are shown in Fig. 1 (solid line) in which the distance traversed by the carmine (expressed as a percentage of the total length of the small intestine) is plotted against the time which elapsed after the animal started to eat. It will be seen that the movement of the carmine is at first relatively fast and then gradually falls off.

#### The effects of anaesthesia and laparotomy

Fig. 1 also shows the effects of anaesthesia and laparotomy. Ether anaesthesia alone (broken line) produced only a small reduction in the rate of propulsion of carmine. In rats subjected to laparotomy at 4 minutes (open circles) there was no further propulsion of carmine after that time. The evidence for this is that the value at 20 minutes in this group is similar to that in the control group of rats which were anaesthetised at 2 minutes and killed at 4 minutes.

In another group of animals subjected to laparotomy, anaesthesia was continued until 60 minutes. In these it was found that the carmine had not progressed any further compared with the rats killed at 20 minutes (Fig. 1). In a similar group killed at 90 minutes (not shown in Fig. 1), the values were spread over a wide range (from 40 per cent. to 80 per cent.), indicating that intestinal activity had returned. Intraperitoneal injection of 3 ml. air or saline at 4 minutes instead of laparotomy gave equivocal results, inhibition of intestinal propulsion occurring in about two-thirds of the animals.

Although the use of ethyl chloride instead of ether as the anaesthetic produced a slightly higher reading in anaesthetised rats at 20 minutes, it did not affect the inhibition pro-

duced by laparotomy. In order to test whether the general trauma of laparotomy was a significant factor, a series was done in which one femur was fractured in anaesthetised animals. In this group no inhibition of intestinal propulsion occurred. Control experiments showed that the falls in blood pressure produced by fracture of the femur and laparotomy were similar.

#### The effects of Guanethidine, Neostigmine and Carbachol upon post-operative ileus.

A possible explanation of the production of postoperative ileus is that the intestine is inhibited by a reflex increase in sympathetic tone. Cass and Spriggs (1961) showed that Guanethidine blocks the effect of sympathetic nerve stimulation to the intestine and that intestinal noradrenaline is much reduced 24 hours after an injection of 15 mg/kg subcutaneously. It was decided to test whether pre-treatment with this drug would abolish postoperative ileus. Guanethidine (20 mg/kg) subcutaneously 24 hours before experiment produced obvious diarrhoea and raised the 20-minute figure (normal value 68.5 per cent.) to 75 per cent. (mean of 4 rats). It did not, however, prevent inhibition of intestinal movement following laparotomy.

The possibility that intestinal activity was reduced by a reflex withdrawal of parasympathetic tone was tested by using parasympathomimetic agents. Neither subcutaneous nor intraperitoneal neostigmine prevented postoperative ileus. Even the combined use of guanethidine and neostigmine failed to prevent it. Carbachol, which is known to act directly upon the effector cell, was ineffective when given subcutaneously, but in 3 out of 4 animals values of about 50 per cent. at 20 minutes were found following intraperitoneal carbachol at the time of laparotomy. This value is about midway between the value at 20 minutes for the group subjected to anaesthesia alone (61 per cent.) and that for anaesthesia and laparotomy (36.2 per cent.).

### DISCUSSION

The technique of using carmine as a marker to measure intestinal propulsion has proved satisfactory for the purposes of these experiments, although the physiological importance of the values obtained and of the shape of the curve is probably small. The great advantage of the technique is that the anatomy and physiology of the intestine is not in any way altered before the definitive laparotomy. It should be stressed, however, that cessation of

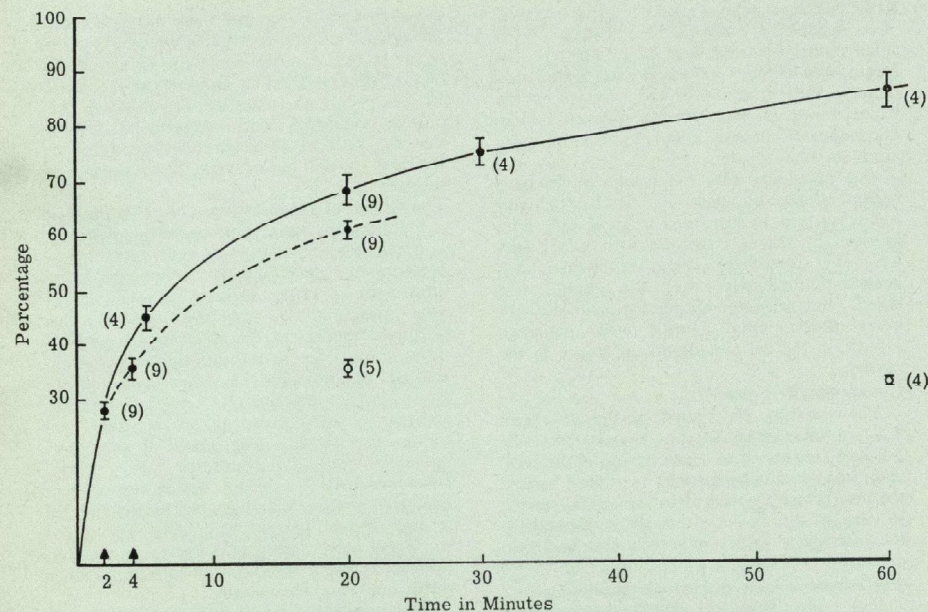


Fig. 1. Movement of carmine in unanaesthetised rats (solid line), unanaesthetised rats (broken line), and rats subjected to anaesthesia and laparotomy (open circles). Ordinate: percentage of small intestine traversed. Abscissa: time in minutes at which the animal is killed. Zero time indicates the moment at which the animal starts to eat. The first arrow at 2 minutes indicates the point at which food is taken away from unanaesthetised animals and at which induction of anaesthesia is begun in the others. The second arrow at 4 minutes indicates the time at which laparotomies were done. The points represent the mean values for each group, the vertical lines the Standard Errors of the Means, and the figures in brackets indicate the number of experimental animals in each group.

movement of carmine through the intestine does not necessarily mean that the intestinal musculature is totally paralysed.

Auer (1907) observed gastric peristalsis in rabbits through the shaved abdominal wall and noted that no further movement could be seen after the abdomen was opened. Normal activity did return some hours after the abdomen was closed. Wakim and Mann (1943) studied ileus in dogs using chronically isolated loops of small intestine and found that ether anaesthesia and exploratory laparotomy produced almost complete cessation of intestinal activity for a minimum of four hours, returning to normal within 24 hours. The main finding presented here, that laparotomy abolishes intestinal propulsion immediately and that this inhibition continues for some time after the abdomen is closed, agrees well with the results quoted above and with clinical experience.

Species differences and the minimal abdominal procedure adopted may account for the fact that the recovery from ileus is considerably quicker in the present series (60-90 minutes) than in previous studies. Both Cannon and Murphy (1906) using cats, and Cannon and Murphy (1906) using cats, and Wakim and Mann (1943) using dogs, gave a minimum of four hours.

The mode of production of postoperative ileus remains obscure. The present experiments indicate that the anaesthetic cannot be blamed as Bisgard and Johnson (1939) suggested, for neither ether nor ethyl chloride alone made any significant difference to the value obtained at 20 minutes. The suggestion that ileus might be one of the effects of the increased adrenal cortical activity following trauma, made by Moore (1953), and supported by Du Plessis (1954), seems improbable in view of the failure of other major trauma such as femoral fracture to produce

ileus, and the fact that it follows immediately upon laparotomy.

Douglas and Mann (1941), studying the ileus produced by peritoneal irritation with Lugol's Iodine in rabbits and dogs found that the immediate and prolonged inhibition thus produced was not affected by vagotomy or adrenalectomy, but was almost abolished by bilateral splanchnic section. These experiments are not strictly comparable with the present series since they were concerned with the ileus of general peritoneal irritation rather than with that following laparotomy. Nevertheless, it was found that Guanethidine in sufficiently high dosage to block the effects of sympathetic nerve stimulation to the intestine and to give rise to intestinal hurry and diarrhoea did not affect the intestinal inhibition produced by laparotomy. This finding suggests that the explanation of ileus does not lie in a simple reflex mediated by the sympathetic nervous system, although the possibility that Guanethidine does not completely block the inhibitory postganglionic sympathetic nerve ending cannot be excluded.

Similarly the observation that neostigmine failed to prevent the inhibition of intestinal movement, even in an animal pretreated with guanethidine, suggests that the explanation does not lie in a simple withdrawal of parasympathetic tone. The only agent used which did produce intestinal movement during the time between laparotomy and sacrifice at 20 minutes was carbachol, and since this is known to act upon the effector cell directly, the finding is probably not of much physiological significance. The movement produced was less than in the control anaesthetised animals indicating that the inhibitory effect of laparotomy had not been completely suppressed.

The most important points arising from the present series of experiments are that they do provide a baseline for the experimental investigation of postoperative ileus, they indicate the immediacy with which ileus follows upon laparotomy, and they suggest that it is not possible to observe, at least in the rat, normal intestinal activity with the abdomen open.

## SUMMARY

1. Gastrointestinal propulsion has been demonstrated in unanaesthetised and anaesthetised rats using a carmine marker technique.
2. Anaesthesia caused only a small reduction in the rate of propulsion of carmine.
3. Laparotomy produced an immediate arrest of propulsion of carmine which lasted for between 60 and 90 minutes.
4. The ileus produced by laparotomy was not affected by guanethidine or neostigmine suggesting that it cannot be explained simply by an increase in sympathetic activity nor by a decrease in parasympathetic tone.

## ACKNOWLEDGEMENTS

I wish to thank Mr. R. A. Dwyer for technical assistance and Ciba Laboratories, Ltd., for supplying guanethidine.

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## NEW SPECIMENS ADDED TO THE MUSEUM DURING THE YEAR 1962.

Museum No.	Specimen	Clinician
A 382	Polyostotic Fibrous Dysplasia	Prof. Scowen
A 551	Adamantinoma of Jaw	Mr. Hankey
A 624	Chondrosarcoma in Ollier's Disease	Mr. Aston

A 641	Osteogenic Sarcoma of Humerus with Pulmonary Metastases	Mr. Williams
B 71	Osteo-arthritis of Knee-Joint	Dr. Hayward
R 222	Gout of Knee-Joint	Dr. Bodley-Scott
B 237	Malignant Synovioma of Shoulder-Joint	Mr. Hunt
E 14 a	Embolus in Patent Foramen Ovale	Presented by Dr. Bradley-Watson
E 115	Systemic Lupus Erythematosus—Heart and Kidney	Dr. Spence
F 16	Aortic Atheroma	Dr. Bodley-Scott
F 238 a	Pulmonary Arterio-Venous Aneurysm	Dr. Cullinan
G 158	Carcinoma of Tip of Nose	Mr. Jayes
G 229	Carcinoma of Tongue	Mr. Birnstingl
H 144	Aspiration Pneumonia in Newborn Infant	Dr. Harris
H 168	Diffuse Scleroderma—Lung	Dr. McKenna
H 235	Hodgkin's Disease—Lung	Dr. Balme
H 250 a	Bronchogenic Carcinoma	Mr. Hill
J 17	Taritar of Canine Tooth	Presented by Mr. Walter
L 171	Secondary Melanoma—Small Intestine	Prof. Taylor
L 244	Acute Appendicitis	Mr. Badenoch
M 170	Femoral Hernial Sac containing Appendix	Mr. Tuckwell
N 2	Brown Atrophy of Liver	Prof. Scowen
N 4	Amyloid Disease of Liver	Dr. Spence
N 12 c	Thrombosis of Hepatic Veins (Budd-Chiari Syndrome)	Mr. Hunt
N 35	Old Amoebic Abscess of Liver	Dr. Bodley-Scott
N 120	Hodgkin's Disease—Liver	Dr. Bodley-Scott
N 263	Carcinoma of Gall-Bladder	Mr. Hunt
P 51	Hodgkin's Disease—Lymph Nodes	Prof. Scowen
P 82	Amyloid Degeneration of Spleen	Mr. Naunton Morgan
P 136 c	Gaucher's Splenomegaly	Mr. Todd
P 177	Myxoedema—Thyroid Gland	Dr. Bodley-Scott
P 275 c	Phaeochromocytoma of Adrenal Gland	Prof. Taylor.
Q 24	Infarction of Kidney	Dr. Hayward
Q 38	Diffuse Scleroderma—Kidney	Dr. McKenna
Q 212	Myelomatosis—Kidneys	Dr. Bodley-Scott
Q 270	Carcinoma of Ureter	Mr. Badenoch
S 40	Tuberculous Epididymo-Orchitis	Mr. Badenoch
T 34	Tuberculous Meningitis	Mr. O'Connell
T 128	Disseminated Sclerosis—Brain Stem	Dr. Bodley-Scott
U 220	Glomus Jugulare Tumour	Mr. Capps
V 71	Mycosis Fungoides	Dr. Spence
W 60	Thecoma of Ovary with Carcinoma of Uterus	Mr. Fraser
W 306	Carcinoma of Vagina	Mr. Todd
TE 152	Congenital Reduplication of Colon	Mr. Hunt
I 17	Obstruction of Ileum by a Bone	Mr. Naunton Morgan
I 67	Shrapnel in Muscle	Prof. Taylor

A few more 1962 specimens not yet completed will be included in the 1963 list.

### THREE SPECIMENS OF PARTICULAR INTEREST FROM THE BONE SECTION

#### POLYOSTOTIC FIBROUS DYSPLASIA

A.382 A right femur, tibia and fibula sectioned longitudinally to show gross

dysplasia with multiple cysts and areas of sclerosis. The femur is also deformed by an old malunited fracture. In addition there is a myxomatous tumour in a muscle adjacent to the femur. 1962.

#### Microscopic Examination

Sections of the bones show areas of replacement by fibroblastic and myxomatous tissue, intermingled with dysplastic bone of varying density. The cysts appear to have resulted from degeneration of the myxomatous tissue. The changes are those of fibrous dysplasia. (In addition to the above changes, several deposits of secondary spheroidal-cell carcinoma are present.) The muscle tumour is a myxomatous fibroma.

From a woman, aged 55, who died with multiple metastases from carcinoma of the left breast.

Twenty-six years previously the patient had had an operation at another hospital for a cyst in the jaw, and nine years previously the right femur had been fractured. For four years several painless lumps had been present in the right lower limb. The patient was admitted to this hospital nearly two years before death, when the diagnosis of polyostotic fibrous dysplasia was established after pathological and radiological investigations. The serum calcium was 9.8 mgm. per 100 ml., and the serum inorganic phosphate 2.9 mgm. per 100 ml., both values being within normal limits. Radiological changes were seen in the left half of the skull, the left humerus, the right half of the pelvis, both femora, the right tibia and the left fibula.

At post mortem the skull showed asymmetrical dense sclerosis mainly affecting the left frontal region, and sclerotic areas were also found in the upper end of the left femur. In the muscles of the right thigh there were numerous encapsulated, lobulated tumours similar to the one shown in the specimen.

#### CHONDROSARCOMA IN OLLIER'S DISEASE (DYSCHONDROPLASIA)

A.624 The lower half of a left femur, with the tibia from the same limb, both bones having been sectioned in a sagittal plane to show innumerable, bluish, cartilagenous masses in the marrow cavities. On the anterior aspect of the femur there is also a large bony and cartilagenous protrusion. In the upper half of the tibia there is a softer, partly-myxomatous and carti-

lagenous tumour, showing areas of haemorrhage and cystic degeneration; its malignant nature is apparent from the manner in which it has eroded through the cortex of the bone and into the knee joint. 1962.

#### Microscopic Examination

Sections of the femur show typical skeletal enchondromatosis, with irregular islands of hyaline cartilage intermingled with the bone structure.

Sections of the tumour in the upper tibia show a chondrosarcoma infiltrating and destroying the cortex of the bone.

Removed by a per-trochanteric amputation from a man, aged 53, whose history dated back to the age of 7, when he fell and fractured his left femur, which was plated. Further fractures of the left femur and left tibia subsequently occurred, and the presence of an enchondroma was first diagnosed by biopsy at the age of 14. Lumps appeared at various sites on the limb, and there was intermittent trouble with the knee joint. Eighteen months prior to amputation the knee became very weak and somewhat painful, and the upper part of the tibia began to expand. Later an X-ray showed increased bone destruction, and malignant change was confirmed by biopsy, but there was some delay before the patient consented to operation.

#### OSTEOGENIC SARCOMA OF HUMERUS WITH PULMONARY METASTASES

A.641 A right humerus sectioned to show expansion and partial destruction of the upper end by a hard whitish tumour. A slice of a lung is also mounted to show metastases. 1962.

#### Microscopic Examination

The growth is a typical pleomorphic osteogenic sarcoma. Neoplastic bone formation is also present in the pulmonary metastases.

From a boy, aged 16, who had a six months' history of pain in the right shoulder. The diagnosis of osteogenic sarcoma was confirmed by biopsy two months before death, and a course of radiotherapy was given. Shortly before death the patient became increasingly breathless due to the lung metastases.

## MYCOBACTERIUM SMEGMATIS IN CLEAN SPECIMENS OF URINE

by T. R. G. Carter and Richard Petty

### INTRODUCTION

THE acid-fast commensal organism, *Mycobacterium smegmatis*, was originally described by Alvarez and Tavel<sup>1</sup> in 1885 and was the first acid-fast organism to be demonstrated after Koch's discovery of the tubercle bacillus in 1882. (Hansen had described the first member of the genetic group in 1874—the leprosy bacillus.) Its presence in urine is well known to be a source of confusion in the microscopic examination of urinary deposits for the presence of tubercle bacilli. But it is commonly stated that in practice no difficulty should arise, since *Mycobacterium tuberculosis* will resist alcohol decolorisation while *Mycobacterium smegmatis* will not. Weber<sup>2</sup> in 1903 showed that *Mycobacterium smegmatis* in smegma is easily decolorised with alcohol, but strains of the organism isolated by Möller<sup>3</sup> in 1902 were strongly resistant to both alcohol and acid. Surprisingly, we have not been able to find in the extensive literature on the mycobacteria a formal study either of the frequency with which *Mycobacterium smegmatis* is found in the urine or, more importantly, the frequency with which acid-alcohol-fast strains occur.

### METHODS AND MATERIALS

It was obvious that the first objective of our investigation would have to be the development and assessment of suitable techniques to facilitate the reliable identification of the organism.

When this had been achieved an attempt was to have been made to correlate the incidence of contamination of clean specimens of urine with their method of collection. With this object in view the investigation was performed upon a random series of specimens from all wards and departments of this Hospital. This proved to threaten our time schedule and was, therefore, abandoned, but it would obviously be a rewarding and interesting line for further research. It was possible, however, to obtain a figure representing the overall percentage of specimens contaminated with acid-fast and acid-alcohol-fast bacilli.

The project was divided into three parts:

- I. The investigation of methods of culture of the primary inoculum of *Mycobacterium smegmatis*.

- II. The investigation of methods of culture of *Mycobacterium smegmatis* from urine.

- III. The investigation of the series of "clean specimens of urine" from female patients.

#### I. Methods of Culture of the Primary Inoculum of *Mycobacterium smegmatis*.

A primary inoculum of *Mycobacterium smegmatis* was grown on nutrient agar slants at 37°C and the following trials performed:

1. Subcultures of the organism on nutrient agar plates at 37°C and 20°C in order to observe rate and type of growth.
2. Subcultures on blood agar plates at 37°C and 20°C.
3. Subcultures by a micro technique in Dubos medium (both with and without bovine albumen) at 37°C and 20°C.
4. Subcultures by micro technique in lysed blood medium at 37°C and 20°C.
5. Subcultures by micro technique in nutrient broth medium.
6. Subcultures by micro technique in lysed blood, nutrient broth and Dubos media after washing in 6 per cent. Sulphuric acid for twenty minutes.

#### The Micro Technique

A modification of the method suggested by Pryce<sup>4</sup> for the culture of the tubercle bacilli was used.

The principle of this technique depends upon the growth of the organism on a micro slide  $\frac{1}{4}$  by 1 inch cut from a 3 by 1 inch microscope slide. This was immersed in the relevant liquid medium and the resulting colonies observed directly by microscopy.

For our purposes this technique was varied so that the micro-colonies could be stained by the Ziehl-Neelsen method without risk of dislodging the organism, Kinyoun's method<sup>5</sup> of cold staining having been found unsatisfactory.

The slides were primed for the reception of the organism with a smear of 5 per cent. egg albumen sterilized by Seitz filtration (bovine albumen was found to have inadequate adhesive properties). The film of egg albumen was gently dried and a loopful of the inoculum and a loopful of the egg albumen were then

Table I

Growth of urinary organisms and *Mycobacterium smegmatis* on microslides after exposure to 6% Sulphuric acid for various times:

Minutes	6	8	10	12	14	16	18	20
Urinary and contaminating organisms	+	±	—	—	—	—	—	—
<i>Mycobacterium smegmatis</i>	+	+	+	+	+	+	+	+

Ten minutes was chosen as the minimum time effective for the inhibition of organisms other than *Mycobacterium smegmatis*.

mixed on the slide and allowed to dry. The slide was immersed in the medium contained within a 5 c.c. screw cap bottle and incubated.

### Results

The trials performed using solid media plates showed a satisfactory growth of the organism in the typical form of rough, waxy colonies of an off-white colour at either 37°C or 20°C after 72 hours' incubation.

The investigation of the micro techniques showed that the growth of the organism was abundant in lysed blood medium at 37°C after 72 hours, but less satisfactory in nutrient broth and Dubos media at either temperature.

#### II. Methods of Culture of *Mycobacterium smegmatis* from Urine.

##### (a) Conventional Methods.

The aforementioned solid media were inoculated with centrifuged deposits from "clean specimens of urine" sent to the laboratory for routine investigations, but it became rapidly clear that any colonies of *Mycobacterium smegmatis* that might have been present were being totally obscured by the overgrowth of other organisms.

The following procedures were performed in an attempt to inhibit the growth of these extraneous organisms:

1. The Antibiotics: A cross-section of the organisms encountered was checked for sensitivities against the following antibiotics using the ditch plate method with blood agar medium:
  - Tetracycline 50 µg/ml and 250 µg/ml.
  - Penicillin 10 units/ml and 100 units/ml.
  - Streptomycin 250 µg/ml.
  - Sulphonamide 250 µg/ml.
  - Erythromycin 25 µg/ml.
  - Chloramphenicol 250 µg/ml.
  - Neomycin 250 µg/ml.
  - Polymixin 250 µg/ml.
  - Ampicillin 100 µg/ml.
  - Methicillin 100 µg/ml.

Controls of a pure strain of *Mycobacterium smegmatis* were put up concurrently and it was found that the organism itself was sensitive to all the antibiotics used (cf. Lack et al<sup>6</sup>).

2. Various dilutions of gentian violet and malachite green in nutrient agar: At the dilutions of these agents to which *Mycobacterium smegmatis* was insensitive the contaminating organisms were insensitive also.

##### (b) Micro Methods

As with solid media it was found that there was present an overgrowth of contaminating organisms, but, in this case, it was possible to show that this overgrowth actively inhibited the proliferation of the *Mycobacterium smegmatis*. Sulphuric acid was then investigated to determine its inhibitory properties.

##### Sulphuric Acid as an Inhibitory Agent

1. Micro slides of a pure strain of *Mycobacterium smegmatis* were washed in 6 per cent. Sulphuric acid for 20 minutes, washed in sterile water and cultured in Dubos, lysed blood, and nutrient broth media. Growth was evident after 5 days at 37°C in lysed blood medium.
2. Micro slides of urinary organisms were subjected to the same treatment and their growth was shown to have been satisfactorily inhibited.
3. A series of urinary organisms, including *Escherichia coli*, *Staphylococcus faecalis*, and *Proteus* species, on micro-slides were exposed to 6 per cent. Sulphuric acid for varying times with concurrent controls of *Mycobacterium smegmatis* (Table 1).

#### III. The Investigation of a Series of Clean Specimens of Urine from Female Patients.

##### Methods

From the information gleaned during the preliminary trials the following technique was developed and adopted:

The "clean specimen of urine" under investigation was centrifuged and the deposit

Table II

Clean specimens of urine	Acid-fast bacilli	Acid-Alcohol-fast bacilli	Positive micro-cultures
150	No. (%) 35 (23)	No. (%) 4* (3)	6 (4)

\*Only 31 of the specimens showing acid-fast bacilli were checked for their alcohol-fast properties.

Table III

Frequency with which acid-fast bacilli occurred singly or were associated with epithelial cells or infection.

Clean specimens of urine showing acid-fast bacilli	Associated with epithelial cells	Discreet acid-fast bacilli	Uninfected urine	Infected urine
35	No. (%) 21 (60)	No. (%) 14 (40)	No. (%) 35 (100)	No. (%) 0 (0)

was:

1. Stained by the Ziehl-Neelsen method and decolorised by 25 per cent. Sulphuric acid. If any acid-fast bacilli were observed, their alcohol-fast properties were checked by treating the slide with 74 O.P. spirit for ten minutes.

2. Micro-cultured in lysed blood medium, having been washed for ten minutes by 6 per cent. Sulphuric acid and subsequently thoroughly washed in sterile water.

The cultures were at first incubated at 37°C for five days, but, as satisfactory growth did not take place, times of incubation were increased progressively up to twenty-one days. Specimens in which acid-alcohol-fast bacilli were seen were also cultured by conventional methods for *Mycobacterium tuberculosis*; none were isolated.

## RESULTS

A total of 150 routine "clean specimens of urine" from female patients were investigated with the results shown in Table II.

### Ziehl-Neelsen Staining

Typically the organism appeared either as single acid-fast bacilli or in clumps of 2 to 6 closely associated with epithelial cells. The urine in these cases was usually free from other organisms. In no case was the presence of acid-fast bacilli demonstrated when the urine was heavily infected. Table III.

### Morphology

The organisms which resisted acid, but not alcohol, were short rods with round ends and parallel sides, slightly curved or straight, and ranging in length from 2 to 3  $\mu$ .

Of the four acid-alcohol-fast bacilli demonstrated, one showed morphology similar to that of the acid-fast bacilli. The remainder showed beaded forms of irregular shape.

### Micro-culture

Of the thirty-one urines in which acid-fast bacilli were demonstrated, in only five were acid-fast bacilli seen after attempting to grow the organism by the micro-culture technique. In one of these, the cultured organisms were both alcohol and acid-fast, and beaded and irregular in shape. Of the others, two showed the growth of micro-colonies, one of which had been incubated for five days and the other for twenty-one days. Neither of these organisms was alcohol-fast.

Of the four urines containing acid-alcohol-fast bacilli, in only one could the organism be demonstrated on the micro-slide after culture, and it then no longer resisted alcohol decolorisation.

The remainder, after twenty-one days' incubation, showed clumps of three to six organisms, but no growth of micro-colonies.

## DISCUSSION

That 23 per cent. of the clean specimens of urine from female patients that we examined should be contaminated with acid-fast bacilli is perhaps the most dramatic observation made during the course of the investigation. We have found no reference in the literature to the frequency of occurrence of *Mycobacterium smegmatis* in urine but while the figure obtained by us is high, unless particular care is taken to avoid preputial contamination, it could be still higher.

The methods of collection of clean specimens vary considerably and this must influence the rate of recovery of *Mycobacterium smegmatis*. Obviously the most satisfactory method of collection with regard to the purity of the specimen is that of catheterisation, but the accompanying dangers of this technique more than outweigh the advantages offered by it to

the pathologist.

Möller<sup>3</sup> observed that certain strains of *Mycobacterium smegmatis* show acid alcohol-fast properties. This was born out by the incidence of 13 per cent. of these strains in the organisms in this series. It is obvious, therefore, that the distinction between *Mycobacterium smegmatis* and *Mycobacterium tuberculosis* cannot reliably be made utilising tests based on the principle that *Mycobacterium smegmatis* is not alcohol-fast.

## SUMMARY

1. Twenty-three per cent. of the Clean Specimens of Urine from female patients were observed to be contaminated by acid-fast bacilli.

2. Thirteen per cent. of the acid-fast organisms isolated showed alcohol-fast properties.

## CURRENT INVESTIGATIONS AND RESEARCH PROJECTS IN THE HOSPITAL AND THE MEDICAL COLLEGE

### Surgical Professorial Unit

1. An experimental and clinical study of the fate of autogenous vein grafts.
2. A comparative study of the efficiency of internal and external cardiac massage.
3. Post-operative intestinal motility and observation.
4. Haemodynamic changes accompanying arterial obstruction.
5. An experimental and environmental study of cross infection in surgical wards.
6. A comparative histological and histochemical study of the arterial wall in atherosclerosis and thrombo-angiitis obliterans.

### Department of General Pathology and Morbid Anatomy

#### Professor Spector and Dr. Willoughby

1. The role of SH and NH<sub>2</sub> groups in the *in vivo* release of histamine by injury (in collaboration with Mrs. J. Frears).
2. The suppression of inflammatory changes by inhibitors of amine decarboxylases and oxidases.
3. A study of the vascular permeability factor obtained from lymph node cells and its possible role in delayed hypersensitivity reactions.
4. The mechanism of excess mucus secretion in injured mucous membranes.
5. The production of connective tissue fibrinoid.
6. (In collaboration with Dr. Brown of Pharmacology.) The mechanism of the skin necrotising action of staph. pyogenes toxin.

#### Dr. Barbara Smith

A histochemical study of normal and dystrophic skeletal muscle.

## ACKNOWLEDGEMENTS

We should like to thank Professor R. A. Shooter for encouraging us to do this work, and Dr. F. O'Grady for his most generous advice and help throughout.

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- 4.—Pryce, D. M., 1941. J. Path. Bact., 53, 327.
- 5.—Kinyoun, J. J., 1915. Amer. J. Publ. Hlth., 5, 867.
- 6.—Lack, C. H. et al., 1957. J. Clin. Path., 10, 204.

### Dr. Finlayson

A comparative study of atherosclerosis.

### Dr. Stansfeld

Necrotising vasculitis.

### Dr. Cureton

X ray studies of pathological specimens.

### Department of Bacteriology

#### Professor Shooter and Dr. O'Grady

1. Hospital infections.
2. Chemotherapy.
3. Pathogenesis of urinary tract infections.

#### Dr. Heath

A study of respiratory viruses.

### Department of Chemical Pathology

#### Dr. Anderson

1. The measurement of thyroid function.
2. The nature of urinary melanogens.
3. The inhibition of alkaline phosphatase.

#### Dr. Lehmann

1. A study of abnormal haemoglobins.
2. The investigation of pseudocholinesterase.

#### Dr. Robinson

1. Urinary ketosteroids in adrenal tumours.
2. Isolation of urinary steroid alcohols.

### Department of Haematology

#### Dr. Brewer

1. Antibodies in acquired haemolytic anaemia and in Rh disease.
2. Albumin as a restorer of blood volume in shock.

#### Dr. Story

1. Blood platelet changes in anaemia.
2. A study of thrombocytopenia and bleeding disorders.

**Eye Department****Mr. H. B. Stallard**

1. Irradiation of malignant intra-ocular neoplasm by  $^{60}\text{Co}$  applicators combined with chemotherapy.
2. Various surgical techniques for partial cyclectomy.
3. Reconstruction of congenital defects of the tarsus.

**Mr. J. H. Dobree**

1. Evolution of lesions of diabetic retinopathy.
2. Formation of filtering blebs in glaucoma surgery.

**Mr. R. B. Harcourt**

Orbital manifestations of Wagener's Granulomatosis.

**Mr. D. W. Hill**

Investigation of vascular retinopathy.

**Mr. J. E. Cairns**

Use of I.D.U. in virus infections of the cornea.

**E.N.T. Department**

**Mr. Fuller** is perfecting a transistorised laryngectomy speech aid in conjunction with the Physics Department. Mr. Fuller is also studying the problem of delayed radio-necrosis of the tympanic ring.

**Orthopaedic Department**

1. Fractures of the calcaneum, and functional anatomy of the calcaneum.
2. Cervical spondylosis.
3. Recurrent dislocation of the patella.
4. Orthopaedic problems in the myelodysplasias.
5. Periarthritis of the shoulder.

**Department for Venereal Diseases**

1. Penicillin and Streptomycin resistance in gonorrhoea.
2. Culture of Trichomonas vaginalis.
3. Effect of Durenan combined with Streptomycin in the treatment of non-gonococcal urethritis in the Male.

**Department of Thoracic Surgery**

1. The physiological changes associated with profound hypothermia used in open heart surgery.
2. Blood changes using the above method.

**Department of Neurological Surgery**

(see page xv)

**Diagnostic Radiology Department****R. A. Kemp Harper, M.D.**

1. Complications of gastrectomy and partial gastrectomy.
2. Radiological features and differential diagnosis in Crohn's disease and ulcerative colitis.
3. Radiological study of gastric and intestinal motility in the immediate post operative period (in collaboration with the Surgical Unit).
4. Review of 60 cases of Scleroderma, with special reference to colonic changes.
5. Ciné radiography in post operative cholangiography.

**G. Simon, M.D.**

1. Principles of chest X-ray diagnosis.
2. Unilateral lung translucency.
3. Chronic bronchitis; radiological aspects of a 5-year follow-up.
4. The place of radiology in undergraduate teaching.

**G. du Boulay, M.B.**

1. The radiological evidence of raised intracranial pressure in children.
2. Clinical use of a 12-in. image amplifier.
3. Orbital angioma diagnosed by phlebography.
4. Orbital phlebography in the diagnosis of haemangioma of the orbit.
5. Use of television in radiology and the storage wheel.
6. Spasm of intracranial arteries in relation to its cause.
7. Teleciné in neuroradiology.
8. The natural history of intracranial aneurysms.
9. Calcification in chromophobe adenoma.

**I. Kelsey Fry, D.M.**

1. Ciné radiographic study of defaecation with special reference to rectal prolapse.

**D. C. Jackson, M.B.**

Lymphangiography in the investigation and control of retroperitoneal glandular masses.

**Department of Radiotherapeutics**

1. A study of the oxygen effect on tumour response to irradiation using hydrogen peroxide by intra-arterial infusion. (**Mr. Whittle.**)
2. A study of lymphatic distribution in patients with intra-abdominal lymph node neoplasms, primary and secondary, by lymph-angiography. (**Mr. Whittle.**)
3. A study of thyroid activity in patients with breast cancer.
4. Retinoblastoma. Irradiation of retinal neoplasm by direct irradiation ( $\text{Co } 60$ ) through the lens. This is combined with systemic chemotherapy with cyclophosphamide. In conjunction with the Department of Ophthalmology.
5. The application of mechanical analogues to the solution of the correct method of applying radiation to different parts of the human body, viz.: in arcing and rotation techniques, taking into account the different shapes of patients at different levels in the body. (With Department of Physics.)
6. Information storage of patients' filter requirements direct from the patients' contours and feeding this into an automatic shaping machine, so producing the required replacement compensating filters. (With Department of Physics.)
7. 15 MeV X-ray and electron therapy treatment of carcinoma of the bronchus, pancreas, stomach, rectum and cerebral tumours.

**Department for Diseases of the Skin**

1. Investigations of quantitative and qualitative aspects of sebaceous gland production of sebum, particularly as related to acne vulgaris.
2. Investigation of immunoproteins in lupus erythematosus.
3. The part played by Demodex in Acne Rosacea.
4. The investigation of basophil counts in treated and untreated urticaria produced by systemic allergy.
5. The study of normal and abnormal keratinization, particularly as directed toward psoriasis and its aetiology.
6. The function of acetylcholine in the skin.

7. Capillary microscopy in lupus erythematosus.
8. Investigation of Xanthomatosis.

**The Physics Department and Radiobiology Unit****A. Radiation Research**

(Effects of ionizing radiation on matter, particularly on living tissue.)

1. Investigation of radicals produced by radiation using the flash absorption spectroscopy technique.
2. Investigation of radicals produced by radiation using the electron spin resonance technique.
3. Effects of radiation on enzymes.
4. Effect of age and radiation on the growth of ascites tumour cells in vivo.
5. Radiation survival curves in HeLa cells in different gas media.
6. Radiation sensitivity of spontaneous and radiation-induced lung tumours in vitro.
7. Cell studies in mice by autoradiography using tritiated thymidine.
8. Effect of fractionation of radiation dose on tumours and normal tissues.
9. The influence of age of mammals on their acute and long-term sensitivity to radiation. Life-shortening and ageing effects of ionizing radiations.
11. Dose-rate effects in mice.
12. Effect of hypoxia on radiation sensitivity of mice.
13. Protection from radiation-induced sterility in mice.
14. Radiation protection of high pressure inert gases in mice.
15. Physiology of hypoxia in mice and dogs using perfusates of low and high oxygen tension.
16. Measurement of oxygen tension in neoplastic and normal tissues by the polarographic technique.
17. Histopathology of radiation-induced lung tumours.
18. Effect of radiation and diet on weight changes in mice.
19. Induction of lens opacities by radiation in mice of different ages.

**B. Radiation Physics**

(Mainly dosimetry)

20. The use of Perspex and Red Perspex for the measurement of high doses of radiation.
21. The use of lithium fluoride for thermoluminescent dosimetry in the range of 0.1 to  $10^9$  r.
22. Yield of secondary electrons from thin foils in a high energy electron beam.
23. Calorimetric techniques in dosimetry.

**C. Medical Physics**

24. The use of 15 MeV electrons in therapy.
25. Clinical uses of radioactive isotopes.
26. The rationale of fractionation in radiotherapy.

**D. Nuclear Physics**

27. Effect of disintegration of light nuclei by bombardment with high energy Helium-3 nuclei.
28. Effect of disintegration of light nuclei by bombardment with high energy neutrons.

**Anatomy Department****Professor A. J. E. Cave**

1. The intimate structure of the cetacean and pinnipede reniculus.
2. Cranial morphology and visceral anatomy of the Rhinocerotidae.
3. Mammalian lymph node structure (with Dr. F. J. Aumonier).

**Dr. O. J. Lewis**

1. Morphology of the crural flexor musculature.
2. The evolution of Primate pedal structures.

**Dr. F. L. D. Steel**

1. Experimental study of effects of a variable gravitational field upon differential growth.
2. Multivariate analysis of Primate osteometry.

**Dr. P. S. C. Bunnig**

1. The anthropology of the talo-calcaneal joint.
2. Investigation of the intrinsic vasculature of leg muscles.

**Dr. R. M. Simons**

Structural variation in the peroneal tendons.

**Department of Physiology****Circulation and Respiration**

1. The reflex respiratory and circulatory effects of stimulation of the isolated perfused aortic arch chemoreceptors and baroreceptors. (**M. de Burgh Daly and Julie L. Hazzledine.**)
2. The mechanisms underlying the cardiovascular responses observed in ventilation hypoxia. (**M. de Burgh Daly and Julie L. Hazzledine.**)
3. Reflex haemodynamic changes in the pulmonary circulation resulting from stimulation of the carotid body chemoreceptors. (**M. de Burgh Daly.**)
4. Physiological properties of transplanted veins. (**I. P. Griffith.**)
5. The control of respiration with particular reference to respiratory reflexes occurring at a spinal level. (**Ann M. Alderson.**)

**Autonomic nervous system**

6. The synthesis and release of the sympathetic postganglionic transmitter: the relation between the output of transmitter and organ response on stimulation of sympathetic nerves. (**B. N. Davies.**)
7. Mode of action of some hypotensive drugs. (**B. N. Davies.**)

**Peripheral nervous system**

8. Physiological properties of plasma taken from patients with myasthenia gravis, with special reference to its action on neuromuscular transmission. (**J. D. Parkes.**)
9. Comparison of the neuromuscular blocking action of decamethonium on respiratory and limb muscles. (**Ann M. Alderson.**)

**Morphology**

10. Comparative histology of lymphoid tissue. (F. J. Aumonier.)
11. Morphological studies on the splenic circulation. (F. J. Aumonier.)

**Anaesthetics**

12. Lung function studies after general anaesthesia. (P. V. Cole.)
13. Examination of halothane in closed-circuit anaesthesia. (P. V. Cole.)
14. Critical review of obstetric analgesic machines. (P. V. Cole.)
15. Studies on sterilization of local anaesthetics by irradiation in the linear accelerator. (P. V. Cole.)

**Methodology**

16. Comparison of the rates of uptake of oxygen by absorbents. (D. C. Moore.)

**Department of Pharmacology****Mode of action of centrally-active drugs**

Particular interest in this field derives from the lack of knowledge on the mode of action of these drugs on the brain. The object of this research is to obtain information which will be helpful to the treatment of mental disease in man. The experimental approach, which involves the use of isolated tissues, anaesthetized preparations and human beings, takes the following directions.

1. Action of drugs on peripheral synapses of the autonomic nervous system in the anaesthetized preparation.
2. Effects on transmission using the isolated skeletal neuromuscular junction as a model of a synapse.
3. Modification by drugs of the output of transmitter by direct measurement at the ganglionic and neuromuscular synapses in the intact and isolated preparation.
4. Comparative drug sensitivities of rat, rabbit, cat and kitten autonomic ganglia.
5. Synaptic transmission in the perfused frog spinal cord and its modification by drugs.
6. Effects on autonomic efferent pathways in the medulla oblongata of the cat.
7. Distinctions between peripheral and central effects of drugs on autonomic responses in the same animal.
8. Human responses, autonomic, psychosensory and psychomotor to drugs.

**Human experimental pharmacology**

9. Olfactory, visual, auditory and electrocardiographic responses to drugs and correlation with changes in skin resistance and finger blood flow.
10. Pharmacological aspects of the clinical trial technique.
11. Pharmacological and clinical studies on the diuretic action of triamterene.

**Other projects**

12. Action of anticholinesterase agents upon peripheral nervous structures.
13. Mode of action of amphetamine on the adrenergic neurone.
14. The pharmacology of the  $\alpha$ -toxin of Staphylococcus pyrogenes.
15. Liberation of pharmacologically active compounds in tissues by drugs.

16. Micro-electrode techniques for the study of muscle cell responses to drugs.
17. The moving fluid electrode and the measurement of depolarization of cells.
18. Activity of proteolytic enzymes on pharmacological responses of mammalian smooth muscle.
19. Application of electronic techniques to pharmacological problems.
20. Study of unit construction in the development of multipurpose electronic devices for biological applications.
21. Exploration of tropical forest natural products for pharmacological activity.
22. The pharmacology of the bronchial tree with special reference to long duration bronchodilation.

**Department of Biochemistry**

1. Investigations on the mechanism of antibody formation and the structure of antibodies, involving studies on the formation of antibodies to polyhaptenic antigens, studies on the breakdown products of antibodies, and the fate of injected protein antigens in lymphoid tissue.  
Investigations on the uptake of protein antigens into the lungs of normal and immune animals following intravenous injection, and a study of the biochemical properties of normal and immune lung tissue.  
Investigations on the mode of action of haemolytic complement.  
Studies on the radioprotective action of injected spleen cells, with particular reference to the metabolism of blood proteins.
2. Investigations into the zinc metabolism of normal and neoplastic tissue, with particular reference to changes in the distribution and activity of zinc-containing enzymes.
3. Investigations into the biochemical effects of radiation, with special reference to its general effects on pure enzymes, its effects on intracellular membranes and the liberation of enzymes, on metabolic processes in subcellular particles, and on the formation of peroxides. Studies on the metabolism of unsaturated fatty acids, with special reference to peroxide formation, the biochemical properties of peroxides, and the mode of action of Vitamin E.
4. A study of sebaceous gland activity with special reference to the effect of individual variation and of environmental and hormonal factors on the amount and composition of sebum produced in health and disease (acne).
5. Paper chromatographic investigations on urines from patients showing various metabolic disorders.
6. Recovery of the medical knowledge of South American Indian tribes whose culture is in imminent danger of collapse through the impact of civilisation, and the isolation and chemical study of substances from plant and animal sources from British Guiana having demonstrable pharmacological activity.
7. A study of the stereochemistry and biosynthesis of marrubiin (a natural product used in cough medicines).

8. Preliminary work on the chemistry of furan acids, substances of great potential interest from the pharmacological viewpoint.
9. Investigation of the free acids in Pyrethrum "marc" with a view to the isolation and identification of a dermatitic agent.
10. A study of the isoelectric point of collagen, its association with mucopolysaccharides and influence on bioelectric potentials.
11. Development of a differential assay method for the components of vitamin B<sub>6</sub> in human urine (present in 0.1  $\mu$ g. quantities, and subject to variation during isoniazid therapy for tuberculosis).
12. Study of the chemistry and spectra of imidazole compounds with special reference to the active sites of enzymes.
13. An investigation of the attachment of enzymes to solid supports and the consequent effect upon the enzymic and physico-chemical properties.

**Department of Neurological Surgery**

1. The cerebro-spinal fluid circulation on which observations have been made in the past are continuing.
2. Intervertebral disc protrusions on all levels in the spinal canal, as well as associated degenerative changes in the cervical region.
3. Spontaneous intracranial haemorrhage and its surgical management.
4. The surgical and other treatment of intracranial gliomata.
5. The management of intractable pain.
6. The surgical treatment of Parkinson's disease and other dyskinesias.

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# ST. BARTHOLOMEW'S HOSPITAL JOURNAL

## CLINICAL AND RESEARCH SUPPLEMENT

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Supplement No. 4

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## PROFOUND HYPOTHERMIA

A technique for open-heart surgery, using the patient's own lungs as the oxygenator.

R. L. Hurt,

Department of Thoracic Surgery

THE use of hypothermia for open-heart surgery is now well established as a safe technique for the treatment of many types of congenital and acquired cardiac defects. The body temperature may be reduced to as low as 10°C. with or without the use of a heart-lung machine.

### THE HYPOTHERMIC CONCEPT

The induction of hypothermia lowers the metabolism of the tissues which therefore require less oxygen and a reduced blood flow. The brain is the tissue most susceptible to lack of oxygen and so the limiting factor in this technique is the period that the brain is able to survive without oxygen. At normal body temperature (37°C.) the brain may suffer permanent damage if the blood supply is cut off for more than two minutes. At lower temperatures, however, a longer period of circulatory arrest is possible—at 30°C. nine minutes and at 15°C. as long as one hour. These periods will provide sufficient time for an operation to be performed on the opened heart in a relatively bloodless field. The type of operation will determine the length of circulatory arrest required and therefore the degree of cooling.

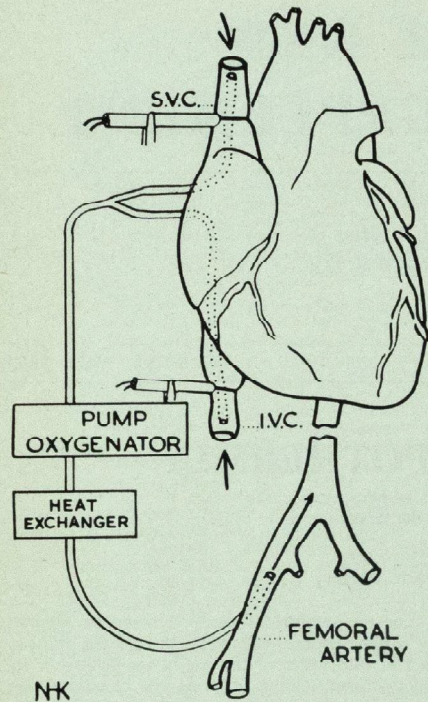
The temperature of the body may be lowered by surface cooling (exposure to cold air, immersion in cold water or the use of ice packs) or by blood-stream cooling (passing the blood through a heat exchanger), with or without the use of a heart-lung machine. The grades of hypothermia in clinical use may be described as mild, "conventional" or profound.

### Mild Hypothermia

Mild hypothermia (down to 34°C.) is induced by surface cooling of the whole body or part of the body by cold air. It is indicated following head injuries or intracranial surgery if cerebral oedema and consequent cerebral ischaemia is likely to develop. It is also valuable in the treatment of peripheral vascular disease following arterial occlusion or arterial endarterectomy.

### "Conventional" Hypothermia

Conventional hypothermia is induced by surface cooling of the whole body by immersion of the anaesthetised patient in a bath of cold water. When the temperature has been lowered to 30°C. (nasopharyngeal temperature, which approximates closely to that of the brain) the circulation may be arrested for nine minutes with complete



**Fig 1.** The flow of blood during extracorporeal circulation. The blood flows by gravity from the inferior and superior vena cava into the pump oxygenator (heart-lung machine). After oxygenation, the blood is pumped via a heat-exchanger to a femoral artery. The femoral artery cannula is directed proximally so that the blood flows through the aorta in a retrograde direction and then to the rest of the body.

return of normal cerebral function after operation. This will provide sufficient time for the correction of certain abnormalities such as the secundum type of atrial septal defect or pulmonary valve stenosis. Other abnormalities, such as ventricular septal defect, tetralogy of Fallot, primum type of atrial septal defect or aortic stenosis are more difficult to treat and require a longer time for operation. They must be corrected by a

different technique, either under profound hypothermia or with the use of a heart-lung machine.

#### Profound Hypothermia

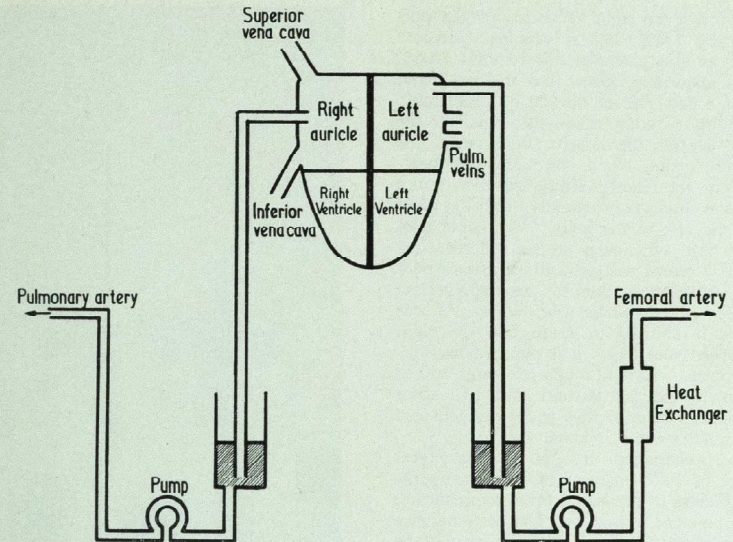
Profound hypothermia implies the reduction of the body temperature to 10-15°C. by blood-stream cooling with the use of a heat-exchanger. It will permit circulatory arrest for a period of sixty minutes, which is sufficiently long for the correction of most types of intra-cardiac defect. Since the heart has ceased to beat at this temperature, the operation field is relatively dry, or even completely dry, and the operating conditions are ideal. If necessary, a further period of recirculation will provide still more time for the repair of the intracardiac defect.

A clear distinction must be made between profound hypothermia in association with the use of a heart-lung machine and profound hypothermia by the Drew technique. Profound hypothermia to 15°C. in association with a heart-lung machine (Fig. 1) allows the blood flow to be reduced with a consequent reduction in blood damage (the limiting factor in the duration of heart-lung bypass), or even to be stopped so as to provide a completely dry operation field inside the heart during certain difficult periods of the operation. Profound hypothermia by the Drew technique (Fig. 2), however, is fundamentally different in that there is no artificial oxygenator, and the patient's own lungs are used for respiratory exchange. There is, therefore, less damage to the blood and consequently less post-operative bleeding. In this technique two pumps are utilised to take over the action of the right and left ventricles, which cease to provide an adequate output at a temperature of about 25°C. due to the onset of ventricular fibrillation (in which case the output ceases altogether) or to extreme bradycardia.

Since November, 1961, we have increasingly used the Drew technique of profound hypothermia in preference to the Melrose heart-lung machine. In this report I will describe our experience of this technique of open-heart surgery.

#### THE DREW TECHNIQUE OF PROFOUND HYPOTHERMIA

The body temperature cannot be lowered with safety below 30°C. by surface cooling for, as mentioned above, ventricular fibrillation is likely



**Fig. 2.** The flow of blood during profound hypothermia. The blood is drawn off the right atrium into a reservoir, and is then pumped into the lungs via a cannula introduced through the right ventricle into the pulmonary artery. The blood passes through the lungs into the left atrium, and is then drawn off into a reservoir. It is pumped through a heat-exchanger into a femoral artery, the cannula being directed proximally so that the blood flows through the aorta in a retrograde direction and then to the rest of the body.

to occur at about 25°C., and the heart will then cease to function as a pump. But in 1959 Drew and his colleagues conceived the brilliant idea of continuing the cooling process down to 15°C. by using two pumps to take over the action of the heart before it fails and ceases to provide an adequate circulation.

#### The Apparatus (artificial heart)

The machine used for profound hypothermia consists of a compact double-pump unit (Fig. 3), incorporating two reservoirs and a heat-exchanger. The two reservoirs, which act as artificial atria, are made of large diameter polyvinyl chloride tubing with stainless steel end-pieces. A screw occlusive device compresses the atrial drainage line and controls the flow of blood into the reservoir. The "ventricles" are standard rotary

pumps (Melrose design), incorporating occlusive rollers. A heat exchanger is included in the left heart circuit. Disposable plastic tubing is used for most of the blood circuit and consequently there are only a few parts which require cleaning after each case.

The machine is primed with four pints of citrated blood not more than three days old. Heparin is added to this blood and also given to the patient before cooling begins. At the conclusion of warming protamine is given to the patient to neutralise the heparin.

#### Management of Cooling and Rewarming

A median sternotomy followed by a vertical pericardial incision provides direct access to the heart. Cannulae are introduced into the left and right atria (via the respective atrial appendages)

and also through the right ventricle into the pulmonary artery (Fig. 2). A cannula (directed proximally) is also placed in the femoral artery.

Blood is allowed to drain into the left atrial reservoir at a flow rate of 60-120 ml./Kg./min., depending upon body size—the smaller the patient the greater the relative flow rate. The pump returns the blood through the heat-exchanger into the femoral artery and then (since the cannula is directed proximally) into the aorta and so to the rest of the body. As cooling progresses the right ventricular output and therefore the left atrial return will fall, either due to poor ventricular contraction due to the hypothermia or the onset of ventricular fibrillation. At this stage blood is allowed to drain into the right atrial reservoir from which it is pumped back into the pulmonary artery through the lungs and so back again to the left atrium and left atrial reservoir. Stabilisation of flow is rapidly achieved and little adjustment is necessary.

Cooling is continued until a nasopharyngeal temperature of 15°C. is reached. This temperature is very close to the actual brain temperature. It is important not to cool too fast, as otherwise the temperature gradients in the patient will be too large, and the brain itself will not remain sufficiently cool during the period of arrested circulation. The time taken for cooling should be 30-40 minutes. At 15°C. (or lower if the repair of the defect is likely to be difficult and a longer period of arrest is anticipated) the pumps are stopped and artificial respiration is discontinued. The heart is motionless, the operation field is completely dry, and ideal operating conditions are present.

When the appropriate surgery has been completed rewarming is commenced and is continued until a temperature of about 35°C. has been reached. During the warming period the heart may start beating spontaneously, slowly at first and then later more quickly. On the other hand, it may fibrillate and either revert to normal rhythm spontaneously or require electrical defibrillation. Surprisingly there is seldom any difficulty in re-starting the heart, though if the bundle of His has been damaged during the surgical repair it will be necessary to insert electrodes into the myocardium for connection to an artificial pacemaker. When the right ventricle is beating

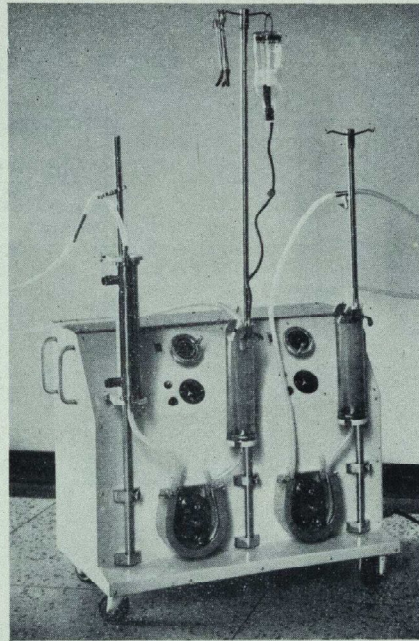


Fig. 3. The profound hypothermia unit. The heat-exchanger, left-heart reservoir, and right-heart reservoir are mounted on the left-hand, centre, and right-hand columns respectively. The two pumps are at the base of the unit.

adequately the right heart bypass is discontinued. The left heart bypass is maintained until the body is sufficiently warm. Finally protamine is given to neutralise the effect of the heparin.

#### Management of pulmonary flow

In Fallot's tetralogy, there is often considerable narrowing of the pulmonary valve and right ventricular outflow tract, but there is never any real difficulty in cannulation of the pulmonary artery via the right ventricle if a rigid steel cannula is used.

In some cases of ventricular septal defect the pulmonary artery pressure is grossly elevated due

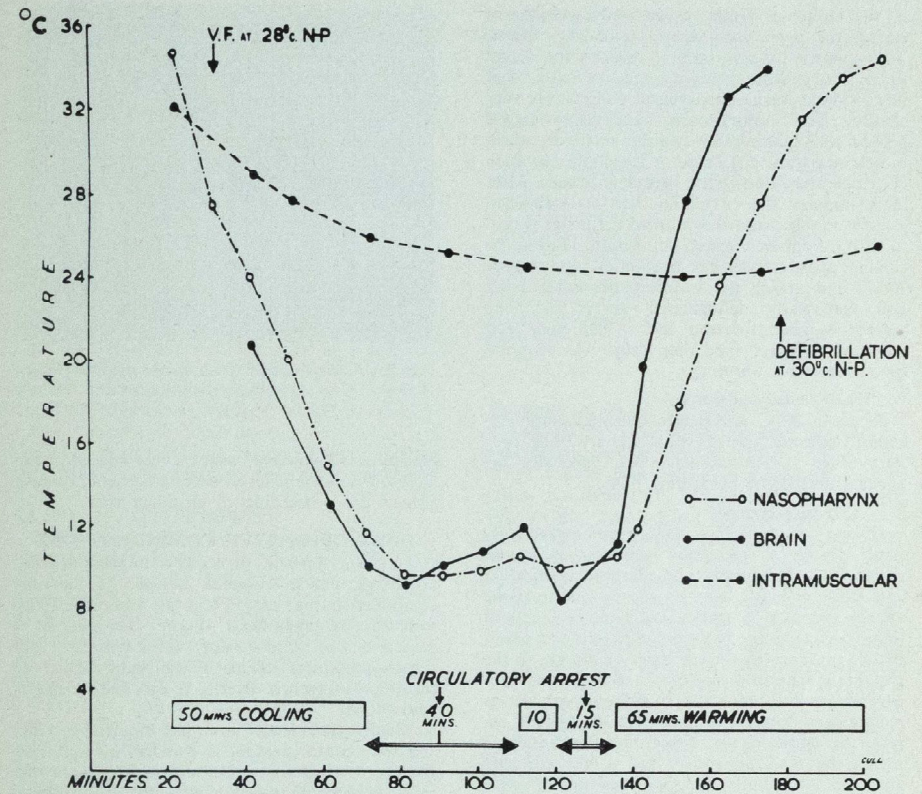


Fig. 4. The temperature changes during an operation under profound hypothermia (craniotomy at Oldchurch Hospital, Romford, for aneurysm of circle of Willis). The brain temperature approximates very closely to the nasopharyngeal temperature.

to an associated raised pulmonary vascular resistance. In such cases it may be difficult to obtain satisfactory pulmonary flow, but if the lungs are ventilated with 100 per cent. oxygen and if a tape is placed around the pulmonary artery to prevent pulmonary regurgitation, then a satisfactory flow can usually be obtained.

#### OBSERVATIONS DURING COOLING AND RE-WARMING

##### 1. Temperature changes

The graph shown in Fig. 4 was made during an operation under profound hypothermia for intracranial aneurysm at Oldchurch Hospital, Romford. Due to the situation of the aneurysm

in the circle of Willis, it was only possible to excise the aneurysm after circulatory arrest. The opportunity was taken to record the actual brain temperature and it will be seen that this followed the nasopharyngeal temperature very closely. The intramuscular temperature lagged behind very considerably and this relatively warm muscle mass was the cause of the slight elevation of temperature during the period of arrest. After forty minutes the circulation was re-established for ten minutes, and this allowed a further period of fifteen minutes arrested circulation. During the cooling phase ventricular fibrillation occurred at 28°C. and during the warming phase the heart was electrically defibrillated at 30°C. The patient weighed fourteen and a half stone and therefore a longer time than usual was required for cooling and warming.

## 2. Electro-encephalograph

At about 20°C. the electro-encephalograph becomes isoelectric, no electrical activity being present (Fig. 5). A normal trace gradually reappears during the rewarming phase.

## 3. Acid-base changes

During the period of cooling and rewarming, some degree of metabolic acidosis occurs, as shown by a fall in pH and plasma bicarbonate, and a rise in blood lactate. This is due to tissue anoxia and may be partly explained by reduced tissue perfusion due to vaso-constriction and partly by the presence of a large mass of muscle in the patient which does not reach such a low temperature as the brain and therefore continues its metabolism during the period of circulatory arrest. In addition the donor blood required to prime the machine always has a low pH and this too contributes to the development of a metabolic acidosis.

To counter this change in acid-base balance sodium bicarbonate 4-7 mEq./Kg. body weight is added in divided doses during cooling and rewarming.

## 4. Potassium

It has been found that there is always a fall in blood potassium following operation under profound hypothermia. This is surprising, since some degree of haemolysis of donor blood always occurs after operation and it would have been expected that the relatively high intracellular

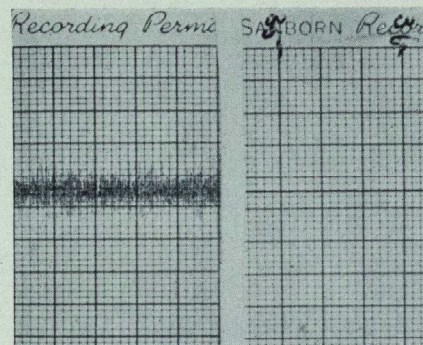


Fig. 5. Electroencephalogram during profound hypothermia. Normal body temperature on the left and 12°C. on the right. Paper speed 0.25 mm./sec.

potassium would have caused a rise and not a fall in blood potassium level after operation. Investigations are proceeding to elucidate this.

## POST OPERATIVE COMPLICATIONS

Too long a period of cerebral ischaemia, leading to permanent cerebral damage, is the only complication that may occur as a result of this technique of open-heart surgery *per se*. It is caused by too rapid cooling of the patient (leading to inadequate cooling of the brain itself) and possibly by cerebral arterial spasm due to unduly cold blood.

Though this complication has occurred in other thoracic centres, notably in Sweden, no such case has occurred in our series, and it is thought that this has been due to strict adherence to the principle of gradual cooling of the patient and the avoidance of a temperature gradient of more than 15°C. between the nasopharynx and the blood entering the patient.

## COMPARISON WITH HEART-LUNG BYPASS

The apparatus for profound hypothermia is very much more simple than a heart-lung machine and requires a smaller volume of blood for priming. Since there is no oxygenator or coronary sinus sucker system to remove blood from the

open heart, there is less damage to the blood and therefore less bleeding after operation. It is this progressive blood damage that is the time-limiting factor in the use of a heart-lung machine. In addition the technique provides ideal operating conditions—a bloodless field and a motionless heart—identical to those in a cadaver.

The only major disadvantage of the technique is that the time available for the intracardiac procedure is limited to sixty minutes, though extra time is possible if the operation is done in two stages with a short period of perfusion in between. A possible disadvantage in cases of mitral incompetence is that in some centres it is thought desirable to view the mitral valve whilst the heart is beating so that the site and cause of the incompetence may be accurately assessed and the efficiency of the repair estimated. On the other hand, the Mayo Clinic group, who undertake this type of surgery with an extremely efficient heart-lung machine, cool the patient to a level at which the heart ceases to beat. Further experience is necessary to determine this point.

## CLINICAL EXPERIENCE

Open-heart surgery was first commenced at St. Bartholomew's Hospital in October, 1959, and up to November, 1961, seventy open-heart operations have been carried out by Mr. O. S. Tibbbs and Mr. I. M. Hill using the Melrose artificial heart-lung machine. Since this time increasing use has been made of the profound hypothermia technique and we have now operated on seventy-five cases by this method. During the same period only eleven operations have been carried out using the Melrose heart-lung machine. Except for cases of mitral incompetence, which at present we think are better operated on using a heart-lung machine, we have found that the profound hypothermia technique is preferable for the following reasons.

1. There has been considerably less physiological disturbance to the patients after operation, who have consequently had a smoother convalescence.

2. The demand on the blood bank has been less, partly due to diminished post-operative bleeding and partly due to smaller machine priming volume.

3. The operating conditions provided for the

surgeon have been almost ideal.

The cases operated on have included nearly all types of congenital and acquired heart disease that are at present treated by open-heart surgery.

	No. of cases	Age in years	Discharged from hospital
Tetralogy of Fallot	20	4½-22	19
Ventricular septal defect	12	3½-40	9
Congenital non-calcified aortic stenosis	9	10-22	9
Congenital calcified aortic stenosis	16	37-65	11
Rheumatic aortic stenosis	2	37-54	2
Atrial septal defect	11	4½-48	10
Pulmonary stenosis	2	27-43	1
Mitral incompetence	1	33	0
Miscellaneous	2	13-58	1
TOTAL	75	3½-65	62

## Tetralogy of Fallot

Twenty patients, whose average age was 13 years, have been treated, and there was only one death due to heart block in a patient aged 4½ years. In these cases of the tetralogy of Fallot (ventricular septal defect combined with stenosis of the right ventricular outflow tract) a considerable portion of the thickened right ventricular muscle was excised from just below the pulmonary valve in all cases. In only two cases was there any narrowing of the pulmonary valve itself, though this was often bicuspid. The ventricular septal defect was closed by direct suture in fourteen cases and by a patch of Teflon felt in six cases. Our present policy is to use Teflon since so often the margins of the V.S.D. are muscular and hold stitches poorly. These results are most gratifying for a group in which there is a very great risk of producing heart block by damage to the bundle of His during the suture of the septal defect.

## Ventricular septal defect

Twelve patients, whose average age was 14½ years, have been treated and in this group there were three deaths, two due to heart block and one due to infarction of the left ventricle after which it was impossible to re-start the heart. One of the cases who developed heart block had virtually a single ventricle due to one large defect and multiple small ones. The defect was closed by direct suture in all cases.

**Congenital non-calcified aortic stenosis**

Nine patients, whose average age was 14 years, have been treated without a death. In two patients the stenosis was due to a subvalvar diaphragm. In the remaining seven patients the valve was bicuspid with only a rudimentary third commissure. In most cases only two commissures were incised for fear of producing incompetence.

**Congenital calcified aortic stenosis**

Sixteen patients, whose average age was 48 years, have been treated, with five deaths. In this older group in whom the onset of symptoms was often delayed until middle age, the valve was always heavily calcified and sometimes apparently quite immobile. Again the valve appeared to have been bicuspid with only a rudimentary third commissure. The valve cusps have been carefully decalcified, in some cases using dental instruments, and always with great care to avoid free calcified particles falling into the left ventricle and producing a cerebral or coronary embolus on the return of heart beat. It has often been surprising how the removal of a relatively small amount of calcified material has resulted in a relatively mobile cusp. Valve or cusp replacement has not been attempted. Despite the presence of a grossly hypertrophied left ventricle which might be expected to be readily affected by lack of oxygen during the period of arrested circulation, there has not been any great difficulty in obtaining return of ventricular contraction during the warming phase.

**Rheumatic aortic stenosis**

This group, in which the valve may be calcified, must be differentiated from congenital calcified aortic stenosis. In these cases the valve is tricuspid and there is usually evidence of other rheumatic valve disease. In the two cases aged 37 and 54 years in this group, the valve was calcified only in the older patient. Both patients had a successful relief of their stenosis.

**Atrial septal defect**

Eleven cases, whose average age was 27 years, have been operated on under profound hypothermia rather than conventional hypothermia, because a pre-operative diagnosis of anomalous pulmonary venous drainage into the right atrium, the presence of a possible primum defect, or

severe pulmonary hypertension had been made. Two cases proved to be a primum type of defect and these were both closed with a Teflon patch. There was one death in this group in a patient who had associated tricuspid incompetence and mitral stenosis.

**Pulmonary stenosis**

Two cases of pulmonary stenosis have been treated. One patient aged 43 years had an isolated infundibular stenosis with a normal pulmonary valve and unfortunately died from congestive heart failure of uncertain aetiology two weeks after operation. The other patient, aged 27 years, with pure pulmonary stenosis and a patent foramen ovale, made an uninterrupted recovery.

**Mitral incompetence**

An attempt to repair mitral incompetence in one patient aged 37 years who had severe pulmonary hypertension led to a fatal outcome following the onset of gross pulmonary oedema at the conclusion of operation.

**Miscellaneous group**

One patient in this group was aged 58 years and had an atrial septal defect and mitral incompetence. He unfortunately died from heart failure following repeated episodes of ventricular fibrillation. The other patient had had a previous total correction of a tetralogy of Fallot, but unfortunately his V.S.D. reopened. He made a good recovery following repair of the defect with a Teflon patch.

**CONCLUSION**

Profound hypothermia has been used for seventy-five cases of congenital and acquired heart disease, including tetralogy of Fallot, ventricular septal defect, congenital and acquired aortic stenosis, and atrial septal defect. The patients' ages have varied between 3½ years and 65 years. The apparatus is extremely simple to use and maintain and has a relatively small priming volume.

The over-all mortality has been 17 per cent. and this compares favourably with other reported series using perfusion with a heart-lung machine. Most of the deaths have occurred in

very bad risk cases, a large proportion being calcified aortic stenosis. The results in tetralogy of Fallot have been especially gratifying. It is our present policy to use this technique for all patients requiring open-heart surgery, except those that are suitable for operation under "conventional" hypothermia (secundum atrial septal defect and pulmonary stenosis) and also cases of mitral incompetence.

**ACKNOWLEDGEMENT**

My thanks are due to Mr. O. S. Tubbs for his constructive criticism of this manuscript.

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## CURRENT INVESTIGATIONS AND RESEARCH PROJECTS IN THE HOSPITAL (cont.)

**Dr. Cullinan's Firm**

1. Studies on small intestinal morphology.
2. Studies on fluorescence and exfoliative cytology in gastric ulcer and carcinoma.
3. Small intestinal influences on carbohydrate absorption.
4. The effect of portal systemic anastomosis on glucose tolerance in cirrhosis (in conjunction with Mr. A. H. Hunt).
5. Ten-year follow-up on diabetic patients.
6. Fundus changes in diabetes and the effect of low animal fat diet (in conjunction with the Eye Department).
7. Blood keto-acids in vitamin deficiency states.
8. Fat mobilization in diabetes and endocrine disorders.

**Dr. Spence's Firm**

1. Investigation of virus infections in chronic bronchitis. (Dr. Stark.)
2. Studies of para-influenzal viruses and their antigenic composition. (Dr. Stark.)
3. Absolute starvation in the treatment of refractory obesity. (Dr. Stark.)

**Dr. Bodley Scott's Firm**

1. Investigation of immunity mechanisms in reticuloses. (Dr. G. Hamilton Fairley; Dr. M. J. L. Patterson.)
2. Investigation of haemolytic anaemias in reticuloses. (Dr. G. Hamilton Fairley; Dr. M. J. L. Patterson.)
3. Assessment of treatment and investigation of the pathological changes in Hodgkin's disease. (Dr. G. Hamilton Fairley; Dr. M. J. L. Patterson.)

**Mr. Naunton Morgan's Firm**

1. Investigation of the blood supply of tumours of the large bowel and rectum using micro-radiographic technique.
2. In vitro perfusion of carcinomas of the colon fol-

- lowing removal at operation and the experimental investigation of factors controlling dissemination of carcinoma cells using cytological and radiological methods.
3. The development of technique for the physiological investigation of factors controlling patients in normal states and in patients with rectal prolapse using a cine-radiographic and image intensifier.
4. Clinical trials of regional intra-arterial infusion with high doses of cytotoxic agents for inoperable malignant disease of the gastro-intestinal tract.
5. The adjuvant use of cytotoxic drugs in operations of malignant disease.
6. Clinical assessment and early treatment of neonatal spina bifida cystica.
7. Cine-radiographic and physiological assessment of the urological complications of spina bifida-vesico ureteric reflux.
8. Identification of cancer cells in the blood stream of patients during operative procedures (in association with Dr. Alan Salisbury, Pathology Department).

**Mr. Badenoch's Firm**

1. Investigation of change in population of bacteria in chronic urinary infection. (Mr. A. W. Badenoch, Mr. J. E. A. Wickham, Dr. O'Grady, and Mr. Patrick Smith.)
2. Investigations of the effects of autotransplant on kidneys of dogs. (Mr. J. E. A. Wickham and Mr. A. W. Badenoch.)
3. Investigation of duodenal Ph. (Mr. Brian Richards.)
4. Investigation of ano-rectal reflexes in relation to megacolon and prolapse. (Mr. I. P. Todd.)
5. Investigation of colonic motility. (Mr. I. P. Todd.)

**Mr. Tuckwell's Firm**

1. An experimental study of renal function in biliary obstruction (with **Dr. R. Cattell**).
2. Cholecystitis glandularis proliferans.
3. Early diagnosis of Scleroderma, with particular reference to vasospastic phenomena.
4. Vascular causes of unequal limb growth (in conjunction with Royal National Orthopaedic Hospital).

**Department of Neurology**

1. Follow-up of myelopathy associated with cervical spondylitis.
2. Study of the association of Leber's Disease with disseminated sclerosis.
3. The prognosis of neuralgic amyotrophy with special reference to recurrences of the disease.
4. Experiments on copper metabolism.
5. Studies on the intravenous injection of Vitamin B<sub>12</sub> Co. isotope.
6. The relationship of migraine and angina in young persons.
7. Studies on the significance of salivation in Parkinsonism.
8. Loss of consciousness in patients with migraine.

**Department of Psychological Medicine****Clinical and Psychophysiological studies of depressive illness (supported by Medical Research Council) including:**

1. Study of autonomic functions.
2. Cardiovascular changes.
3. Muscle tension changes.
4. Conditioning during different stages of illness.
5. Variations in physiological functions in sleeping and waking states.
6. Variations of physiological functions in sleeping and waking states with clinical changes occurring with drug therapy or E.C.T.

**RECENT PAPERS BY BART'S MEN**

- Adrian, Lord. Priorities in medical responsibility. *Proc. roy. Soc. Med.*, 56, July, 1963, pp. 523-528.
- The reaction of degeneration. *Proc. roy. Soc. Med.*, 56, June, 1963, pp. 439-443.
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**The following studies are also in progress:**

7. Controlled study of Nortryptiline in the treatment of depression.
8. Completion of clinical and metabolic study of post partum psychosis.
9. A study of cholinesterase levels in psychiatric disorders.
10. Follow up study of patients referred for termination on psychiatric grounds.
11. The effect of parenteral monoamine oxidase inhibitors in resistant cases of depression.
12. Controlled trial of a new drug in anxiety states.

**Studies of Monoamines**

13. In urine to attempt to differentiate genetically specific types of depression.
14. In platelets to investigate the role of binding sites in the aetiology of depressive illnesses and the effect of antidepressants on such an illness.
15. In post mortem brain tissue to investigate the variation in concentration of monoamines in depressed patients compared with controls and also the effect of antidepressant drugs on these concentrations.
16. By feeding essential amino acids such as tryptophan, to investigate which of the brain monoamines is important in the aetiology of depressive illnesses.
17. The metabolism of monoamine oxidase inhibitors in vivo and its relation to the clinical effectiveness of the drug.
18. Study of relationships between biochemical changes with antidepressive drugs and clinical improvement.

**Psychosomatic and related studies:**

19. Inter-relationships of aetiological factors in asthma, urticaria and vasomotor rhinitis.
20. Aetiology of premenstrual asthma.
21. Aetiology of premenstrual urticaria.
22. Aetiology of premenstrual vasomotor rhinitis.
23. Treatment of congenital dyslexia.

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# ST. BARTHOLOMEW'S HOSPITAL JOURNAL



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FEBRUARY, 1963

## Editorial

The new library at Charterhouse can now be judged to be a great success if the numbers of students and others taking Library Suppers in College Hall are taken into account. Many return to continue their studies in comfort, refreshed by a meal calculated to be light enough to avoid that post-prandial somnolence well-known to those attending the lectures in Pathology and Bacteriology after a hasty lunch—perhaps there is still a case for missing the rush-hour and arriving in time for compulsory lectures at 9 o'clock. It is not one of the intended functions of a library to provide resting-places for the weary—this is one of the indispensable functions of the two Abernethian Rooms—it should provide firstly all the books and periodicals its users require, and secondly a suitable atmosphere in which to work. For students living in flats, especially with non-medical friends, distractions are too numerous to mention, resulting in periods of work interspersed with longer periods of other activities. For them it is essential that one of the Hospital libraries remains open during the evenings, and provides all the necessary text-books; this the new library does and is also a sufficiently pleasant place of work to act as a counter-attraction to even the "pavender or pub" or the College Hall Bar.

Besides text-books the libraries must pro-

vide a range of periodicals whose price continually spirals upwards. At present many of these are kept in the departmental libraries and it is hoped that when the Research Library is built on as an extension, they will become more freely accessible by being housed there. By this centralisation some duplication will be avoided; for instance, of the five copies of "Nature" in various parts of the Hospital and College not one appears in either of the main libraries. But in order not to affect the convenience of having departmental libraries current numbers should be kept in their appropriate places, and the bound volumes put into the main library.

Those who clamour for more books and periodicals must remember that the Bart's Medical College Libraries are only one unit among about a dozen in the University of London. Thus within the University duplication is considerable and unavoidable if the standard of library facilities is to be maintained; however, some Hospitals are well known for specialisation in their libraries, such as U.C.H. for its collection of Physiological books. Different hospitals should be encouraged to build up a special collection beyond their own immediate needs—a system similar to that operating in London public libraries which appears to work effectively.

Comment this month suggests that students should spend more time in hospitals other than Bart's to gain further experience of disease, a view which is widely held and certainly deserves consideration. The Editor would be pleased to receive contributions to this column from any reader with ideas which should be more generally known.

## Calendar

### MARCH

- Sat. & Sun. 2 & 3: Dr. A. W. Spence  
Mr. E. G. Tuckwell  
Mr. W. D. Coltart  
Mr. T. B. Boulton
- Mon., 4: Film Society. "Marx Brothers at the Circus", 8.30 p.m.
- Sat. & Sun. 9 & 10: Prof. E. F. Scowen  
Prof. G. W. Taylor  
Mr. H. Jackson Burrows  
Mr. F. T. Evans
- Wed., 13: B.M.S.A. Visit to the National Spinal Injuries Centre, Stoke Mandeville.  
Professor C. Keith Simpson, M.D.: "Crime and the Doctor", 6 p.m., B.M.A. House, Tavistock Square, W.C.1.
- Sat. & Sun. 16 & 17: Dr. R. Bodley Scott  
Mr. Alan Hunt  
Mr. J. N. Aston  
Dr. R. A. Rowen
- Mon., 18th: Augustine Society, "Faith and the Factory Worker", 5.45 p.m.
- Thurs., 21: Abernethian Society: Prof. Woodruff, "Transplantation of Human Kidney", 5.45 p.m.
- Sat. & Sun. 23 & 24: Dr. E. R. Cullinan  
Mr. C. Naunton  
Morgan  
Mr. W. D. Coltart  
Dr. G. H. Ellis
- Sat. & Sun. 30 & 31: Dr. Graham Hayward  
Mr. A. W. Badenoch  
Mr. J. N. Aston  
Dr. R. Ballantine
- Physician Accoucheur on duty for the month of March is Mr. J. Howkins.

## Engagements

BAILEY—FISHER.—The engagement is announced between Alan Richard Bailey and Rachel Gay Fisher.

## The Late Dr. Garry Renn

Mr. and Mrs. Renn, of Grays, Essex, parents of the late Dr. Garry Renn, who was tragically killed in a road accident soon after qualification from this Medical College, have presented some of his effects to the College. These consist of textbooks, a microscope, slides and osteological specimens, which have been deposited in the appropriate departments. This gift is much appreciated, while we deeply regret the circumstances in which it was made.

RUSHMAN—ROGERS.—The engagement is announced between Geoffrey Rushman and Gillian Mary Rogers.

## Births

- CRONK.—On 14th Jan., to Elizabeth (née Ogden) and Dr. Peter Cronk, a brother (Robert James) to Simon and David.
- CROSFILL.—On 24th Dec., to Jean (née Stewart) and Martin Croffill, a son (John), brother for Fiona.
- DEERING.—On 25th Jan., to Sonia (née McMenemy) and Dr. Robert Basil Deering, a son (Neal Andrew).
- MACADAM.—On 2nd Jan., in Buenos Aires, to Diana (née Duncombe) wife of Dr. F. I. Macadam, a daughter (Mary Rose).
- ROLES.—On 23rd Jan., to Wendy (née Donaldson) and Dr. Nicholas Roles, a son.
- VICKERY.—On 28th Jan., to Betty (née Tiffen) and C. M. Vickery, F.R.C.S., a son, brother for Judith, Jane and Christopher.

## Death

WITH.—On 14th Nov., 1962, Dr. P. A. With, M.R.C.S., L.R.C.P., aged 78. Qualified 1912.

## Appointments

University of Birmingham  
Prof. D. V. Hubble has been appointed Dean of the Faculty of Medicine.

University of London  
The Council for External Students have elected Mr. J. B. Hume as Chairman for the Session 1962-63.

The following have been appointed, or re-appointed as representatives of the University on the governing bodies indicated in parentheses:—Sir Francis Fraser, M.D., F.R.C.P. (London School of Hygiene and Tropical Medicine, Board of Management); Dr. C. F. Harris (London School of Hygiene and Tropical Medicine, Court of Governors); Prof. M. de Burgh Daly (Royal Dental Hospital of London School of Dental Surgery).

The title of Reader in Physiology in the University has been conferred upon Dr. Dennis Mendel in respect of the post held by him at King's College.

## University of Oxford Final M.B. Examination Michaelmas Term, 1962

### Passed

Myers, D. M.

### Supplementary Pass List

#### Medicine

Rushton, G. J.

## University of Cambridge Final M.B. Examination Michaelmas Term 1962

### Passed

Aitken, J. M.           Hudson, T. G.  
Ball, M. H.           Stoodley, B. J.  
Greef, A. W.           Thomas, M. J. G.  
Nanson, E. M. (née Wood)

### Supplementary Pass List

#### Part I. Pathology and Pharmacology

Ansell, I. D.           Hession, M. A.  
Barnes, N. D.       Hoare, E. M.  
Cooke, T. D. V.     Mulvein, J. T.  
Cripps, C. M.     Oon, C. T.  
Crowther, D.       Perring, M. A.  
Declany, D. J.     Pickard, R. G.  
Dunn, D. C.       Stewardson, M. P.  
Edmondson, P. C.   Ward, R. H. T.  
Edwards, W. R.     White, R. J.  
Flower, C. D. R.    Wright, A.

#### Part II. Surgery

Fischer, W. G.       Ward, A. M.  
Mercer, J. D.

- <sup>1</sup> Distinction in Pathology,  
<sup>2</sup> Distinction in Pharmacology

## University of London Final M.B., B.S. Examination October, 1962

### Honours

Butler, P. W. P. (Distinguished in Pathology.)  
Howell, F. A. (Distinguished in Surgery.)  
Langley, P. S. (Distinguished in Surgery.)  
Ross, A. P. J. (Distinguished in Surgery.)

### Pass

Balfour, A. J.  
Colin-Jones, D. G.  
Dacie, J. E.  
Davies, N. M.  
Ernst, E. M. C.  
Harvey, J. A.  
Hore, B. D.  
Howes, A. C.  
Hutchinson, D. B. A.  
Ind, J. E.  
Iregbulem, L. M.  
James, J. E. A.  
Joy, P. J.  
Kingsbury, A. W.  
Ladd, G. H. Y.  
Langford, E. M.  
McCarthy, W. E.  
Manchester, K.

Marsh, A. R.  
Newton, J. R.  
Orr, M. M.  
Patrick, P. L.  
Perry, P. M.  
Robinson, L.  
Rushman, G. B.  
Sandhu, M. S.  
Sharp, G. T.  
Shearer, R. J.  
Smyth, N. W.  
Terry, A.  
Tomlinson, R. J.  
Turner, G. M.  
Waller, A. S.  
Watkin, B. C.  
Watson, J. U.  
Wilson, A. I.

## Supplementary Pass List

### Part I

Aldis, P. W.           Minns, S. A.  
Amir-Ahmadi, H.     Phaure, T. A. J.  
Austin, A. J.         Phillips, J. D.  
Clarke, J. M.         Poore, P. D.  
Coates, O. A.         Pope, F. B.  
Davies, R. K.         Pusey, J. H.  
Doran, B. R. H.       Katcliffe, R. M. H.  
Dudley, N. E.         Robertson, A.  
Dupre, P. C.         Rolfe, M.  
Gardner, Z. N. C.     Ruoss, C. F.  
Gleadle, R. I.         Salole, R. M.  
Guest, A. D. L.       Shinebourne, E. A.  
Hadley, D. A.         Stanley, P.  
Hilton, A. M. B.       Stephens, A. D.  
Knight, A. H.         Tam, Y. D.  
Layton, D. C.         Waller, J. O.  
Lettington, W. C.     Ware, E. A. S.  
Lewis, A. A. M.       Whyatt, N. D.  
Lopez, J. T.           Williams, C. R.  
Lotfi, D.              Wilson, R. G.  
Maw, A. R.            Wise, K. S.

### Part II

Bergel, R. C.           Casson, A. J.  
Blake-James, R. B.     Doney, B. J.  
Bootes, J. A. H.       Healey, J.  
Brooks, B. G. B.       Perriss, B. W.  
Britz, M.

### Part III

Davies, R. K.

### Part IV

Bergel, R. C.           Brooks, B. G. B.  
Birch, A.              Britz, M.  
Blake-James, R. B.     Davies, R. K.  
Bootes, J. A. H.       Perriss, B. W.

## Conjoint Board Final Examination October, 1962

### Pathology

McCarthy, W. E.       Lopez, J. T.  
Waller, J. O.           Jennings, M. C.  
Wise, K. S.           Hilton, A. M. B.  
Aldis, P. W.           Hardy, J. D.  
Amir-Ahmadi, H.       Gleadle, R. I.  
Austin, A. J.           Tam, Y. D.  
Clarke, J. M.           Shinebourne, E. A.  
Dudley, N. E.           Ruoss, C. F.  
Dupre, P. C.           Rolfe, M.  
Caine, P. W.           Phillips, J. D.  
Coates, O. A.           Pusey, J. H.  
Lewis, A. A. M.        Phaure, T. A. J.  
Lotfi, D.              Minns, S. A.  
Leaver, P. K.           Maw, A. R.  
Layton, D. C.           Ware, E. A. S.  
Knight, A. H.

### Medicine

Iregbulem, L. M.       Hore, B. D.  
Dacie, J. E.           Terry, A.  
Howells, D. B. M.     Patrick, P. L.  
Ward, R. H. T.         Michael, G.  
Ind, J. E.              Waller, A. S.  
Britz, M.              Langley, P. S.  
McCarthy, W. E.       Waller, J. O.  
Balfour, A. J.         Turner, G. M.

**Surgery**  
Iregbulem, L. M. Sharp, G. T.  
Dacie, J. E. Ernst, E. M. C.  
Ind, J. E. Zeegen, R.  
Britz, M. Shearer, R. J.  
Davies, N. M. Harvey, J. A.  
Birch, A. Howell, F. A.  
Terry, A. Colin-Jones, D. G.  
Patrick, P. L. Wilson, A. I.  
Michael, G. Watson, J. U.  
Langley, P. S. Winter, J. M.

**Midwifery**  
Britz, M. Waller, A. S.  
Davies, N. M. Rushman, G. B.  
McCarthy, W. E. Zeegen, R.  
Balfour, A. J. Davies, R. K.  
Hore, B. D.

The following have completed the examination for the Diplomas M.R.C.S., L.R.C.P.:—

Iregbulem, L. M. Waller, A. S.  
Dacie, J. E. Langley, P. S.  
Howells, D. B. M. Turner, G. M.  
Ward, R. H. T. Harvey, J. A.  
Britz, M. Howell, F. A.  
Balfour, A. J. Colin-Jones, D. G.  
Hore, B. D. Wilson, A. I.  
Terry, A. Rushman, G. B.  
Patrick, P. L. Winter, J. M.  
Michael, G.

**Conjoint Board  
Final Examination  
January, 1963**

**Pathology**  
Bootes, J. A. H. Scriven, P. C.

## BRITISH MEDICAL STUDENTS ASSOCIATION

### SUMMER PROGRAMME

#### National Clinical Conference

This will be held in Glasgow from Tuesday, 26th March, until Saturday, 30th March. The total cost to students including travel and accommodation will only be £6. The programme includes lectures, ward rounds and demonstrations. Several Bart's students went to the Clinical Conference in Aberdeen last year and thoroughly enjoyed it.

#### Pre-Clinical Scandinavian Summer School

This will be held in Aarhus, Denmark, from 11th-30th August. The fee will be £26 exclusive of travel.

#### Clinical Summer Schools in Scandinavia

1. Copenhagen County Hospitals from 5th to 26th August, for which the fee will be £26, exclusive of travel.

2. University Hospitals in Aarhus, Oslo,

Brooks, B. G. B.  
Russell, A. L.  
Whyatt, N. D.  
Gurry, B. H.

Phaure, T. A. J.  
Pain, V. M.  
Ware, E. A. S.  
Tam, Y. D.  
Minns, S. A.  
Layton, D. C.  
Bootes, J. A. H.  
Brooks, B. G. B.  
Russell, A. L.

**Surgery**  
Brooks, B. G. B.  
Russell, A. L.  
Waller, J. O.  
Ward, A. M.  
Hilton, A. M. B.

**Midwifery**  
Ware, E. A. S.  
Tam, Y. D.  
Minns, S. A.  
Bootes, J. A. H.  
Brooks, B. G. B.  
Russell, A. L.  
Lotfi, D.  
Knight, A. H.

The following have completed the examination for the Diplomas M.R.C.S., L.R.C.P.:—  
Brooks, B. G. B. Ward, A. M.  
Russell, A. L.

Gothenburg and Copenhagen from 5th to 25th August, with 5 days in each city. The fee will be £36, exclusive of return fare.

Application forms will be obtainable from B.M.S.A. representatives and should be received not later than 1st May, 1963.

#### Students International Clinical Conference

This will be held in Copenhagen from 11th to 31st August, and the subjects to be studied are psychiatry, clinical neurophysiology, neurology and neurosurgery. The fee will be £26. Applications must be received by 15th May, 1963.

#### Medico-Social Visit to Russia

This has been arranged for 5th-20th September and will cost £70 inclusive of travel. Places to be visited include Moscow, Leningrad and Warsaw.

J.V.B.

Gardner, Z. N. C.  
Pott, N. H.  
Oon, C. T.  
Pakiam, A. I.

#### Medicine

Hilton, A. M. B.  
Whyatt, N. D.  
Lotfi, D.  
Dudley, N. E.  
Hardy, J. D.  
Gurry, B. H.  
Rolfe, M.  
Aldis, P. W.  
Austin, A. J.

#### Surgery

Leaver, P. K.  
Coates, O. A.  
Gleadle, R. I.  
Lewis, A. A. M.  
Shinebourne, E. A.

#### Midwifery

Amir-Ahmadi, H.  
Aldis, P. W.  
Scriven, P. C.  
Stephens, A. D.  
Gardner, Z. N. C.  
Leaver, P. K.  
Pusey, J. H.  
Jennings, M. C.

## FIFTY YEARS AGO

Malt extract and malt with cod-liver oil are items in which extravagance, by the patients' manner of taking, occurs to a very large degree. The usual procedure is to dip the domestic teaspoon (which is a good deal larger than the medicinal one) into the jar of malt, and by a certain amount of manipulative skill get out as *much* as possible. This has been found to weigh as much as 280 gr. Even the domestic teaspoonful of malt, properly measured, only weighs about 80 gr., so that it is obvious that the dose taken by the patient is greatly in excess of that ordered.

The Hospital variety of malt extract, with or without cod-liver oil, seems to be such a palatable article that, from the patient's point of view, one never gives sufficient. The prescription of a much smaller dose than is actually desired would be the best way of overcoming this difficulty.

A large number of patients have their medicines ordered *and given* for fourteen days. Many return to the hospital seven days later, are seen, and owing no doubt to the stress of work in the surgery, the prescriptions are repeated without the last date being observed.

Many patients attend the Casualty Department for some weeks or even months, the result being that the prescription papers are filled with a long list of various kinds of medicines that have been required at different times. The tired prescriber on a busier morning than usual is tempted to write "*Rep. omnia*", leaving it to the pharmacist and patient to "fight out" the exact requirements. The patient usually demands that the words be taken literally. An extract from such a paper is here given, the period covered by it being several months. The preparations that had been ordered were as follows:

Hst. seneg. ammon, *quart hor.*  
Linct. scill. opiat., *p.r.n.*  
Hst. gent. c rh., *ter die.*  
Hst. sennæ co. *mane.*  
Lin. sap.  
Pil. cal. c jal.  
H.M.S. c M.S., *ter die.*  
Lotio plumbi.

The patient demanded the *eight* preparations, and was technically within her rights. The prescriber, on being seen, reduced the number to *two*. It would tend to economy if the exact medicines required were indicated on each occasion.

## LAST MONTH

Appendices have always been a fascination to me; I refer of course to literary appendices. The word appendix was first used, it seems, in 1549, as "an addition subjoined to a document or book, having some contributory value, but not essential to completeness". Whenever I read this definition I feel sorry for the poor appendix, tagged on to the end of the story, a sort of postscript, an irritating non-essential. However, I think our sympathies are wasted, for the appendix, by its very nature, is quite happy with the wealth of information it contains. Let me illustrate this with an example.

Appendix XIII of that well known book "*Isotopic Tracers*", a product of our medical college, is a mine of information. There, set out on one clear page, is the 64-times table from 0 to 309. Think how incredibly useful that is to the farmer, say with 64 cows, each of which consumes 91 sacks of meal a year. At a glance this table tells the farmer he will require 5,824 sacks a year. Or to the astronaut who has been circling the Earth for 64 hours at an average speed of 17 thousand miles per hour. How many miles has he travelled? Appendix XIII makes it 1,088 thousand. Then of course 64 is 8 squared or 2 raised to the sixth power. Thus the appendix helps those people that spend hours working out problems about ancient kings, who put a grain of wheat on the first square of a chess board, two on the next, four on the next and so on.

The uses are infinite; regularly in one's daily life appendix XIII can be of service to you. Why not go into the library now with a large pair of scissors and cut out page 504 from this book? Don't let the librarian see you, and if he does don't tell him I sent you. "Anxious" of Kensington High Street writes, "At the moment I am employed in an editorial position on two publications in the hospital as well as having a post of some importance in the Students' Union. Do you think this is too much? I seem to be losing friends fast and would be grateful for any help you can offer".

Dear "Anxious", you omit to mention that in one of the publications you are running a gossip column which, in my opinion, is the real cause of your social failure. About your S.U. position—don't let that worry you, few if any Bart's students really care about the Union.

## AN OUTBREAK OF STAPHYLOCOCCAL SEPSIS IN THE THORACIC SURGICAL UNIT

by D. R. DUNKERLEY

FOR two hundred years writers have pointed out the dangers of going into hospital, for the patient may acquire there a disease which he did not have on admission. An early account is that of J.-R. Tenon, who in 1788 in his "Mémoires sur les Hôpitaux de Paris" frankly described the great Hôpital-Dieu. The patients lay four to six in a bed, and the average mortality for the whole place was 20 per cent., while "recovery from surgical operation was, in the nature of things, a rarity" (Garrison, 1929). The problem of hospital infection was greatly reduced by the efforts of Florence Nightingale, who led the campaign to improve hospital hygiene, and Lord Lister; but surgical infection continued at a lower rate. The meagre figures available for the first part of this century indicate that 5 per cent. to 15 per cent. of wounds became infected after clean operations.

In 1939 Devenish and Miles from U.C.H. drew attention to an outbreak of staphylococcal infection originating from a single source, a surgeon. They initiated the long series of reports of infection by staphylococci which have continued to the present day. As new antibiotics underwent preliminary trial they were found effective against staphylococci; on general release each was used with enthusiasm, and sooner or later staphylococci developed resistance to nearly all of them. Certain multiple resistant strains showed a propensity to rapid and extensive spread among patients and staff in hospitals. They caused severe lesions difficult to treat owing to the antibiotic resistance, they were difficult to eliminate from the ward and if the patient took them home, he and his family were liable to suffer from boils over periods of months or years.

From Australia in 1954 came a report by P. M. Rountree and her colleagues describing an apparently new strain reacting with phages 80 and 81, which had caused an epidemic in a surgical ward (Isbister et al, 1954). A year later she was writing again to say that reports were coming in from all over Australia of

epidemics due to 80/81 (Rountree and Freeman, 1955). Soon afterwards papers from Canada (Bynoe et al, 1956), the U.S.A. (Shaffer et al, 1957, Blair and Carr, 1958) and Britain (Gillespie and Alder, 1957, Williams, 1957) traced the rapid spread of this strain. By 1958-60 it had become the most widely encountered of the relatively limited number of resistant strains liable to cause outbreaks of infection.

The Thoracic Surgical Unit of this hospital reported in April, 1962, the occurrence of four cases of sepsis caused by antibiotic resistant staphylococci in the previous eight weeks. One of these was a paronychia, the other three post-operative infections of some kind. This may not seem exceptional in eight weeks, during which some 55 operations were performed, but on examination of the records it was found that no cases of staphylococcal sepsis had been detected on that unit for twelve months.

An investigation was undertaken to find the sources of the staphylococcus, and if possible to trace the original source. This report is presented as an example of how, by relatively simple methods, the history of the outbreak may be traced and the ward cleared of infection.

### Materials and Methods

The ward contains patients of both sexes and consists of a ten-bed room, four four-bed rooms, and four single rooms which may be used for isolation. One of the four-bed rooms is used as a recovery room where all post-thoracotomy patients spend at least 24 hours. All such patients have a week of prophylactic penicillin, 15.6 mega-units in all, commencing with their premedication.

Nasal swabs were taken from all patients, nurses in both ward and theatre, the surgical staff and the domestic staff on three occasions—16th and 24th April, and 1st May. Some swabs had been taken prior to 16th April. All coagulase-positive staphylococci

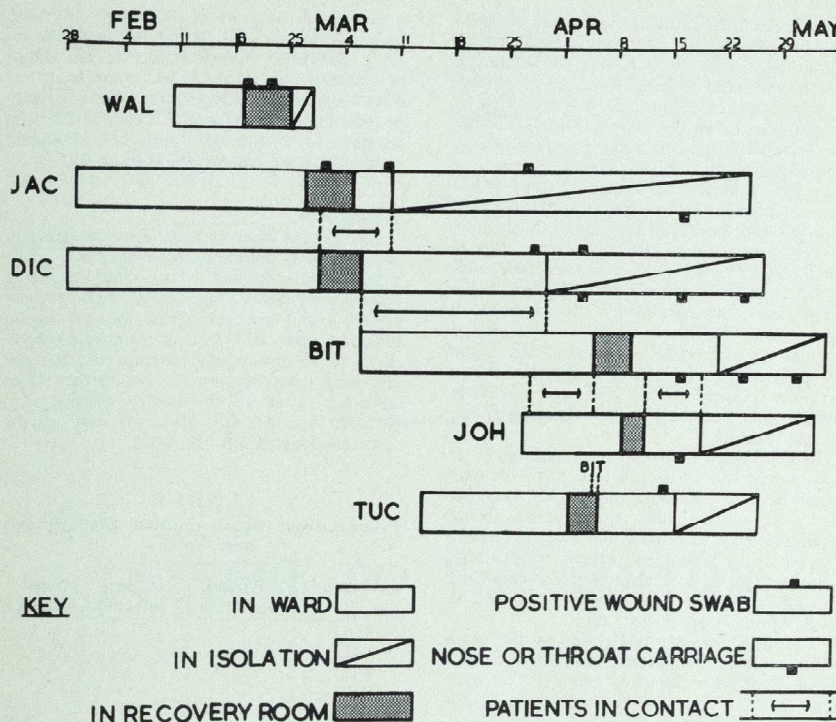


Chart showing patients' movements and times when in contact.

were tested for antibiotic sensitivities and sent to the Central Public Health Laboratory at Colindale who kindly phage-typed them.

### Results

Six patients were involved. The first patient, WAL, died before our investigation began, and the organisms isolated from him were not phage-typed. The other five were shown to carry or be infected with type 80/81, resistant to penicillin and tetracycline (see Table).

From the bacteriological results and the account of the patients' movements extracted from the ward record book, a chart was constructed, a simplified version of which is reproduced here.

WAL was admitted on 10th February, from another hospital known to be troubled with staphylococcal infection. At operation on 19th February, an infected carcinoma of the oesophagus was resected: culture yielded *Staph. aureus* resistant to penicillin and tetracycline. On 21st February, a similar organism was found in his sputum. He was moved into a single room, where he died shortly afterwards.

JAC entered the recovery room, following operation, on 27th February, two days after WAL had left it, and he remained there 7 days. On 1st March, while he was still there, a resistant staphylococcus was isolated from his tracheostomy and his sputum. After returning to the ward he developed a wound infection from which a resistant staphylococ-

cus was cultured, and was moved into isolation on 10th March. By the time detailed investigation began, the wound was sterile and it was not possible to phage-type the organism. However, on 16th April, he was found to be a nasal carrier of the resistant strain 52/80/81/+, which is closely related to, and known to develop easily from 80/81. It is postulated that JAC acquired the organism from WAL, that it infected his wound and sputum, and that this was the strain later found in his nose.

The third patient, DIC, spent four days in the recovery room and a further four days in the same room in the ward with JAC. Two weeks later, on 28th March, he developed a paronychia. This was shown to be caused by type 80/81, and he was subsequently found to be a nasal carrier of this strain. He almost certainly acquired it from JAC, and it is likely that he first became a nasal carrier, later infecting himself.

BIT, the fourth patient, was admitted on 5th March, and as he and DIC were the only small boys in the ward, they were together for most of the next three weeks, being separated now and then for reasons mainly disciplinary. There was ample opportunity, therefore, for BIT to acquire the resistant organism in his nose, and, as was discovered on 24th April, in his throat also.

The fifth patient, JOH, was in the same room as BIT for thirteen days until on 6th April, both were found to carry the resistant type 80/81. This was his only contact with a known carrier.

The sixth patient, Miss TUC, was the only female affected, and had had no contact with the other patients, except that she shared the recovery room for two days with BIT. On 14th April she developed a wound infection from which type 80/81 was isolated.

The recovery room itself was examined bacteriologically on 6th April, while BIT was in residence. No staphylococci were found on the sinks, blankets, curtains, or in the dust. The mechanical respirator was free from staphylococci.

The transfer sequence may be described thus: WAL—JAC—DIC—BIT—JOH and TUC. Each step is fairly clear, except for the first. WAL was never actually in the same room as JAC, although the latter entered the ten-bed room the day after WAL left it, and the recovery room two days after he left. Experience in other wards has shown that various routes of transfer are possible. The organism may have remained in the dust, on bedding or on other items in the rooms. Or

a member of the recovery room staff may have become a carrier and passed the organism to JAC. Whatever the route, it may reasonably be assumed that as WAL had come from another hospital, as the organism was already present at operation, and as this was the first recognition of it in the unit, he introduced it into the ward and passed it on to JAC.

#### Management

All infected cases and carriers were isolated, and this was achieved by 19th April. The nasal carriers applied 1 per cent. neomycin cream to the nostrils twice daily. JAC received erythromycin and novobiocin for his wound infection, and BIT had a neomycin throat spray in an unsuccessful attempt to clear the organism from his throat. No further cases developed after all the known sources were isolated, and by 4th May, the last of the involved patients left the ward.

TABLE  
Patients from whom resistant Staphylococci were isolated.

Name	Wound Infection	Other Infection	Nasal Carriage
WAL		(+)	
JAC	(+)	(+)	+
DIC		+	+
BIT			+
JOH			+
TUC	+		

+ Organism isolated and phage-typed.

(+) Organism isolated but not phage-typed.

#### Summary and Conclusions

By swabbing all the people who might have been involved, and charting out the possible contact situations from the ward record, the spread of the antibiotic resistant staphylococcus 80/81 could be traced back to its origin. The use of phage-typing made it clear that the infections were due to the introduction of a new strain into the unit, for during the period of our investigation a number of other phage-types with various antibiotic resistances were isolated, but these presumably lacked the ability of 80/81 to colonise and infect a series of patients. The infecting strain was eliminated from the ward by isolating and treating the affected patients until they were discharged. When all the sources had been removed, further sepsis ceased.

#### Acknowledgements

I am indebted to Mr. O. S. Tubbs and Mr. I. M. Hill for permission to work in their wards and to Professor R. A. Shooter for much encouragement and advice. My thanks are due to Miss Anne Brooke for technical assistance. The work was supported by a research grant from the Treasurer and Governors of the Hospital.

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## LETTERS TO THE EDITOR

Dear Sir,

Concerning the obituary of my Father published in the December issue of the Journal, it has needed a physician to draw attention to a surgical error which crept into the paragraph describing the Vintage Years at the hospital. It will come as no surprise to your readers to be told that it was that stickler for accuracy, Dr. George Graham, who observed that Sir D'Arcy Power was stated to have been President of the Royal College of Surgeons. He was in fact on the Council from 1912-1928 and was for many years honorary librarian to the College but he was never President.

Mr. Reginald Vick has pointed to a less historically important but rather more amusing fact. If the photograph of the Staff, reproduced on page 301, is studied, it will be seen that in the back row of the group towards the left hand end there is a hiatus. In the original this was occupied by Mr. Watson, later Sir Charles Gordon-Watson, but as he had not at that time been elected to the Staff he was later expunged from the picture.

In writing this letter perhaps it is also not out of place to record that my Father died in 1962, not 1961 as stated in the heading to the obituary.

Yours faithfully,

Michael Harmer.

\* \* \*

Dear Sir,

In the annual report of the college council, the hope is expressed that at some future date a "rowing" tank will be installed. Meanwhile, surely there can be no objection to a "bank tub" being put in to the Nurses' swimming bath. This could be suspended from the roof, or on "davits". I feel sure that the Nurses would be willing to sacrifice one or two hours a week of their swimming time in order to help the Boat Club to train more students and to win more races.

Yours truly,

Malcolm Donaldson.

## THE DUCTS OF LUSCHKA

by I. A. YING

### INTRODUCTION

WE are taught of the existence of aberrant bile ducts communicating between the intra-hepatic biliary tree and the gall bladder. These were first described by Hubert Luschka in 1863 and there is a great deal of confusion as to what Luschka really described. However, the significance of the ducts from a practical point of view is not to be denied.

In the following case, a communication between the right hepatic duct within the liver and the bed of the gall bladder was demonstrated by cholangiography at operation.

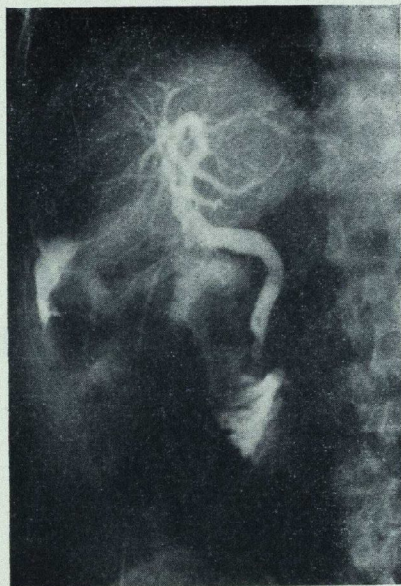
### CASE HISTORY

Mr. W. S., aged 55, a tool maintenance engineer, first went to hospital in 1938 (then aged 31) because he was jaundiced. A diagnosis of cholelithiasis was made, but his jaundice subsided and nothing was done. Ever since then he had had occasional vague abdominal pain in the right hypochondrium.

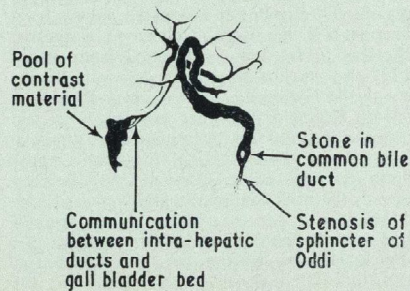
In September 1958 he had a small haematemesis and passed a melaena stool, and was treated medically for peptic ulceration. In May 1959 he had another haematemesis and melaena and was investigated (at another hospital). He was found to have hepatosplenomegaly; a barium meal and enema showed no lesion, but a cholecystogram demonstrated three stones.

At operation he was found to have gross cirrhosis hepatis, and, with a history of haematemesis and melaena, it was thought that he was a possible candidate for a porta-caval anastomosis. Hence, a cholecystotomy was done in order to leave the area around the Foramen of Winslow untouched. Later, a barium swallow demonstrated large oesophageal varices. The porta-caval anastomosis was done in November 1959 at St. Bartholomew's Hospital.

He started to have recurrent symptoms of gall bladder disease and in May 1961 he was re-admitted for a cholecystectomy.



Operative Cholangiogram showing back flow of contrast material to the gall bladder bed.



At operation the gall bladder was found to be greatly thickened and contained numerous small stones. It was removed; 45 per cent. hypaque was then injected into the stump of the cystic duct through a fine polythene tube.

This operative cholangiogram (fig. 1 and explanatory sketch) shows moderate dilatation of the biliary tree, a stone at the lower end of the common bile duct, stenosis of the sphincter of Oddi and backflow of contrast through aberrant bile ducts of Luschka to the gall bladder bed, where a pool of contrast material has collected.

The operation then proceeded as follows: The cystic duct was tied off. Through a duodenotomy incision, the sphincter of Oddi was divided and the mucosa of the lower end of the common duct sutured to the duodenal mucosa so as to constitute a sphincteroplasty. The stone in the common duct was removed and the biliary passage well irrigated to ensure that there was no other calculus present. A fine polythene tube was inserted to drain the common duct and the duodenotomy was closed. A Penrose drain was inserted to the bed of the gall bladder. The wound was closed in the usual manner, with catgut, stainless steel sutures and skinclips. No attempt was made to suture the leaking ducts of Luschka, and little bile-stained fluid drained from the tube.

The patient made a good recovery from the operation but became ill again in 1962. He died of liver failure on 30th June. At post-mortem it was found that he had developed a primary carcinoma of the liver. The sphincteroplasty had succeeded in keeping the passage through the Ampulla of Vater widely patent. The porta-caval anastomosis was only 9 mm. across, but otherwise entirely satisfactory.

### DEFINITION

In 1863 Hubert Luschka described certain small ducts in the wall of the gall bladder which occurred both on the peritoneal and hepatic surfaces of the viscus. They were seen to communicate with one another in many places, but he never found any of them opening into the lumen of the gall bladder or into the intra-hepatic ducts. Luschka believed these to be aberrant bile ducts which represented metamorphosed remnants of the embryonic primordium of the liver.

In 1927 Béla Halpert gave a clearer description of these aberrant bile ducts in the gall bladder wall. He found that they occurred more frequently on the hepatic aspect

and usually along the edge of the vesicae fellae, but also on the peritoneal surface. They are often found running together with small blood vessels. The ducts were seen to branch and anastomose with one another or to communicate with bile ducts emerging from the liver, but they never opened into the lumen of the gall bladder. They lie mainly in the perimuscularis and generally run parallel to the surface of the gall bladder.

The occasional occurrence of islets of hepatic tissue in the periphery of the perimuscularis suggests a possible relationship with the Luschka ducts. These islets are usually separated from the liver by a strand of connective tissue. They support Luschka's theory that the aberrant bile ducts are derived from the embryonic primordium of the liver. The Luschka ducts must not be confused with the out-pouchings of the gall bladder mucosa which are often found in chronically inflamed gall-bladders and which were first described by Rokitsky in 1842 and re-described by Aschoff in 1905.

### HISTOLOGY

The ducts of Luschka have a characteristic wall which has the same structure as the intra-hepatic ducts. The lumen is generally less than 0.3 mm. in diameter and is lined by columnar epithelium somewhat lower than that in the gall bladder mucosa. The epithelium is surrounded by a cellular connective tissue layer, rich in circularly arranged white connective tissue fibres.

### INCIDENCE

The following series was reported by Béla Halpert:

Number of gall bladders examined	Number of cases in which true Luschka ducts were found.
10 embryos and fetuses ranging from 25 to 370 mm.	None
10 infants aged 1 month to 9 months.	5
120 patients aged 16 to 75 years in which the gall bladders had been removed surgically.	1

It must be pointed out that gall bladders of the prenatals and infants were examined in their entire length, some of them cut serially. However, in the surgical cases, in about only 100 cases was there a definite plan or system applied in selecting the part of the gall bladder taken for microscopic examination.

Between 1923 and 1925 Halpert and Malloy examined a further series of gall bladders removed surgically. The available material of the Pathological Laboratory of the Boston City Hospital was utilised. Of 300 gall bladders removed, they selected about 200 which did not show post-mortem changes. True Luschka ducts were seen in nearly 10 per cent. The discrepancy between the two series is difficult to explain.

#### DISCUSSION

From the above, it is seen that the percentage of patients in whom the aberrant Luschka ducts may be present is not known exactly. In one group they were present in about 0.8 per cent. of the adult patients, and in the other they were present in about 10 per cent. Also, there appears to be an increased incidence in infants, but the significance of this is uncertain since only 10 infants' gall bladders were examined in the series. Nevertheless, even if we take the smaller figure, namely 0.8 per cent., it is a high percentage of patients in whom there is a risk of leakage of bile after cholecystectomy. Haberland, in 1925, was one of the first surgeons to draw attention to the practical significance of the ducts of Luschka. He reported that he had been rather puzzled as to why unexplained leakage of bile occurred in some cases after cholecystectomy. He was convinced that the leakage was not from the stump of the cystic duct and this led him to investigate the matter further. He demonstrated by X-rays of human cadavers (after the injection of opaque material into the bile

ducts) the existence of branches of the intra-hepatic bile ducts which ran into the subserosa of the gall bladder. Quite clearly, these are identical with the aberrant ducts originally described by Luschka.

#### CONCLUSION

These aberrant bile ducts are very unlikely to be detected during the course of a cholecystectomy operation. They can be the source of a biliary leak which will lead to biliary peritonitis or localised biliary abscess, and this in turn can lead to other unwelcome complications. Most surgeons therefore consider it wise, if not imperative, always to drain the region of the gall bladder bed after cholecystectomy however dry it may appear to be. The possible presence of ducts of Luschka should never be overlooked.

#### ACKNOWLEDGEMENT

I should like to thank Mr. A. H. Hunt for his invaluable help. I should also like to extend my thanks to Mr. Cull, the Medical Artist, and the Dept. of Medical Photography for their help in preparing this article.

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## THE CITY OF LONDON BATTALION

by J. A. PARRISH

DO you know the name of the church outside Bart's across from the Old Bailey? Have you ever visited the Tower of London?

St. Sepulchre's, the Tower and Bart's have a common link with the Royal Fusiliers. Since 1957, the City of London Battalion of the Royal Fusiliers (T.A.) has had an R.M.O. from Bart's; St. Sepulchre's is their City church and in it hang the regimental battle honours. Each year on Remembrance Sunday, the Fusiliers have a march-past along Holborn and a service in the church, and those on duty at the hospital on that weekend may have

heard and seen something of this.

#### The Formation of the Regiment

On 11th June, 1685, King James II authorised Lord Dartmouth, who was Master-General of Ordnance and Constable of the Tower of London, to raise a regiment from two independent companies which had for a long time formed the Garrison of the Tower, and from ten companies drawn from the Trained Bands of the City. This new regiment, the 7th of the Line, was to be raised as an Ordnance regiment, its duties being the protection of the guns of the Artillery. It was

to be armed with a new type of flintlock musket known as a "fuzil", and as the regiment was the first of its kind in the English service, the King named it "Our Royal Regiment of Fuzileers".

#### The City of London Battalion

This battalion was first raised in the City in 1859 as Rifle Volunteers; in 1883 it was renamed the 1st Volunteer Battalion Royal Fusiliers and adopted the badge and uniform of that regiment. Until the end of Queen Anne's reign (1714) all guns had stamped on them the Royal badge of the Union Rose surmounted by the Crown, and this was the first badge of the Royal Fusiliers. (Two of these early guns, with the rose surmounted by the Crown stamped on them, may now be seen on the steps leading to the Fusilier Museum.) In 1751 the Union Rose was incorporated within the Garter, and this, with the Crown over it, has been the badge of the Regiment ever since.

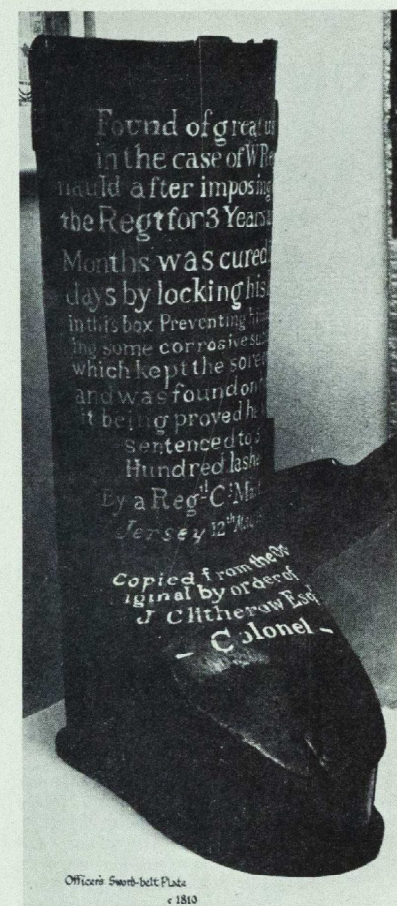
This began the association of Volunteers with Regulars and many served together in the 2nd Battalion R.F. in the South African War. In 1908 it was renamed the 1st (City of London) Battalion, the London Regiment R.F. This lengthy title was abbreviated to the 1st Londons and under this name fought in the Great War.

In 1937 the title was changed again to the 8th (1st City of London) Battalion R.F. and as such fought in the World War in North Africa and Italy as part of the 56 London Division.

In April, 1961, as a result of the reorganisation of the Territorial Army, 624 Light Anti-Aircraft Regiment R.A. (R.F.) T.A., which had itself before 1947 been the 9th Battalion R.F., was amalgamated with the 8th Battalion to form what is now the City of London Battalion, R.F. (T.A.).

The battalion has its Headquarters at Balham with companies at Streatham and in the Tower of London. The regimental headquarters are also at the Tower, and there the Fusiliers opened to the public in November the Fusilier Museum which is of considerable interest and an additional attraction to the Crown Jewels and the Bloody Tower.

One of the pieces from the museum is shown in the photograph and suggests that the army was a little more definitive in its treatment of malingering in 1808 than we are over a century later in M.O.P.'s, and with the vogue for resurrecting old techniques may yet be made use of by our dermatological colleagues.



Inscription on boot:—

"found of great use in the case W. Reginauld after imposing on the Regiment for 3 years and 6 months was cured in 12 days by locking his leg in this box preventing him applying some corrosive substance which kept the sore open and was found on him—it being proved he was sentenced to 5 hundred lashes by a Regimental Court Martial. Jersey, 12th May, 1808."

## COMMENT

### TIME OUT OF BART'S ?

THE other day I went up to the wards hoping to examine a few patients. On the first ward that I visited, I was told by the Sister that only students on the firm were allowed to examine patients. My first reaction was one of indignation, but this abated when I was told that the patient I wished to examine had been seen by fifteen students already. In fact this incident, although an extreme example, served to illustrate to me one of the limitations of a teaching hospital, that there are simply not enough patients to go round.

Apart from this, another disadvantage of a teaching hospital is that it is not very common for a patient admitted as an emergency to be seen on admission. This is mainly due to the fact that only a third of the day is spent in the hospital, and much of this time is already filled with lectures and ward rounds. As a result, common conditions, such as bronchopneumonia, myocardial infarction and acute abdomens are not seen until the signs and symptoms have been modified by treatment or operation.

One solution to these difficulties is that more time should be spent in hospitals other than the teaching hospital from which the student qualifies. This would enable him to see many of the commoner complaints and emergencies and would also give him a chance to gain considerable confidence in his ability to appreciate physical signs. He would be given more responsibility and would be made to feel more a part of the medical team. Furthermore, as only one or two students need be resident at one time, the medical staff would be able to give far more individual help with the students' problems.

Bart's students already spend some of their clinical training in other hospitals. At pre-

sent two months' midwifery and two weeks' surgery are the most that can be spent in this way. This may be more if the student is lucky enough to have a revision period. Surely it would be possible to make room in the present curriculum for a further four to six weeks, perhaps arranged something on the following lines: two weeks' orthopaedics during the specials appointment; one or two weeks in a fever hospital during the childrens appointment; and two weeks during second-time medicine. Alternatively, rather than split this time up it could be taken as a four to six week elective period. These are merely suggestions and others may have different ideas as to how this time should be spent.

Apart from working in other hospitals, every student should be given the chance to spend a week in general practice. At present it is only possible for him to do this during his holiday periods. This week could well replace the week spent visiting Bethnal Green during the childrens appointment. Rather than talking about the child in relation to his environment, it would be possible to visit the child in his own home, surely a far better way of studying the subject.

The function of the teaching hospital is to teach, and this it does by means of lectures and ward rounds. But the non-teaching hospital, because of its relatively greater number of patients, is more suitable for gaining clinical experience. Most students find the time spent outside the hospital one of the most interesting parts of their clinical training, and at other hospitals schemes similar to the one suggested above are already in operation. Surely it is time that Bart's students were able to do likewise ?

E.M.H.

## SPORTS DIARY

### March

- March 2 Rugby 1st XV v. Streatham (H).  
Rugby A XV v. London Irish (H)  
Soccer 1st XI v. Trinity Hall, Cambridge (H).
- March 5 Swimming Team v. University College.
- March 6 Soccer 1st XI v. Charing Cross Hospital (H).
- March 7 Swimming Team v. Northampton College.
- March 9 Rugby 1st XV v. Aldershot Services (A).  
Rugby A XV v. Radcliffe Infirmary (A).  
Soccer 1st XI v. College of Estate Management (H).

### Editorial

For the past month (January), practically all outside sport has had to be cancelled. This has meant a dedicated effort by the keener team players to indoor training and practice. Glowing reports from students using the "re-conditioned" gymnasium suggest that the work put into the scheme has been very worthwhile. The gym provides the Rugger Club with cover for team training; their fitness will be needed particularly for their postponed Cup Match when the pitches are playable again.

One of the few clubs that continues to flourish despite the atrocious weather conditions is our Cross-Country team. They have run so well—better than ever this season—that the name of Bart's is genuinely respected by opposition not only from the London Colleges, but also from teams as far afield as Ireland. On 2nd February, Bart's excelled themselves in the United Hospitals' Cross Country Championship. They retained the Kent Hughes Cup by a greater margin than ever before. N. Pott achieved something of an ambition by beating a former American distance champion from St. Mary's, and is to be congratulated.

Another highly successful Club at Bart's has been our Canoe Club. S. Phillips, C. Evans, and B. Watkin have distinguished themselves against National and International opposition and succeeded in winning two National Titles,

- March 12 Squash Team v. Escorts (H).  
Swimming Team v. Imperial College.
- March 13 Rugby 1st XV v. Public School Wand. (H).  
Soccer 1st XI v. London Hospital (A).
- March 16 Rugby 1st XV v. Loughborough College (H).  
Rugby A XV v. City Police (H).
- March 19 Squash Team v. Jesters (H).  
Swimming Team v. King's College.
- March 23 Rugby 1st XV v. Oxford (A).
- March 26 Squash Team v. Staff (H).
- March 30 Rugby 1st XV v. Treorchy (H).  
Rugby A XV v. Royal Dental College (A).

plus numerous Class events at meetings throughout the country. G.H.

### SWIMMING CLUB

#### United Hospitals Water Polo League

In the final positioning at the end of the season the 1st team found itself once again second to St. Mary's in the first division. This, although a creditable position, leaves much to be desired for St. Mary's were much weaker this year than previously and we should have beaten them. Our failure to do so merely reflects a certain lack of training and an almost certain lack of enthusiasm. Every other hospital team was successfully beaten, although we had hard matches with Guy's and The London.

The five-a-side arrangement worked to our advantage with the second team, as it is much easier to find two teams of five reasonably experienced players than, say, six or seven. The second team put up a good showing, although they were unfortunate to meet several hospitals only entering one team and as a consequence were soundly beaten. Again more enthusiasm coupled with training would be well rewarded.

The term has therefore been reasonably successful for the club, but we look forward to putting up a much better show in this term's University League.

## CANOE CLUB REPORT

The Canoe Club have just finished their first full year and can look back on the season with satisfaction, having won two National titles and finished runners-up and third in two other National events. Apart from their racing successes, a number of students have been taught the elements of watermanship and safety in a boat and several Freshmen have come on very well.

In the early part of the long-distance racing season, S. Phillips dominated the Class 3A field, winning at Bedford and Twickenham. In the latter race J. Flatman, a relative newcomer, gained a good second.

C. Evans and B. Watkin, after a mixed early season of "seconds" and "thirds", won their last five doubles races. They finished up by beating the Northern and Midlands crews in the London River race over twenty one miles (during M.B. finals!), thus winning the National Class 7 title. In the sprints B. Watkin won a British title during the canoe championships at Boston, paddling number four in the 10,000 metres Royal Canoe Club K4; he was also runner-up in the 1,000 metres at the same meeting. Together with C. Evans he paddled to third place in the British K2 10,000 metres.

The Club entered all the major regattas, including the International on the Serpentine, and now owns three excellent long-distance racing canoes. New members are very welcome, and with some hard winter training should meet with success in the coming summer. Bart's Canoe Club is now well established at National level.

## RESULTS

### Long Distance :—

Oxford—2nd Class 5; 3rd Class 4A.  
Twickenham.—1st and 2nd Class 3A; 4th Class 5.

Bedford—1st Class 3A.  
Poole—3rd Class 6A.

Worcester—2nd Class 6A.

Chelmsford—1st Class 7A (New Record).

Bath—1st Class 7A (New Record).

Exeter—1st Class 7A.

Midlands—1st Class 7A (New Record).

London River—1st Class R2M.

### Sprints :—

Royal C.C. Regatta—1st K4; 3rd K2.

Richmond Regatta—1st K4; 2nd K1.

Birmingham Regatta—2nd K4.

Sunbury Regatta—1st Relay; 2nd K4; 3rd K2.

Teddington Regatta—1st K2; 1st K4.

Isleworth Regatta—1st K2.

## CROSS COUNTRY REPORT

### Wednesday, 28th November. University League I at Mitcham.

Before this, the third League match, Bart's were lying second to University College with King's College, who were our hosts for the day's race, next behind us. We were without our captain, P. Littlewood, who was ill, and we were therefore anxious about the outcome of the race.

The course was extremely flat, quite fast and offering various prospects of the local gas-works, industrial estates and railway sidings. The leading bunch of five runners ran off course since there were no King's men with them, but they rejoined the field and ran through it to maintain their position.

J. Farrington and P. Yates of U.C. won. Bart's places were T. Foxton, 4th, D. S. Tunstall-Pedoe, 6th, N. Pott, 8th, then a long gap with R. Thompson, 24th, R. Pickard, 41st, and F. Hardy, 45th. This race illustrated the fact that to have three men in the first ten does not help your league result as much as having five men well up. King's beat us in this league race, but not by a sufficiently wide margin to overtake us in the league aggregate.

### Saturday, 5th January. U.H. Club Handicap. 5½ miles.

This race was held at Barnet with a foot of snow on the ground. P. Littlewood was back marker with N. Pott and T. Foxton thirty seconds in front and other runners stretched out to a maximum of seven minutes ahead—a formidable gap to close.

As the faster runners came through, the competition became keener, whilst the front markers, still in the lead with only a mile to go, were spurred on to efforts they would never make at the back of the field. However, on the long ascent through to Hadley Common, with the deep snow sapping everyone's strength, Pott and Foxton ran through to beat the Handicapper and snatched a close victory from Fielding of the Middlesex.

### University of London Cross Country Club Dublin Trip. 12th and 13th January.

P. Littlewood (U.L. C.C.C. captain) selected T. Foxton and D. Tunstall-Pedoe to go to Dublin with London University Cross Country team. London University were supposedly running cross country against Clonliffe Harriers on the Saturday and then in a Road Race on the Sunday.

We arrived in a Dublin free from snow only to wake up on the Saturday morning to find it three inches deep. For the thirty minutes

previous to the cross country race there was a blizzard. The "Clonliffe selected team" contained a small minority of actual Clonliffe men so that London University were running against an Irish representative team—in fact, according to one official "all the boys who aren't in England". Not surprisingly London lost the match. Bart's places were P. Littlewood 7th, T. Foxton 11th, D. Tunstall-Pedoe 17th. The snow continued, so the much publicised road race was cancelled. However, as Eire Television had been going to film it, we were asked to assemble at the Santry Stadium. This, the track where Elliot broke the world mile record, was under three inches of snow.

It was decided to run a 20-minute *Parlanf* (2 runners run a continuous relay, sharing the running as they think best; the pair running the greatest distance wins) and a Bart's combination, P. Littlewood and D. Tunstall-Pedoe, convincingly beat the Irish and the other London University pairs by some two hundred yards. This was much too complicated for Eire Television, so the moment the *Parlanf* finished an official announced, "All right boys, now let's have a half-mile race for the cameras". After ten minutes' respite, with the camera accompanying the runners on a car driven around the track, the half-mile field set off.

D. Tunstall-Pedoe led for the first three hundred yards, lay second until the final bend and then struck in the home straight to win by a yard in 2 min. 17 secs.!

Having satisfied Eire Television, the team devoted themselves to draught Guinness and Irish Coffee (the best way of taking Irish whisky).

### Wednesday, 23rd January. St. Mary's Hospital Hyde Park Road Race.

This annual road race is open to all the teaching hospitals in London. Being the first road race of the season it usually provides a valuable guide to the coming season's form. This year, however, the weather had turned it into one long 5½-mile skate.

The race was won by L. Steiglitz, ex-U.S.A. 10,000 metres champion (St. Mary's), with Bart's packing 2nd, 3rd and 4th and having six men home in the first ten.

Individual performances were not taken seriously—either you can skate or you blame your footwear—but Pete Littlewood did well to come second to Steiglitz and Bart's were happy to retain the cup with such a clear-cut victory.

### Saturday, 26th January. Queen Mary College Invitation 7½-Mile Championship at Dytchleys, Essex.

This race, usually over thick clinging plough, is reckoned one of the toughest in the fixture list. It attracts University teams from all over the country and there is a separate trophy awarded for the best London College—until this year the possession of either University College or Imperial College. Bart's were without R. Pickard, one of our reliable scoring men and a great asset when the going is slow, but when we arrived at Dytchleys we found that University College were without three of their best men. So having chased University College in the League and in the University Championships, this seemed to be our chance to beat them.

The plough was frozen solid with loose snow in the furrows, whose depth was therefore hidden. At the start N. Pott and T. Foxton led, with P. Littlewood and D. Tunstall-Pedoe well up. After a mile and a half we hit the frozen plough. Whilst others stumbled and cursed, Terry Foxton cruised over it like a hovercraft, chased by P. Littlewood and the Cambridge University Secretary, Heron. On the next bit of road the field closed up on the leaders again, but on repeating the two-mile circuit of plough and road Foxton and Littlewood broke away and Foxton, running the race he has deserved for the whole season, opened up a gap over some loose snow and went on to win with Littlewood seven seconds behind him. N. Pott, who had been in bed for two days with a septic toe in the previous week, did not have the speed for the final 1½ miles of road but finished 8th. D. Tunstall-Pedoe lost a lot of places on the plough, made up some of them on the road only to develop cramp and finish 33rd. R. Thompson ran very well to take 56th place in a large field and F. Hardy and R. Sanders ran well to finish 78th and 82nd respectively.

Scoring six men per team the results were:

1. Leeds University	...	...	90
2. Sheffield University	...	...	94
3. Oxford Tortoises	...	...	151
4. St. Bartholomew's Hospital	...	...	178
5. University College	...	...	235
6. Sandhurst	...	...	252
7. King's College, London	...	...	293
8. Imperial College, London	...	...	298
9. Guy's Hospital	...	...	417

Winner of the John Banks Trophy for London Colleges :—

St. Bartholomew's Hospital

Thus we collected a new trophy and since Foxton, Littlewood and Pott all ran so well, they will be competing for London University over the same course in the Universities Athletic Union Championships on 9th February.

#### United Hospitals Cross Country Championships for the Kent Hughes Cup. 2nd February, 1963.

After their victory in the Queen Mary College 7½ the previous week, Bart's cross country team were in no mood to trifle with the Hospitals Championships over 5 miles of snow covered woods and common at Barnet. The question was not whether Bart's would win, but by how much; and who would win the individual race.

Under normal conditions, L. Steiglitz (St. Mary's), the ex-U.S.A. 10,000 metres champion, who has run a mile in 4 mins. 4 seconds, would have been the unquestionable favourite, but with several inches of snow on the ground the "savants" were "putting their money" on powerful Nick Pott.

Pott, wearing spiked shoes over the icy course, broke away after Cockfosters Hill and went on to win by more than half a minute. L. Steiglitz, after making a slight detour off the unmarked course, came in just in front of P. Littlewood, the winner of last year's race. With T. Foxton next in 4th position, D. Tunstall-Pedoe 6th and R. Pickard 9th, Bart's 5 scoring men were all home.

It must be disappointing for runners such as F. Hardy (11th), R. Sanders (16th) and R. Hale (26th) not to score when even St. Mary's in 2nd place went down to 22nd for their 5th scoring man. Bart's cross country prowess is such that if this championship race had been St. Bartholomew's Hospital versus the rest of U.H., we would have won (scoring 7) by 50 points to 56; and this without R. Thompson, one of our most promising runners, who was ill.

#### Results

	mins.	secs.
1. N. Pott (Bart's) ...	31	50
2. L. Steiglitz (St. Mary's) ...	32	35
3. L. Littlewood (Bart's) ...	32	40
4. T. Foxton (Bart's) ...	32	55
5. J. Brotherhood (St. Thomas's) ...	33	15
6. { D. Tunstall Pedoe (Bart's) ...	33	43
{ A. Napier (Charing X) ...	33	43
9. R. Pickard (Bart's) ...	35	25
11. F. Hardy (Bart's) ...	35	47
16. R. Sanders (Bart's) ...	36	46
26. R. Hale (Bart's) ...	38	40
39. A. Lewis (Bart's) ...	41	56

#### Teams

1. St. Bartholomew's Hospital: 1-3-4-6-9=23
2. St. Mary's Hospital: 2-8-10-12-22=54
3. Guy's Hospital: 13-14-17-23-24=91

#### GOLF CLUB REPORT, 1962

The season, in retrospect, proved to be one of considerable success for the Hospital Golf team. The first team played through three rounds of the Hospitals Cup to reach the final which we lost three games to two. The match was played at Sunningdale against St. Thomas' Hospital and the Cup was lost on the 18th green—two matches being all square at the 17th. It is fair to say that we were unlucky to lose both these matches on the last green. The other Cup matches were played against London Hospital and Guy's—the latter suffering a humiliating defeat by 5 games to none. The following people have played in the Cup team through the season: T. Stephenson, J. Miller, J. Waller, J. Rush-ton, F. Miller, S. Thomas, T. Coltart, and C. Richards—Stephenson, the Captain, played very well and won all three matches.

The other fixtures during the season were enjoyed by all. The team fielded was not always the strongest, due to examinations and other commitments.

Played 8. Won 3.

A debatable defeat was inflicted by the staff at Denham and this year's fixture is eagerly awaited. Mr. Hankey's team also defeated us despite the fact that we were strengthened by the inclusion of two members of the staff, Dr. P. Borrie and Mr. J. O. Robinson.

#### MEN'S HOCKEY CLUB

Cup Match v. St. George's & R.D.H. Result 1-1 draw, abandoned. Played at Chislehurst, 12 Dec., 1962.

As a result of the late arrival of the opposition, this match was started half an hour late on a dark December afternoon. An added handicap to the playing of good hockey was the fact that St. George's had been unable to find a neutral umpire and had press-ganged a member of their Ladies' team to officiate. Thus, with some misgivings, the game was begun.

After 10 minutes of Bart's pressure, St. George's scored a lucky goal, when a shot from outside the circle hit a post, the rebound being pushed into the net by one of the

opposing forwards. Bart's had the better of the rest of the half and deservedly drew level just before half-time with a shot from a long corner.

The interval was waived as a result of the imminent darkness. In the second half St. George's did most of the attacking and only some surprisingly agile goalkeeping by S. Phillips prevented them from scoring. The Bart's forwards were seeing very little of the ball. As the sleet, which started soon after half-time, soon became a veritable snowstorm, nobody saw very much of it!

It now became almost impossible to play decent hockey and both life and limb were in danger. The two captains therefore agreed to abandon the game some 15 minutes before the end, deciding that discretion was the better part of valour.

We would like to thank Laurie White for his preparation of the pitch, which remained in good condition despite the weather. Our lady umpire did her job well and deserves our congratulations for not allowing some bad language to colour her judgment of the game.

Because of the inclement weather, the replay has now been postponed three times and the chances of playing in the near future seem

pretty slim at the time of writing. Thus it may be necessary for the result of this match to be decided by a panel of experts. We would welcome volunteers.

Team: S. Phillips, J. Harrison, A. C. Robertson, P. W. Caine, R. S. A. Thomas, T. Billington, M. Nightingale, A. Bateman, D. Glover, H. Da Silva, A. Edleston.

#### BOOK REVIEWS

**Principles of Chest X-ray Diagnosis.** Second edition, by George Simon. Butterworths, London, 1962.

The second edition of George Simon's book on the radiology of the chest appears six years after the first, and a very welcome sign it is. Written primarily for aspiring radiologists and chest physicians, it contains systematic descriptions of the various radiological appearances with which we are all familiar, for example homogeneous opacities, ring and linear shadows. These are then considered in terms of differential diagnosis. Students may find the arguments a little heavy going at times, but the book has much to offer them. The illustrations are accompanied by short case histories and present little clinico-pathological problems in themselves. Many intra-thoracic disorders are particularly amenable to radiography, such as calcification of the pericardium and diaphragmatic herniation of the stomach, and the illustrations form useful starting points for further study.

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A New Book  
for Bart's Men  
— by Bart's Men

Aids to **SURGERY**

By Michael Harmer, M.A., M.B. (Cantab.), F.R.C.S. (England). Surgeon to the Royal Marsden Hospital and the Institute of Cancer Research, Paddington Green Children's Hospital and St. Andrew's Hospital, Dollis Hill. Sometime Chief Assistant on the Pink Firm;

and G. Maurice Lunn, M.A., M.Chir. (Cantab.), F.R.C.S., (England). Surgeon to the Metropolitan Hospital, St. Leonard's Hospital, and St. Andrew's Hospital, Dollis Hill. Sometime Chief Assistant on the Green Firm.

One of the senior titles in the Students' Aids Series *Aids to Surgery* provides the essentials of surgery in handy concise form for use by medical students as an aid to their studies, and a summary of surgery for those who may have need for a quick reference.

The introduction and first four chapters deal with the general aspects of the subject and the remaining twenty-two chapters cover the surgery of various regions and systems of the body. This edition has been considerably revised to take into account recent progress and certain portions of the previous edition have been omitted. New sections have been included on fluid balance, burns, chemotherapy, and the chapters on cardiovascular surgical conditions, head injuries and the bladder and prostate have been rewritten so that the entire book is as up-to-date as possible.

9th Edition 360 pages. 26 illustrations. 13s. 6d.  
postage 1s.

**Baillière, Tindall & Cox**

7 & 8 Henrietta Street, London, W.C.2

St. B.H.J., February, 1963

Here is a book which may profitably be opened by any of us. George Simon, who has made significant contributions to the subject himself, realises the difficulties in radiological interpretation, and insists that detailed and factual descriptions of shadows must precede diagnostic conclusions. If the book does no more than bring home this point to its readers it will have served its purpose, but it contains far more than that. Indeed, it is a survey of diseases of the chest seen from the viewpoint of an eminent radiologist.

**Dr. Timothy Bright, 1550-1615. A Survey of his Life with a Bibliography of his Writings** by Sir Geoffrey Keynes. London, Wellcome Historical Medical Library, 1962. Pp. 47. 21s.

This book, which begins a new series of publications by the Wellcome Historical Medical Library, is a beautifully produced but slight addition to the canon of Sir Geoffrey Keynes's bibliographical writings. Bright was physician to Bart's 1585-91, an incidental achievement compared with his contribution to "shorte, swifte and secrete writing" or shortland *Characterie*, 1588, and his chief medical work *A treatise of melancholie*, 1586, which remained for more than two hundred years the only book on psychiatry by a physician to a London teaching hospital until Sir Alexander Crichton's *An inquiry into the nature and origin of mental derangement*, 1798. It may even have been known to Shakespear since some scholars see similarities between it and certain passages in *Hamlet*; and with Andreas Laurentius' *Discourse of . . . melancholike diseases*, 1599, takes its place as the immediate precursor of Robert Burton's classical *Anatomy of melancholy*, 1621. It is of interest that among Bright's lesser writings is a small piece "De Traduice" which forms a chapter in a volume published at Marburg in 1590 entitled *Psychologia* (No. 21 in this bibliography) but unfortunately Sir Geoffrey tells us nothing of its content nor how Bright came to write it. R.H.

**How to Live with Your Heart** by Dr. G. Barry Carruthers. A doctor explains. . . . Evans Brothers Limited, 10s. 6d.

I wouldn't show this to a heart patient. It doesn't hold out a hand—it's a hypochondriac's paradise; every symptom and fearful complication avuncularly explained, from the wily spirochaete to congestive failure. That said, what is projected is done well (though vaguely marred by the jolly corpuscle approach)—but for whom? No, as I say, for someone living with their hearts, not for Joe Bloggs, either—despite the Orphean Cook's tour that introduces the stupendous C.V.S. More a lightweight symposium than a fireside chat (selectively read, perhaps, a good primer for introductory students), this is a book of prophylaxis for the converted layman—a regrettably scarce species. The cover smacks of Charing Cross Road, which is a pity. M.P.S.

**BOOK RECEIVED**

G. Kersley, "The Rheumatic Diseases", 4th Edition.

# ST. BARTHOLOMEW'S HOSPITAL JOURNAL



Vol. LXVII, No. 3

MARCH, 1963

## Editorial

At the end of January a Medical Weekend was held at Cumberland Lodge in Windsor Great Park, where thirty-four students met to discuss Medical Education with the Dean of St. George's Hospital, the Director of the National Foundation for Educational Research, a Professor of Medicine and a General Practitioner. Many subjects were discussed among the different groups, ranging from "The ambiguous status of the medical student, as seen both by himself and those studying a progressive and expanding discipline within an archaic and authoritarian framework", to "The attitude of senior nursing staff to women medical students". However, one of the most widely discussed topics was that of the liaison between staff and students; in some medical schools this is provided for by the existence of "Staff-Student Curriculum Committees". This system is found in only four of the London Teaching Hospitals and is more common in the provincial Medical Schools. During discussion it was found that

it worked effectively and that the system was useful to both students and staff. The representatives of Schools without it felt that this could prove a useful innovation, although in the case of Liverpool and Sheffield liaison on teaching matters was "so good that a Committee was unnecessary".

The whole question of the Medical Curriculum is being examined by a B.M.S.A. Committee, whose report should be ready by the end of the year, and it would be better that a Staff-Student Committee, if it should come into existence, be formed before this report is published. Those which are already in operation have proved useful from the point of view of both students and staff, and such a system could easily prove a success in Bart's.

## The Fountain

Ice finally melted from the Fountain, after coating it since Christmas, on 8th March. Both the Fountain and its attendant goldfish have survived their ordeal.

**Robert Foster Moore**

A Service of Remembrance for the late Robert Foster Moore, O.B.E., F.R.C.S., J.P., will be held in the Church of St. Bartholomew-the-Less, West Smithfield, on Friday, 5th April, at 12.45 p.m. An obituary will appear in the April Journal.

**This Issue**

Dr. P. J. Lindop, Ph.D., M.R.C.P., works in

**Engagements**

HILL.—TAUSZIG.—The engagement is announced between Dr. Anthony F. Hill and Julie M. Tauszig.

JORY.—SHEPHEARD.—The engagement is announced between William John Jory and Carolyn Shepheard.

**Births**

GRAY.—On 13th Feb., to Jill (née Hoyte), wife of Dr. Denis John Pereira Gray, a son (Peter John Pereira).

HOOKER.—On 28th Feb., to Copper (née Northey), and Dr. David Hooker, a son.

LEHMANN.—On 2nd Feb., to Julia (née Williams), and Dr. Nigel Lehmann, a daughter (Amanda Tracy).

**Deaths**

MARSHALL.—On 26th Feb., Eric Stewart Marshall, C.B.E., M.C. Qualified 1906.

NICHOLAS.—On 18th Feb., Cecil Francis Nicholas, M.R.C.S., L.R.C.P. Qualified 1903.

RENWICK.—On 16th Jan., Robert Renwick, M.R.C.S., L.R.C.P., aged 41. Qualified 1946.

SCOTT.—On 2nd Nov., 1962, Aleck Lauriston Scott, M.R.C.S., L.R.C.P., Lieutenant-Colonel R.A.M.C. Qualified 1898.

THURSTON.—On 17th Jan., Lionel Victor Thurston, D.S.O., M.R.C.S., L.R.C.P. Qualified 1904.

WATKYN-THOMAS.—On 31st Jan., Frederic William Watkyn-Thomas, F.R.C.S. Qualified 1914.

WESTERMAN.—On 8th Jan., Arthur Westerman, M.D. Qualified 1900.

WILSON.—On 3rd Feb., Philip Frederick Wilson, M.B., B.Ch., aged 79. Qualified 1911.

**Appointments***Royal College of Physicians.*

Dr. E. R. Cullinan was re-appointed as college representative on the Metropolitan Regional Medical Recruitment Committee for 1963 and 1964.

The following candidates were elected to membership: D. A. Birkett, B. P. Harrold, M. J. L. Patterson, T. W. E. Robinson, D. C. L. Savage.

*Royal College of Surgeons of England.*

Mr. H. Jackson Burrows was appointed the Robert Jones Lecturer for 1963.

**Monday, 15th April**—Matter for the May Journal should be sent to the Editor by this date.

the Radiobiology Unit at Charterhouse, and has published papers on the "Ageing Effect of Ionising Radiations" and on "Protection against Radiation Effects by Hypoxia."

Mr. E. A. J. Alment, M.R.C.S., L.R.C.P., M.R.C.O.G., is Consulting Gynaecologist to the Northampton and Kettering Group of Hospitals.

D. Dunn is in his final clinical year.

**Change of Address**

Dr. S. Shere,  
1, Hermitage Lane,  
Barming,  
Maidstone, Kent.

Dr. A. G. Dawrant,  
2, Rossett Holt Grove,  
Harrogate, Yorks.

Dr. W. B. Jepson,  
The Old Cottage,  
Hollingbourne,  
Maidstone, Kent.

Mr. J. E. Gerard-Pearse,  
"Cliff Edge",  
Belle Vue Road,  
Weymouth, Dorset.

Dr. S. D. Sturion,  
c/o C.M.S.,  
6, Salisbury Square,  
London, E.C.4.

**Calendar****APRIL**

Sat., Sun. 6 & 7 April: Dr. A. W. Spence  
Mr. E. G. Tuckwell  
Mr. W. D. Coltart  
Dr. Ian Jackson

Sat., Sun. 13 & 14 April: Prof. E. F. Scowen  
Prof. G. W. Taylor  
Mr. H. Jackson

Sat., Sun. 20 & 21 April: Mr. T. B. Boulton  
Dr. R. Bodley Scott  
Mr. Alan Hunt  
Mr. J. N. Aston  
Mr. F. T. Evans

Thurs., 25 April: Abernethian Society, 5.45 p.m., Dr. H. V. Dicks, "Psychology of Marital Tension".

Sat., Sun. 27 & 28 April: Dr. E. R. Cullinan  
Mr. C. Naunton  
Morgan  
Mr. W. D. Coltart  
Dr. R. A. Bowen

Physician Accoucheur on duty for the month of April is Mr. G. Bourne.

**THE FIRST BLUE UNIFORM**

by NELLIE J. M. KERLING (Archivist of St. Bartholomew's Hospital)

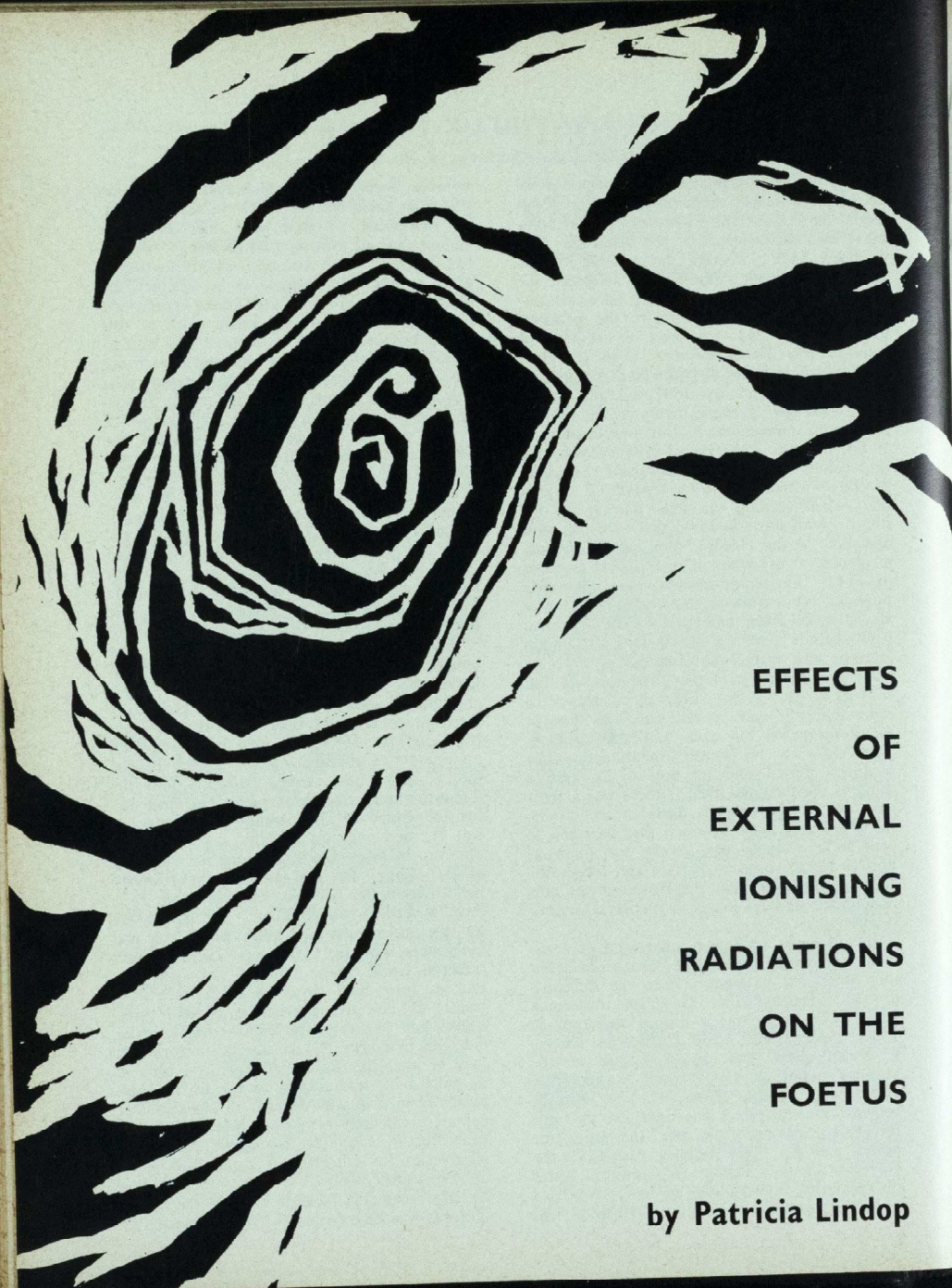
IN 1539 the suppression was ordered of all religious houses and institutions in England. As a result the Priory of St. Bartholomew was surrendered to the King on 25th October, 1539. Though the position of the Hospital was not immediately affected, the situation must have become very uncertain until the King finally listened to the petitions of the Mayor and Aldermen of the City of London. On 27th December, 1546, the Hospital was granted to the City and in the next month on 13th January, 1547, a Letter Patent was issued giving every detail of the organisation and endowment of this new institution.

The minutes of the Board of Governors now responsible for the Hospital, show the many problems which had to be settled. It is evident when reading the first Journal of this Board which starts in 1549, that in many ways discipline in the Hospital was lacking, owing, no doubt, to the years of uncertainty previous to 1547. The rules for the new institution provided for a Matron and eleven sisters who all had to be given material for their uniforms. From details given by the Bishop of London after he had visited the Hospital in 1316 we know that the sister at that time was wearing a dress of grey cloth. There is no reason to think that this was altered until the time of the Reformation but after 1547 this original grey cloth is no longer mentioned. The medieval period and its institutions were a thing of the past and even if there was a remnant left of the original dress of the sisters, the Governors must have felt that they had to provide a suitable new livery for them as well as for the beadles, porters and other officials to emphasise that the Hospital was now re-founded and no longer a medieval organisation.

It will never be known what kind of arguments were used during the discussions about this topic, but it appears from the Accounts of the Treasurer that Governor Alderman John White, who was a draper, delivered in 1549 "russet frieze" cloth for liveries. Frieze, a Welsh cloth, was generally one of the cheaper materials and "russet" apparently refers here to the colour, that is reddish-brown. This material was used for the uniforms of the Matron, the cook, the butler, the porter and for eight beadles. In 1551 the Governors took a further step towards better discipline by ordering that all sisters who had served at least one year in the Hospital had

to wear livery, a rule which makes one think that they had become slack in that respect. In November of that year the Governors agreed that all officers had to wear "blue of Mr. White". Unfortunately no information is given in the first Journal as to whether the same Governor John White, draper, persuaded his fellow Governors to choose cloth of this colour because he had it in stock and wanted to sell it, or whether blue was chosen as being the most practical colour; but whatever the reason, draper John White sold to the Hospital blue cloth at seven shillings and four pence a yard for the liveries of the cook and the porter. The butler and the steward received cloth of the same price which in the Accounts of the Treasurer is called "of the new colour", which was presumably blue since all the officers were ordered to have this colour. Only for the Matron the Hospital purchased cheap red Welsh frieze which was only one shilling and ten pence a yard. Perhaps she did not fancy the new blue and preferred red, especially as it was so near Christmas.

The next time new material had to be bought Mr. White was no longer one of the Governors, he resigned in September, 1552, and instead Governor Sir William Harper, a merchant-tailor, sold blue cloth to the Hospital early in 1553. He may have delivered material of a slightly inferior quality or the prices may have come down, but the Treasurer must have been pleased to find that for the livery of the beadles and sisters he was charged only six shillings a yard instead of seven shillings and four pence for the cloth of Mr. White. For the Matron who obviously had to be better dressed, he paid seven shillings a yard to Sir William. Yet the colour for the sisters was not quite fixed, for two Governors who in 1554 were asked to buy material, could choose material "of suche colour as they shall thynk meate". The Accounts do not give particulars of their purchases and one does not know what was decided in that year for the sisters' uniform. It may be that the choice fell again on blue as so much of it was already in use in the Hospital. Even if it was decided to have another colour, it can only have been used for a short time, for in 1555 the Governors ruled that all liveries for officers and sisters had to be of the same colour. As the officers were already dressed in blue since 1551, the sisters' uniform was blue from that time onwards.



EFFECTS  
OF  
EXTERNAL  
IONISING  
RADIATIONS  
ON THE  
FOETUS

by Patricia Lindop

St. B.H.J., March, 1963

WE are living in an age of unprecedented technological advance and are using methods in medicine for the effects of which we must of course hold ourselves responsible. This applies not only to the use of nuclear energy or X-rays in diagnosis and treatment, but to all our practice. It implies a responsibility for all that we do which extends beyond the individual patient, whether it is by increasing the genetic load in the population by improving neonatal survival, or by increasing the economic load to the population by prolonging life into old age, without as yet prolonging full health. The possibility of adversely affecting the unborn child is of real concern, and we need to be aware of the relative advantages and disadvantages of any procedures which we adopt.

#### Biological effects of ionizing radiation

Ionizing radiation, in the form of X-rays,  $\alpha$  or  $\beta$  particles, whether it is from outside or inside the body, has the potential for producing biological damage in the tissue irradiated. The quality of the damage produced is independent of the physical character of the radiation, although the different sorts of radiation or particles have different quantitative effects.

Exposure of the whole body to radiation, e.g. to X-rays, in large enough doses can result in damage. Somatic damage is that suffered by the individual exposed, and evident in the tissues irradiated, but which is not handed on to the next generation. This somatic damage can be acute or long term, according to the time of onset of symptoms, which often depends on the size of the radiation dose. Acute effects are seen in man after whole body exposure over a short time period to doses of 200r or higher. Long term effects are exemplified by the induction of leukaemia or other forms of cancer, aplastic anaemia, cataracts or shortening of lifespan.

Another kind of damage, genetic damage, is due to the exposure of the potential gametes in the gonads. Normally, the offspring develops as a composite of the genetic information put into the original zygote by mother and father, but changes, or mutations, can occur in the chromosomes which may lead to defects in the offspring. Mutations may occur spontaneously in any cells capable of division, but certain substances or conditions are mutagenic and increase the number of mutations produced. Ionizing radiation is such a mutagen, and accounts for the genetic effects of radiation. Examples of mutations producing genetic effects are seen in some miscarriages, still

births, alteration of neonatal sex ratio, achondroplasia, diabetes mellitus, and many physically minor deformities or maldevelopments.

When considering the possible effects of foetal exposure to radiation we must therefore think of these three groups of potential injury, (i) the acute somatic, (ii) the long term somatic, and (iii) the genetic.

#### Special problems of the foetus

The foetus presents an entirely different problem with respect to ionizing radiation from the adult. The embryo presents a dynamic, ever changing and ever more complicated mosaic of cells. It exhibits a high radiosensitivity simply because it consists largely of differentiating and mitotic cells, and since our main criterion of radiosensitivity is the loss of the reproductive integrity of the cell.

Developmental deficiencies and teratologies can be produced by exposing the embryo to relatively low levels of ionizing radiation, but such conditions are not produced by exposing the adult, no matter what dose of radiation is used. For example, probably the most common embryological damage from radiation is microcephaly or deletions in the central nervous system, but these are never produced even at high levels of adult exposure.

At the same time, however, the embryo possesses unique powers of regeneration or reconstruction. From an early stage in development it possesses phagocytes which are active and ready to engulf and remove cellular debris and necrotic cells. With these out of the way, the remaining undifferentiated and undamaged primordial cells are called on by the "organism as a whole" to fill in the deficiencies as best they can, so that an embryo can be topographically apparently normal but reduced through cellular deletions. This leads to microphthalmia, microcephalia, stunting and other evidence of loss of formative materials. Yet the embryo and newborn may appear normal, though miniature or reduced. That it is not entirely normal can be demonstrated in cytological or histological analyses, behaviour tests and reduced lifespan.

Radiation exposure of the foetus does not produce anomalies which are peculiar to ionizing radiations. Similar results are produced as a foetal reaction to any insult. Of all external agents, however, ionizing radiations appear to be the most consistently damaging.

The genetic consequences of foetal irradiation present a problem different from the adult. It must be remembered that a damaged primordial germ cell of a 32 day old human em-

bryo gives rise to a very large number of damaged cells of the adult gonad, so that the latent effect of radiation exposure will be carried to all instead of a fraction of its surviving progeny.

#### Evidence of foetal damage in experimental animals

Every irradiation-produced anomaly in the human foetus has been experimentally produced in the mouse or rat embryo by X-irradiation at a comparable stage of development. This gives some justification for the extrapolation from the effects on these rodents to the human foetus, with regard to specific organ susceptibilities, with the proviso that any statement is prefaced with the word "probable". There is a difference in rate of development between mouse and man, so that the period of greatest radiosensitivity in the human embryo is greatly extended. The organ development during the first 65 days in man, i.e. up to an embryo length of 40.0 mm., can be equated with the organ development in the mouse up to 15½ days. It must be remembered, however, that as far as the radiosensitive neuroblast is concerned, there is no limited period of sensitivity. It is present from about day 25 in the human embryo (day 9 in the mouse) until sometime after birth.

In rodents, the results show that the pre-implantation embryos (to day 5) are very radiosensitive in that after an exposure to 200r from 43-83 per cent. die before 12 days, and the earliest embryos are the most sensitive. There follows a period from between days 6½-12½ when irradiation results in the highest incidence of malformations after birth. After day 13½ abnormalities are again difficult to produce, so that days 6½-12½ must be considered the most susceptible period for most organ systems. This corresponds to approximately the 14th-36th day-old human embryo.

Lower doses, e.g., 25r delivered to the fertilized but uncleaved embryo, i.e. ½ day old in the mouse, will cause 38 per cent. of the embryos to die in utero. 15r at 1.5 days, i.e. the 2-cell state, has been found to produce exencephaly in the mouse, showing that these dose levels are deleterious.

#### Evidence of foetal damage in man

Implantation of the human ovum takes place at about 10 or 11 days after insemination. Radiation sensitivity during this preimplantation period is not known since experiments cannot be carried out. In the human prenatal life the most radiosensitive period probably

occurs from conception up to about 40 days after implantation. It is now believed that an exposure of as little as 40r to the human embryo before day 28 might produce serious abnormalities. After day 40, higher levels of irradiation are necessary to produce a significant proportion of anomalies. Extrapolating from mouse data to the human embryo, there may be a danger of neurological damage at any day up to the first 40 days. Therefore pelvic X-irradiation of the female should be avoided where possible except during the 9 days after the onset of a regular menstruation. This suggestion, made by the workers in this field in 1952 (Russell, I. D., and Russell, W. L.) is quoted in the 1962 report of the U.N. Scientific Committee on the Effects of Atomic Radiation.

Apart from these extrapolations from animals there are some human data available on some of these points.

#### Effects of high doses

After about 40 days, gross teratologies are difficult to produce, although the sensitive neuroblasts and primitive germ cells can accumulate effects throughout gestation. Human data are now appearing in the literature, much of which is coming out of studies in Hiroshima and Nagasaki. It is becoming apparent that low levels of exposure may elicit functional changes which are difficult to measure, or somatic cell changes which may contribute to disease processes many years after exposure.

During the decade after the exposure of foetuses at Hiroshima and Nagasaki, it has been shown that in some cases there was a reduction in head dimensions with mental retardation. The closer the pregnant woman was to ground zero, the more apt was she to produce a microcephalic child, often with other evidence of stunting. Thirty-three children exposed in utero at Hiroshima had head circumferences statistically below normal, 24 of these were exposed between 7-15 weeks gestation. Mental retardation occurred in 45 per cent. of these children. There was a sex difference in these effects, in that the girls showed reduction in mean height, weight and head circumference, whereas the boys only showed reduction in head circumference. Exposure in the second half of the gestational period did not produce such effects. Neurological abnormalities were found in children exposed in utero when less than 2,000 metres from ground zero, but severe neurological anomalies, such as were found in rats and mice, were not produced. This may be due to the poor survival

of children so affected, because the above statements refer to a study of those children who survived up to 6 or 7 years. Such reports will be modified with time, because tests at 6 to 8 years old do not reveal irradiation effects which may not develop until adolescence or later.

The above are the results of local exposure to large doses, approximately 700r or more. But it should be mentioned that there have been reports of foetal irradiation without obvious sequelae, even though exposures were given of 900r at the 5th month, or 4790r during the period 90-112 days.

#### Effects of small doses

There have been reports of deleterious effects produced by low doses. Diagnostic X-ray examination of a pregnant woman at 4, 5 and 6 months was followed by delivery of a child with multiple deformities. A report in 1956 (A. Stewart et al, 1956) lists 168 similar cases, from radiotherapy or diagnostic X-ray, indicating that exposure within the 4th or 5th month had effects equivalent to that in the mouse at 10½ days. One of the problems of some of these severe foetal abnormalities is that they may not produce spontaneous abortion.

One field of foetal effects has received a lot of attention, namely the incidence and onset of the late sequelae of ionizing radiation when the embryo is exposed. It takes several years for cancer to become macroscopic in man after irradiation, and we do not know whether there would be the same long latent period when a more radiosensitive organ system of the foetus is exposed. It is important to evaluate the consequences of foetal irradiation as we do for adults, and to assess the incidence, for example, of leukaemia in childhood.

Alice Stewart and her colleagues reported in 1956, and confirmed in 1958, a higher frequency of prenatal X-ray exposure in those children dying of leukaemia or other forms of cancer than in the control groups. Since then several independent studies have either confirmed or contradicted these findings. The problem is that the relative risk might be so small that only very large statistical studies could demonstrate the presence or absence of an effect. Seven separate investigations have not found a statistically significant excess of cancer mortality in relation to prenatal X-ray exposure, but in none of these was the material large enough to be able to demonstrate the risk.

A recent study, however (MacMahon,

1962) has probably removed much of the controversy.

His study population consisted of 734,243 children born in and discharged alive from 37 large maternity hospitals in the States, in the years 1947-1954. The frequency of intrauterine X-ray exposure in the population was estimated by review of the records of a 10 per cent. systematic sample. Abdominal or pelvic X-rays were recorded in 10.6 per cent. of the single pregnancies in the sample. MacMahon then traced the children who subsequently died of cancer, and of these 15.5 per cent. had had intra-uterine X-ray exposure, the higher frequency of prenatal X-ray in the cancer cases being statistically significant.

Corrections were made for indirect association with birth order and other complicating variables and he finally estimated that cancer mortality was about 40 per cent. higher (relative risk 1.4) in the X-rayed than in the non-X-rayed population. This relationship held for the three major diagnostic categories, leukaemia, neoplasm of the central nervous system and other neoplasms.

The excess in cancer mortality in the X-rayed group was most marked at ages 5 to 7 years, at which time the relative risk was 2.0. The excess risk appears to be exhausted for leukaemia by age 8. The smallest risk in the first 5 years corroborates Stewart's findings. The assumption, however, of exhaustion of risk by age 8 may not be altogether true, since the latent period of other forms of cancer may increase the risk at a later age. A distribution of cases according to the number of films taken, shows a trend towards higher mortality in the more heavily irradiated, which was not statistically significant. There was no evidence of a dependence on the stage of pregnancy at the time of exposure.

MacMahon does not give an estimate of the dose to which the foetus was exposed, but by using the surveys of foetal exposures for similar types of examination over the same years in the United States, it is possible to estimate a mean dose of about 2 rads to the foetus. Using assumptions of a linear dose response relationship for the induction of leukaemia, the estimated doubling dose for leukaemia in the foetus at this dose rate is of the order of 6 rads, about one-fifth of that estimated in the 1958 U.N. report as the doubling dose for similar effects in the adult.

#### Genetic effects of foetal exposure

When we come to consider genetic effects, the foetal gonad doses from X-ray procedures

Type of examination	Mean gonad dose per examination (mrem)*	Genetically significant dose (mrem per year)	Percentage of total population genetically significant dose (total 14.1 mrem)
Obstetrical abdomen	723	2.27	16
Pelvimetry	885	0.60	4.3
Chest	5.5	0.05	0.35

\* 1 mrem = 1/1000 rad

become of even more significance. It is generally accepted that any exposure to radiation will increase the risk of genetic damage, and that of the genetically significant dose to a population, exposures during the first 30 years of life, and of course, prenatally, are considered as adding to the potential pool of genetic damage. Fortunately, with the increased awareness by the medical profession of the hazards of radiation, the genetically significant dose from diagnostic procedures has decreased over the past few years.

From the survey for the United Kingdom, 1957-58, Table I gives some examples of foetal exposure.

From these figures it can be seen that an appreciable contribution to the genetically significant dose is from obstetrical X-rays. The contribution from chest X-rays is extremely low, although the advisability of routine chest X-rays in early pregnancy must still be in doubt.

In conclusion, there is a growing body of evidence for the damaging effects of even

small doses of radiation on the fetus. An awareness of this hazard will do much to reduce unnecessary radiation exposure, and knowledge of its approximate size will enable reassurance to be given to worried mothers when an X-ray really is necessary. In such a way a balance can be achieved between the advantages and disadvantages of this technique.

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## THE GENETIC RESPONSIBILITY OF THE OBSTETRICIAN

by E. A. J. ALMENT

ONE of the principal freedoms allowed to the medical practitioner, and one which has grown rather than diminished since the integration of medicine with government, is the freedom to choose how great or how little responsibility he will accept for events or consequences beyond his immediate bond of service. The fight against disease, whether waged by the instinct of the atheist or the mission of the devoted, is often a crusade confined by the close horizons usual when heart is high and head is down, and upon broader issues judgements are light: fertility is the birthright of man; famine is the care of government; senescence accumulates at the door of national insurance.

Our contracts are between individuals. Thus, whilst in many fields of agriculture and animal husbandry eugenics is applied to the service of man, for man himself the lightening of his genetic burden is left to natural processes. Indeed, in the practice of therapeutics it may be increased, as exemplified by the rising population of diabetics: under control of the disease women gain fertility, by obstetric care their offspring survive, and genetic dominance ensures an increased incidence in successive generations.

Genetic problems enter the scope of the obstetrician and gynaecologist in several ways. As the promotion of fertility and the salvage of foetal life is his deep concern he recognises the part played by lethal genes in reducing woman's procreative capacity.

#### Fertility

In civilised societies about one marriage in ten is childless. Present methods of investigation seldom disclose a definite factor responsible such as aspermia, tubal blockage or failure of ovulation, and the inability of many couples to beget children is largely unexplained. It seems likely that some factor such as a lethal gene operating at the earliest stage of embryonic growth determines certain lines for extinction and accounts for a proportion of infertility cases.

#### Spontaneous abortion

If a lethal gene is operative after the first two weeks of foetal life the clinical manifestation of abortion results. It is estimated that at least half of all early spontaneous abortions are associated with gross foetal defects—a "blighted ovum". Since the principle of foetal salvage is the chief concern in cases of threatened miscarriage it might be supposed that successful therapeutics would increase the likelihood of abnormal fetuses becoming viable. Although the outcome of pregnancy in such cases seems to be determined largely by the state of the embryo, and where a pregnancy threatens to miscarry but survives the foetus is usually apparently normal, its sub-lethal genetic disadvantage cannot be known.

#### Therapeutic abortion

The termination of a pregnancy where the foetus is suspected of being malformed is not allowed to a woman by law unless her life or health are in danger from her morbid fear of the outcome. However, in conditions where a severely deformed foetus is certain to result from the pregnancy, termination could be justified by the hopeless outcome. In such cases, and in all cases where an attempt is made to predict the prospects for future pregnancies after such a disastrous one, chromosomal studies of both parents, any living children and any fresh foetal tissue is useful. A certain proportion of Down's syndrome, for example, can be predicted by demonstrating translocations in two pairs of chromosomes in cells from tissue cultures prepared from this material. As laboratory facilities are increased a far wider use of chromosomal studies will be made in pregnancies overshadowed by previous foetal abnormalities.

#### Antenatal care

Whilst antenatal care is not wholly the responsibility of the obstetrician, it is to him that other members of the maternity services—the general practitioner and the midwife—will look for guidance and progress. It is he,

therefore, who must be alert to such dangers as the teratogenic effects of drugs and the hazards of ionising radiation. Just as the practice of foetal salvage whatever the genetic implications may be regarded as the obstetrician's sin of omission, the principal long-term genetic damage that he can commission is by irradiation of the foetus or the maternal gonads.

It is only a decade since routine X-ray pelvimetry was advocated for every primigravida: a practice which in the light of current radiobiological knowledge would have increased by a third the genetic load carried by the first born into its own reproductive life, and also materially increased that of subsequent offspring from the maternal gonad exposure. In 1957 in Great Britain some 3,600 X-ray pelvimetries were carried out with an average of two films per patient: this comprised about 2 per cent. of all primigravidae only, so that the total genetic effect was small, although in the U.S.A. the proportion was perhaps as high as 10 per cent. of all women in well-equipped hospitals during the 15 years of popularity of X-ray pelvimetry.

Whilst it can be shown that routine pelvic measurement by X-rays is unnecessary—and indeed this investigation can probably be dispensed with entirely without affecting foetal safety—there are occasions when diagnostic radiology in pregnancy is indicated. In fact, abdominal X-ray examination of the foetus adds much greater total genetic dose to the next generation than pelvimetry because it is more widely used: in 1957 some 21,000 films were taken of 15,600 women in pregnancy and the total genetic dose to the foetus was almost four times as great as the total from pelvimetry. However, a single film to show the foetal skeleton, taken postero-anteriorly to minimise the foetal dose, can be justified in hydramnios to show abnormality, in breech presentation, multiple pregnancy, or to determine foetal maturity in the case of an uncertain period of gestation, because all these complications are associated with an immediate foetal risk far higher than the ultimate genetic consequence of the examination. In general, all diagnostic abdominal X-rays in pregnancy should be requested only by an obstetric specialist.

Great care must be taken to avoid all unnecessary foetal exposure during the early weeks of embryonic susceptibility. A routine chest X-ray, for example, which is justified by its detection of unsuspected pulmonary tuberculosis—a serious complication of pregnancy—in 1 in 500 women, is best taken with effi-

cient coning of the beam between the 18th and 24th week of gestation, after the embryonic tissue has fully differentiated and before the foetal size causes its encroachment into the zone of scatter from the thorax.

Other diagnostic films such as pyclograms, cholecystograms, views of the lumbar spine or pelvis and barium studies should never be carried out in pregnancy. In most hospitals now no radiological examination is made of a woman of child-bearing age without an enquiry about the possibility of her being pregnant. The ovaries must similarly be protected from unnecessary irradiation in a woman who might subsequently conceive. The development of the primordial follicles and ova which begins during foetal life is complete at puberty, so that no further oögenesis occurs. Each ovum therefore is vulnerable in its mature state to cumulative radiation effects during the procreative years of a woman's life, and her later offspring will have derived a contribution from any diagnostic pelvic radiation as well as a greater duration of effect from the natural background. If lateral views of the abdomen or pelvis are necessary it is important to change sides for a second film, or if one ovary only is present, to position the patient with that side adjacent to the film.

Hysterosalpingography is an examination of the uterus and Fallopian tubes made in women who are infertile and is therefore a form of pelvic irradiation which quite commonly precedes pregnancy—in about 10 per cent. of cases who have had this investigation. The risk of irradiating a very early embryo can be largely eliminated by confining the examination to the pre-ovulatory phase of the menstrual cycle. The ovarian dose is reduced by short periods of screening and the taking of a single film at the optimum moment for a permanent record. Past studies have indicated an average screening time of 1½ minutes and an average number of 2 films, but with greater care these could be halved. Undoubtedly modern techniques of image intensification and teleradiology will reduce the radiation dosage, and in all screening procedures monitoring dosimetry is desirable.

#### Delivery

The obstetrician's principal aim now is to make childbirth as safe for the child as for the mother. This goal is still a long way off and apart from the natural hazards of birth the operator adds to the toll of physical handicap and cerebral damage with the obstetric forceps. Even spontaneous delivery represents

the greatest hazard of his life to an individual born into a secure modern society, and in the intermittent foetal hypoxia which labour entails none of us can know what modifications have taken place and made us other than we might have been, or what subliminal damage has resulted. Yet even Caesarean section to avoid some special predictable risk of vaginal delivery may result in the birth of a child loaded with genetic disadvantage that would

have been lost *per vias naturales*.

Of all clinicians the obstetrician is perhaps the most concerned with simple issues: he stands in the way of life at its emergence and past him the river runs, bearing its adverse genes like sand in the ever-growing tide towards the distant delta. If he is powerless to clear the stream of its burden he can at least strive to add no more.

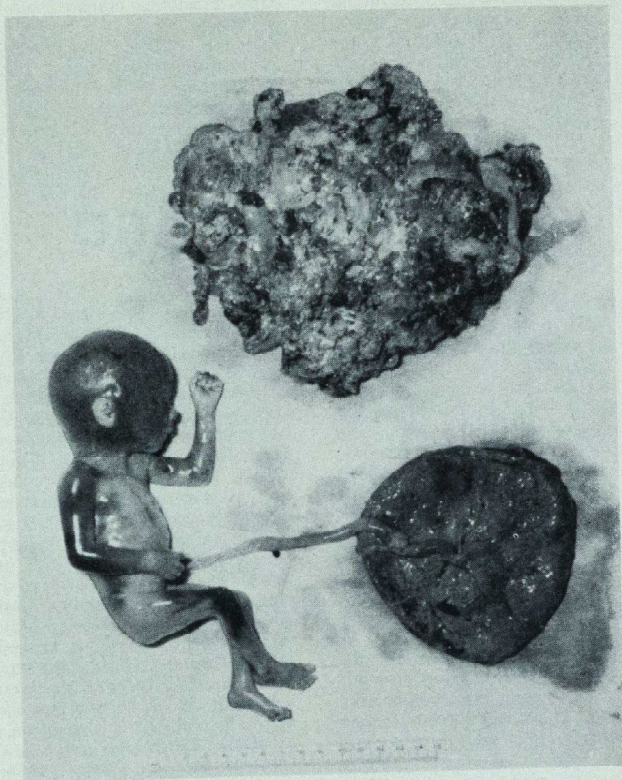
## FIFTY YEARS AGO

"About the time that Paslew was conspiring against Henry VIII, a strange being made his appearance in the neighbourhood, from whence nobody knew. He was known as Nicholas Demdike, and believed to be a wizard. He had married a wild but beautiful girl of the neighbourhood, by name Bess Blackburn. She was a suspect, too, on account of her ancestry, which was as follows: Hard by Whalley Abbey there used to stand a small chapel, to which people who were tired of this world could retire and lead a religious life. In the time of Henry VI a beautiful widow named Isola de Heton retired thither to console herself for the death of her husband, of course under strict vows. But she soon forgot her husband and her vows, and her life became such a scandal that the chapel was dismantled. So much is actual history; but the story goes on, that wandering, an outcast, on the hills near Whalley, she was in danger of losing her beauty and her life too, but for a timely compact with Satan, from whom she obtained a further lease of them—of course at a certain price. Now, on the slope of Pendle Hill there stood an old fortress, always the abode of evil doers, and at this time held by a notorious robber named Blackburn. He took the beautiful ex-votress, Isola de Heton, to live with

him there; till one night, in the midst of a riotous banquet, a dark, sinister man appeared and claimed her as his own. Satan made a double capture that night, for the robber Blackburn also died of terror. From this worthy pair (it was said) was descended Bess Blackburn, wife of Demdike the wizard. These Demdikes had one child, a daughter, who, by all the laws of eugenics, ought not to have been allowed to live. As it was she lived, but got no chance of a good life, for the Abbot Paslew refused the rite of baptism to the children of witches. For this he earned the hatred of Demdike, which, indeed, he had already earned for another reason. For the Abbot had a past. While still a monk, and aspiring to become abbot, he had had a rival for that honour. He had got rid of this rival by a wicked scheme. He accused him of witchcraft, and in consequence the unfortunate man was built up in a dungeon, there to die by inches. But he was miraculously set free—you may guess by whom—and full powers of vengeance upon the Abbot were granted to him—you may guess at what price. And as Paslew's end drew near, the monk, his former rival, reappears as his persecutor—Nicholas Demdike."

# HYDATIDIFORM MOLE

by DAVID DUNN



The still-born foetus with its placenta and the Hydatidiform Mole (Scale in cms.).

**I**N 1752 one of Smellie's pupils "attended a poor woman, who, in the fourth month of her pregnancy, was taken with a violent flooding, which was refrained with opiates, but in three days returned with greater violence, accompanied with strong pains and a frequent straining like a tenesmus. At length she dis-

charged a pot of coagulated blood and Hydatides, adhering to a membranous substance or to one another, like a bunch of grapes of different sizes, from the bigness of a nutmeg to the smallness of a hempseed. The patient was reduced to such a degree that we thought she could not possibly live; nevertheless she grad-

ually recovered, contrary to our expectation". This classic description is one of the earliest of hydatidiform mole, though other cases had been recorded by Hippocrates and Aetius of Amida.

The following is an unusual case seen at Rochford General Hospital:

The patient was a 27-year-old primigravida who first saw her general practitioner on 11th June, 1962, when she was complaining of vomiting. She was found to be six weeks pregnant. The pregnancy appeared to progress normally until the end of June when the patient noticed a slight blood loss vaginally for two days. She was advised to rest for a week in bed, which she did, and the discharge ceased. The fundus was not palpable per abdomen at this time (8 weeks).

A month later, after thirteen weeks' amenorrhoea, the discharge recurred and on examination her own doctor found the fundus to be nearly at the level of the umbilicus. She was sent to the hospital clinic and booked there on 9th August (14 weeks). The height of the fundus now corresponded to a twenty-week pregnancy. The cervix was well closed. Her blood pressure was 125/65 and there was no oedema or albuminuria. Multiple pregnancy was suspected and as the bleeding had ceased she was asked to return in a month.

She then went on holiday and during this time her ankles began to swell. On her return she again saw her doctor who found that her blood pressure had risen to 140/85 and that she had oedema of both ankles. Her urine showed a dense cloud of albumin. She was sent immediately to the clinic from where she was admitted to hospital as a case of pre-eclampsia in a possible twin pregnancy.

On admission on 7th September, 1962, the signs of pre-eclampsia were confirmed. She was found to have gained twelve pounds in weight in the past month, had slight pretibial oedema, albuminuria, and a blood pressure of 140/90. She seemed reliably sure of her dates which placed the period of gestation at nineteen weeks. However, the height of the fundus corresponded to a twenty-eight week pregnancy. The uterus felt generally cystic, but some foetal parts were palpable. The latter finding seemed to make a hydatidiform mole unlikely, but in view of the history, the size of the uterus, and the onset of pre-eclampsia of such severity early in pregnancy, a specimen of urine was sent to the laboratory for quantitative Asheim-Zondek estimation. When the result came through some days later it was positive at 1/1000 dilution. She also

had a slight fever (99°F) and to exclude a urinary infection a clean specimen of urine was sent to the laboratory. This was sterile on culture but showed 20 mg./litre of albumin. The patient was put to bed and given sedative treatment with butobarbitone. Regular estimations of urinary albumin and twice daily blood pressure readings were instituted. For the next few days the slight fever remained and the blood pressure settled at about 125/85. The albuminuria continued to increase and on 13th September had reached 2½ gm. per litre.

On the afternoon of the 14th September the patient complained of backache and at 3.15 p.m. she passed 2-3 oz. of fresh blood per vaginam. At 3.20 p.m. the membranes ruptured and blood-stained liquor drained. An abortion was now inevitable and an intravenous drip was set up and blood cross-matched. At 4 p.m. there was spontaneous delivery of an 11 oz. foetus measuring 9 inches in length. The fundus remained at twenty-weeks size. While awaiting delivery of the placenta large amounts of hydatidiform tissue were passed. Bleeding continued profusely and because of this I/V ergometrine was given. This rapidly controlled the haemorrhage and arrangements were made to examine and evacuate the uterus under anaesthesia. Her blood pressure was now 118/70 and her pulse 96, of good volume. She was transfused with two pints of blood. When examined under the anaesthetic the ovaries were not palpable. The uterus was still eighteen-weeks in size and the os was two fingers dilated. A normal looking complete placenta was found in the cervical canal and was removed. On digital exploration four ounces of hydatidiform tissue were removed from the uterine cavity.

Postoperatively her temperature rose to 100°F and owing to the association of infection with the removal of a hydatidiform mole, a high vaginal swab was taken and a six-day course of Chloramphenicol begun immediately. The swab showed a heavy growth of haemolytic streptococci sensitive to Chloramphenicol. Her haemoglobin had fallen to 57.6 per cent. and two more pints of blood were transfused. Ten days later her pulse and temperature were normal and her haemoglobin was 75.6 per cent. She had no loss per vaginam for five days and she was allowed to return home. She was asked to return to the clinic for observation and again in a fortnight for a further A-Z test. On discharge her condition was very good. Since then she has been re-admitted and transferred to another hospital with symptoms

of the nephrotic syndrome. At the time of writing she is still under investigation.

The histology report on the hydatidiform tissue was that it showed "marked proliferation of the epithelium".

## DISCUSSION

Hydatid degeneration is variously quoted as occurring in 1/750 to 1/20,000 pregnancies. The occurrence of a well-developed normal foetus associated with it is an extremely rare event, though by no means unknown. Two types occur, those in which there is a twin pregnancy, i.e. one degenerate ovum and one normal foetus and placenta (as in this case), and those in which there is a uniovular pregnancy, i.e. a normal foetus attached to a hydatidiform placenta. Of these two the hydatidiform mole in twin pregnancy is more common. Brews in 1939, reviewing a hundred cases of hydatidiform mole seen at the London Hospital over thirty-three years records three cases, two in twin pregnancies and one in uniovular pregnancy. Mueller and Lapp managed to collect twelve cases occurring in uniovular pregnancy.

The presence of a mole is not necessarily incompatible with a living child though this is extremely rare. Rose (1952) reported a normal live 6 lb. 4 oz. baby delivered at term together with a small hydatidiform mole. This occurred in a twin pregnancy. Another case was reported by Taylor (1957). Here a moderate-sized hydatidiform mole was born with a living male infant and a normal placenta. A case of a live child born with a mole in a uniovular pregnancy was described by Brown in 1957. Here the child also had a polycystic liver and did not survive long. In the present case the foetus showed no obvious abnormality and though too immature for a separate existence showed signs of movement for a short while after birth. Thus the presence of the mole does not seem to affect the development of the other ovum of a twin pregnancy, though its presence usually leads to early abortion.

This case also illustrates one or two points which may be of interest. It presents an unusual diagnostic problem. The usual differential diagnosis of excessive enlargement of the uterus in early pregnancy lies between multiple gestation and hydatidiform mole and in this case signs of both were present, a puzzle only explained when abortion occurred.

Cases such as this provide the evidence for the belief that hydatidiform mole and chorion-epithelioma are the result of a "blighted

ovum" and not of a fault in maternal metabolism. Acosta-Sison in 1954 described three cases of chorion-epithelioma in association with a normal foetus and placenta and pointed out that this was incompatible with the "lytic theory" of chorion-epithelioma invasiveness. This held that the malignancy of chorion-epithelioma was due to the absence of a maternal factor which normally lysed trophoblastic cells entering the maternal circulation.

The occurrence of severe pre-eclampsia so early in a pregnancy is also unusual. Melody (1946) emphasized this as a frequent association with hydatidiform mole and wrote that the syndrome of hypertension, oedema, and albuminuria early in gestation should suggest chorionic disease. He quotes Greenhill as saying that toxæmia without mole rarely occurs in early pregnancy. The reason for this association is as obscure as the aetiology of the pre-eclamptic syndrome itself, although some interesting suggestions have been made. Acosta-Sison in 1956 showed that in 85 cases the hypertension did not occur until the fundus reached the level of the umbilicus, and concluded that the raised blood pressure was due to increased abdominal pressure and a raised level of gonadotrophins. Scott (1958) discounted uterine overdistension as an aetiological factor. In his series of 148 cases of uncomplicated hydramnios there was no significant increase in the incidence of pre-eclampsia. An increase was only noted when the hydramnios was associated with abnormalities such as twins, diabetes or hydrops foetalis which are themselves associated with a high incidence of pre-eclampsia. Scott studied a number of cases of hydatidiform mole and hydrops foetalis and suggested that there were similarities between the toxæmic syndromes associated with these conditions. Both gave rise to severe hypertension, oedema and albuminuria of early onset, and rarely to any eclamptic fits. (Though the latter may have been prevented by the early abortion which usually occurs or is induced, cases of eclampsia and hydatidiform pregnancy have been described.) He also noted similarities between the placental histology in these conditions, both being characterised by an abnormal activity of the trophoblast. He suggested that this type of pre-eclampsia associated with "hyperplacentosis" should be considered as an entity, and that it might result from a raised secretion of trophoblastic gonadotrophin relative to the steroids produced by the syncytium. This case shows all the features of the toxæmic syndrome he describes.

## SUMMARY

A case of hydatidiform mole in association with a normal foetus and placenta occurring in a twin pregnancy is described.

The incidence of this condition and a few points which may be of interest, including the early onset of pre-eclampsia, are briefly discussed.

This case is published by kind permission of Mrs. F. Bridge. Thanks are also due to Mr. K. Sutton for corrections and advice and to Mr. G. Tapsall and Dr. Sadiqua Shaikh for a great deal of help and encouragement.

## LETTER TO THE EDITOR

### Dear Sir,

During recent years there has been much discussion for and against the provision of facilities for the student to learn something of general practice—how it should be done, or what should be provided, should it be voluntary or compulsory, and so on and so forth. Most vociferous of those in favour seem to be the students and yet it is most difficult to arrange information in such a way that they will take advantage of all the facilities offered. This Medical College goes a long way to meet these demands and the following programme has been arranged for 1963:—

**Wednesday, 10th July, 1 p.m.** Visit to Dr. McKane's practice at Dunmow. A symposium, "The rural practitioner and his co-operation with the Public Health Services, etc." A tea party with local doctors and members of the Public Health Services has been arranged.

**Friday, 6th September at 1 p.m.** Visit to Dr. Dimock's practice at Hoddesdon. A symposium, "Clinical aspects of general practice—respiratory diseases, stress in medicine, simple procedures used in general practice". Tea is provided.

**October.** Visit to Harlow, "General practice in a New Town".

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### STUDENT ATTACHMENT SCHEMES:

**Short Attachments.** A list of doctors who have volunteered to allow students to join them in their work for a short time at a moment's notice is available in the Sub-Dean's Office. These arrangements allow students to join doctors for a surgery or for a period of visiting whenever they have a few hours to spare. These doctors are within easy reach of the Hospital.

**Long Attachments.** Arrangements can also be made for students to stay with a general practitioner for any time up to a fortnight on application to me in the Sub-Dean's Office.

**Public Welfare Foundation Prize.** Students may enter a report on a case seen in general practice for the Public Welfare Foundation Prize offered by the College of General Practitioners and valued at First, £100, Second, £75, and Third, £50. Particulars and entry forms are available in the Sub-Dean's Office.

I hope that this information will allow students to reserve the appropriate dates which will be confirmed and advertised in detail nearer the time of occurrence.

Yours faithfully,

J. O. McKane,  
 Adviser in General Practice.

## OPERATION Z

### (BART'S SKI CLUB TRIP TO ZÜRS, 1963)

**I**NVASION day was scheduled for a Saturday and taxis containing our personnel in regulation uniform streamed in from the outskirts of London to rendezvous in the Victoria Station bar. Final instructions were issued by our captain, The Spanish Infanta, and the party of 46 hand-picked veterans with a generous smattering of novices boarded the train to set off. Everyone was seated around in groups smoking nervously and discussing plans (in code, naturally—"screwy louis; hooks and crooks wild"), when it was announced that channel conditions would not permit travel. A few more choice code words and disembarkation was carried out successfully, despite some avowals to go it alone.

It seemed that de Gaulle would indeed keep us out of the Common Market; but after a party, several bottles of wine and precious little sleep, the already battle-scarred troops set off. Invasion point, Z, was reached the following afternoon with few casualties—three sore heads and one lost shirt.

The campaign was to be brief and the objective the snow-covered peaks surrounding the valley. Our platoon set off the next morning with great vigour, but, alas, conditions underfoot were treacherous and most of our troops had difficulty in even standing up. The equipment that had been issued to us by the locals did not help much—six-foot wooden-soled boots and two sticks. Despite initial set-backs we persevered and carried out stalwart attacks every day for the next ten, and due to the stout efforts of the natives in providing evening entertainments, morale remained high. Of greatest value were the frothy medicinal tonics handed out by white-coated attendants and extensive loosening exercises to music from both the local physiotherapists and those we had brought with us. The weather was also kind, with only one blizzard to retard our now steady progress.

The whole operation was given new life with the arrival of Queenie a few days after the start of the campaign, but his influence waned somewhat when he became the target of an enemy agent (code name, "The Merry

Widow"), who led him off on several fruitless midnight sorties. Luckily, this was offset by nightly pre-dinner briefings, entertainment being provided by the sergeant (code name "Baldy"), performing take-offs.

Inevitably, there were incidents with the local inhabitants. As always, some of our members were intoxicated, notably "Baldy" and our north country platoon leader, but apart from an occasional skirmish with the local hair-dressing establishment by two overzealous privates and a one-sided argument between our Spanish interpreter and a high-ranking German officer (by the sound of his voice), all went very quietly. One of our officers ("Jay"), however, was seen tempting an enemy pack-horse with a carrot and had to be severely reprimanded. Our commando expert, Louis, by getting his face progressively blacker, managed to form a liaison with the company's public relations officer (code name "Ycass"), who did a great deal to keep him in check, or was it stalemate?

Towards the end of the second week, great progress had been made with only slight injuries (one strained ankle and two sets of torn trousers—those of "Baldy" and his Auntie Sin), but with extensive damage to the enemy. Thanks to successful rearguard action, several large holes had been left on the slopes and several enemy instructors had been seen retreating down the valley, screaming in frustrated disarray. And so, feeling fully vindicated, the party set off home and met several other guerilla bands on the train.

The journey was eventful. A celebration party was held in a specially-designed carriage when even a full-length leg plaster did not dampen the enthusiasm of one of our members. In Basle calamity struck; excessive gymnastics in our coach had conquered the suspension and we had to transfer to a specially refrigerated carriage to cool us down a little. Despite this, the Bart's 69th Cavalry unit arrived home safe and sound, having had a most enjoyable time—the skiing wasn't bad, either!

(D. S. et al.)

## SPORTS NEWS

### EDITORIAL

Although it can be said that Rugby is the sport that takes pride of place at Bart's, to many Club Secretaries it remains an enigma that the Rugger Club manages to attract practically all the spectators that venture forth to watch prestige or Cup matches.

Before Christmas the Soccer team played Charing Cross Hospital in the first round of the Hospitals' Cup. After last season's success both in the Cup and the League, the Soccer club was entitled to not a little support from students and nurses, especially on a Wednesday afternoon. Imagine the disappointment, despite posters and considerable canvassing for support, that the team felt when they had to make do with the non-playing Social Secretary and Treasurer of the Soccer Club plus the travelling reserve! By contrast, Charing Cross had sent down two coaches full of supporters to encourage and cheer their Hospital on.

Moreover, our team of Cross Country runners, it appears, are not entitled to Bart's support in spite of their first rate successes throughout the season. Either several posters announcing the recent Hyde Park Relay Race were ignored or overlooked, or, as is more likely, nobody could be bothered to make the effort to see Bart's run a magnificent race.

G.H.

### RUGGER CLUB REPORT

**19th February, 1963. 1st Round U.H. R.U.F.C. Cup. Bart's v. George's. Bart's won 11 pts.-3.**

After a delay of over six weeks the 1st XV eventually came to grips with, and defeated, a very game George's XV. This game was played on a rock-like pitch and the Bart's XV were, in the main, very reluctant to come to terms with it too often. As a result, George's were on the offensive for the first half with only a well executed "push-over" try by the Bart's pack and neat conversion by Gibson, enabling them to take the lead that form predicted. At half-time Bart's led by 5 pts.-0 and were having to fight hard to maintain this lead.

The second half brought an early shock for the XV, Robinson, the George's centre kicked

a penalty—success at his sixth attempt. Still this did not stir Bart's on and they continued to play as though fate had already declared them the winners. Finally, in the last 10 minutes of the game, the backs managed to elude the George's defenders and slipped over for a try on the right—scorer Phillips. Then in the closing minutes Goodall kicked ahead and Mackenzie raced in for the touch down. Both of Gibson's kicks failed.

A good, open game considering the conditions and the XV benefited from the outing.

Team: E. D. Dorrell, D. Goodall, M. Phillips, P. Savage, E. Sidebottom, A. T. Letchworth, D. C. Pope, J. Hamilton, B. Gurry, A. J. S. Knox, B. Doran, M. M. Orr, J. C. MacKenzie, C. J. Smart, J. Gibson.

**23rd February, 1963. Bart's v. K.C.S.O.B. Lost 3 pts.-8.**

This was a game Bart's lost by missing their chances and not pressing home their attacks fully. Two second half scores by the Old Boys and a penalty by Gibson for Bart's were the only scores in a game played on relatively soft turf. For the first half the Hospital forwards pressed hard and several scoring chances were lost. K.C.S.O.B. were strong at centre and pressed home their attacks with more power than the Hospital backs, who were well served by Ross, making a welcome return after injury.

A goal and a penalty goal put paid to the chance of a win and although Goodall went over in the right corner this was disallowed, and despite territorial advantage throughout it is the points deficit that inevitably counts. The season began with numerous tries being scored but now the Hospital are finding them difficult to negotiate.

Team: E. D. Dorrell, D. Goodall, M. Phillips, P. Savage, E. Sidebottom, A. T. Letchworth, A. P. Ross, J. Hamilton, B. Gurry, A. J. S. Knox, B. Doran, M. M. Orr, J. C. MacKenzie, C. J. Smart, J. Gibson.

**26th February, 1963. 2nd Round U.H. R.U.F.C. Cup. Bart's v. St. Thomas's. Lost 6 pts.-8.**

With tremendous support from the touch-line the XV went straight onto the offensive



Bart's v. St. Thomas's at Richmond (B. Doran, C. Smart, J. Gibson, A. P. Ross).

and pushed back the Tommies XV to their own goal line. The majority of the 1st half was fought out within the Tommies' "25" and ended with Bart's leading 6 pts.-0 thanks to two superb kicks by Gibson. This was almost made 11 pts. when Phillips and Goodall broke clear of the defence and with the back row in support nearly crossed the Tommies' line, Goodall being tackled into touch inches from the line. At this point the Bart's pack, led by Hamilton, were dominating the opposition and Gurry took the ball to the fight back again and again.

The second half began in a similar fashion, Ross and Letchworth kicking the Hospital into a position on the Tommies' "25". Bart's should have made sure of their lead, but as has occurred in recent matches they were unable to score tries. Goodall crashed over in the corner, but was ruled to have dropped the ball. This seemed to spur St. Thomas's to greater things and their left wing slipped a tackle and ran down the touchline and cross kicked. The Tommies' open-side wing forward took a lucky bounce and went over near

the posts—Brookes converted.

At 6 pts.-5 with 12 minutes to go Bart's stormed into the Tommies' half and then from a loose maul in his own "25" Brooks, the centre, kicked ahead and towards the touchline; Dorrell gathered neatly and at the same moment was tackled by the Tommies' winger, the ball ran loose and the opposition centre following up beat the defence to the touch down, Bart's 6 pts., Tommies 8.

The XV fought back and Gibson was just short with two very long range kicks, but nothing succeeded in cracking the Tommies' defence and the minutes passed by. The end came with Bart's encamped on the St. Thomas's "25", trying desperately to regain their deserved lead but to no avail. The whole Bart's side played well, but were beaten by their own inability to score tries.

Team: E. D. Dorrell, D. Goodall, M. Phillips, P. Savage, E. Sidebottom, A. T. Letchworth, A. P. Ross, J. Hamilton, B. Gurry, A. J. S. Knox, B. Doran, M. M. Orr, J. C. MacKenzie, C. J. Smart, J. Gibson.

### CROSS-COUNTRY REPORT Saturday, 23th February, 1963. Hyde Park Road Relay Race.

This race, consisting of 6 laps of 3 miles run around the Serpentine, attracts student teams from all over England and Wales. In all but name it is the Inter-universities and Colleges Road Relay Championship. This year 7 complete teams competed and not one of these was a 2nd team.

There is a cup awarded for the first team to finish and another for the first college to finish which has less than 500 students (The Imperial College Union Cup).

The start was bungled. The pistol did not go off and the more conscientious runners were left waiting for the recall that never came. However, Bart's first runner, Dan Tunstall-Pedoe, gradually worked his way up the field and at halfway was in the leading group of 5 runners. This group stayed together with the lead alternating until the last 600 yards where Llewellyn Smith, the Oxford University Cross Country captain (New College), went away, followed by the Sheffield University runner. Dan Tunstall-Pedoe finished only 5 seconds behind Llewellyn Smith in 3rd position.

Fred Hardy ran the next leg, and although 11 of the 73 runners behind him came past they did not manage to get far in front of him. Hardy, Bart's marathon runner, ran better over this short distance than most of us had hoped he could.

Nick Pott, taking over in 14th position, looked rather uncomfortable on the road (probably an effect of the snow and ice which has prevented the whole team doing as much road work as they should have done) but ran himself right out to finish in 12th position.

Roger Sanders ran the next leg in a time only 10 seconds slower than Fred Hardy's and finished 15th. With this run of Sanders' and two of our best men still to come Bart's were in the hunt for the Imperial College Union Cup and Terry Foxton had to gain as much as he could from Queen's College, Cambridge, who were behind us. Terry gained 4 places and handed over to Pete Littlewood nearly half-a-minute ahead of Queen's College, Cambridge.

However, half-a-minute is not enough even for Pete Littlewood when he is being chased by Mike Turner, Northern Counties Cross Country Champion, ex-U.A.U. Cross Country Champion and International and Cambridge University's 1st string 3-miler. Pete, though running valiantly, was passed by him and by

T. K. F. Johnston of Trinity College, Cambridge, Inter-Counties Cross-Country Champion and Southern Counties Cross-Country Champion.

So Bart's finished in 13th position (compared with 30th last year), only being beaten by Queen's College, Cambridge, among the small colleges.

#### Result

	mins.	secs.
1. Manchester University ...	86	52
2. Durham University ...	88	25
3. Sheffield University ...	88	34
4. Loughborough College ...	88	38
5. University College (U.L.) ...	88	53
6. Leeds University ...	89	08
7. Liverpool University ...	89	16
8. Nottingham University ...	89	43
9. Leicester University ...	89	53
10. Queen's College, Cambridge ...	90	02
11. Trinity College, Cambridge ...	90	27
12. Bristol University ...	90	32
13. St. Bartholomew's Hospital ...	90	36

(Also competing were most Oxford and Cambridge Colleges, Birmingham University, all the Welsh Universities, Southampton University, etc.)

#### St. Bartholomew's Hospital. (Number in brackets indicates position at end of lap.)

	mins.	secs.	posn.
D. S. Tunstall-Pedoe ...	14	18	(3)
F. Hardy ...	15	43	(14)
N. Pott ...	15	16	(12)
R. Sanders ...	15	53	(15)
T. Foxton ...	14	52	(11)
P. Littlewood ...	14	34	(13)

Fastest Lap: D. M. Turner (Queen's College)  
13 mins. 35 seconds.

76 teams completed the course.

Of the 450 runners competing, Tunstall-Pedoe's time was the 14th fastest of the day and Littlewood's the 28th fastest. These were the 4th and 5th fastest times run by London University entrants.

Although this race was widely publicised at Bart's and was run in Hyde Park on a bright, sunny afternoon, the only support our runners received was from their team mates and other London University runners.

#### MOTOR CLUB, Racing Team Report

This coming racing season will see two Bart's men on the Circuits: Ted Carden will

be racing a Turner Ford in Grand Touring and Production Sports Car races; his first outing is on 24th of March at Brand's Hatch in the John Davy Trophy Race.

A newcomer to the racing scene is J. Robinson, who has graduated from 750 specials and has bought a 1957 Lotus XI Le Mans in which he will be competing in sports car events (all being well in 2nd M.B.1). His first competition will be a sprint at Brand's Hatch on 17th March. Anyone who has a potent machine, and wishes to do some racing, will be welcome.

#### SWIMMING REPORT

Over the past few years, the Bart's water-polo and swimming teams have met with a considerable degree of success, which has not unfortunately been maintained in the past few months. For the third year running, we finished second to St. Mary's in the United Hospitals' League, and in the U.L.U. knock-out competition last December, we lost to Imperial College in the semi-finals, also for the third successive year; since then we have not won a match.

There is sufficient talent in the Hospital, including 4 London University Purples, for us to raise a team capable of beating St.

Mary's, Imperial College or any other London college as well as a good many London clubs. What is lacking is any degree of enthusiasm making evident the total absence of team spirit, so vital in any sport. It is a very long time since we have "fielded" the same seven players in successive matches, and even longer since an organised training session was held. Normally the root of apathy lies outside the particular club involved—more is the pity that in this case the actual team members are at fault.

Taking full advantage of having a pool on the premises, the nurses have raised a flourishing swimming team and have had recent successes over other colleges and hospitals.

It is hoped to enter a ladies' team for the first time in the U.H. Championships this summer. Anyone interested should contact Miss M. Mallan or Miss M. Newbold. Perhaps the ladies will once again outshine their male colleagues.

The following have represented the Hospital in recent matches:

R. Groves (capt.); B. Shorey; C. Ruoss; D. Shand; B. Lask; J. Britton; R. Hillier; A. Letchworth; G. Haig; W. A. M. Davies; P. Quinn.

## But whom do YOU consult, Doctor?

*50,000 Doctors in these islands (and 20,000 more overseas!) enjoy the privileges and benefits of membership of the British Medical Association.*

### Q. What are the advantages of membership?

**A.** A weekly copy of one of the world's outstanding medical journals—the *British Medical Journal*.

The use of a first class medical library—by post if necessary.

Advice on all aspects of professional life.

Scientific and clinical meetings and social functions, both local and national.

*These are some of the reasons why the B.M.A. has the large majority of medical men and women, whatever their field of practice, within its ranks.*

Let the B.M.A. be at YOUR service.

### Q. How much does it cost?

**A.** Two guineas for each of the first two years after provisional registration. Reduced subscriptions continue to apply for a further seven years.



For further details please write to the Secretary,  
British Medical Association, B.M.A. House, Tavistock Square, W.C.1

# ST. BARTHOLOMEW'S HOSPITAL JOURNAL



Vol. LXVII, No. 4  
SUPPLEMENT No. 2

APRIL, 1963

## Editorial

The foundations of modern pathology were laid by Virchow in his basic concept of Cellular pathology. However, the early techniques used in Cytology were so difficult that for many years pathologists were more interested in descriptive Histopathology—the study of the pathology of tissues rather than of cells. The work of George N. Papanicolaou has helped in reversing this trend by the founding of the science of Exfoliative Cytology. The importance of this method in the detection of early malignant lesions has been recognised for many years—for instance by Dudgeon of St. Thomas's thirty years ago—but it seems to have been slow in its application to practical medicine and surgery in this country.

This is partly due to the existence of an attitude, which is hard to break down, that "one swallow doesn't make a Summer" or "one suspicious cell in a smear is unlikely to be conclusive of underlying pathology". This in turn is largely based on the reluctance of some pathologists to accept that accurate cytological diagnosis is only learned after years of experience. Therefore if any "National Cytology Service" is to be established, trained technicians must be provided and they must spend at least one year learning the techniques of diagnostic cytology and several more in order to become competent at screening smears for further examination of positives by an experienced cytologist. This fact has been well known for some years in administrative circles, but as yet has had little effect in producing a national plan for provision of such facilities as are found to be of life-saving value

elsewhere. Only 150 out of 730 pathological departments and laboratories in this country examine and report on smears for cytology, and yet a complete scheme could, if used to the full, be capable of preventing 2,500 deaths a year, in this country, from carcinoma of the cervix.

It follows that the second factor in increasing the use of cytology for the early detection of malignant disease is the persuasion of general practitioners to use the service, and through them, and by other means—not least by television—to educate the public to realise the value of a routine examination of this nature. Even the relatively small amount of advertising used by the "Well Women's Clinic" has met with considerable success. This shows that there are many women who would take advantage of a national service of this kind. The question of the frequency of examinations has still to be settled by large-scale research, but its value is clearly demonstrated within the pages of this Journal.

To most students exfoliative cytology, if it means anything, is connected with carcinoma of the cervix. This is not surprising as at present this is the only example of a probably totally preventable malignant disease, and yet there are many applications in other regions of the body where future discoveries may help in "preventing" other disease. In Bart's this is a rapidly expanding service where demand tends to outstrip the supply of technicians so that other investigations, such as chromosome counts properly carried out in a cytology laboratory, cannot be done in Bart's and must be sent to other hospitals.

One solution to the staffing of cytology laboratories has been suggested in the House of Lords—that medically qualified women be employed as part-time cytologists. This also solves some of the difficulties many medical women have in returning to practice by providing the necessary part-time work which is frequently so hard to find and the lack of which results in an increasing waste of medical

## Engagements

- AUBIN—BOLTON.—The engagement is announced between David Frederick Ashton Aubin and Anne Patricia Bolton.
- BAERSELMAN—PERCIVAL.—The engagement is announced between James Baerselman and Gillian Percival.
- EDMUNDSON—CRAIG.—The engagement is announced between William Lewis Edmundson and Sarah Halifax Craig.
- LLOYD-WILLIAM—CALVERT.—The engagement is announced between John Lloyd-Williams and Adrienne Calvert.
- RIDDLE—PAVIE.—The engagement is announced between Peter N. Riddle and Rita M. P. Pavie.

## Births

- BURBRIDGE.—On 9th March, to Audrey (née Downton) and Dr. Nicholas John Burbridge, a son (David John).
- FREEMAN.—On 17th March, to Florence Eleanor (née Thomas) and Dr. Anthony Freeman, a daughter (Elizabeth Christine), a sister for Michael and Susan Jane.
- IVORY.—On 20th March, in Florida, U.S.A., to Eleanor and Dr. Peter B. C. B. Ivory, a daughter (Anne), a sister for Mark.

## Deaths

- FOSTER MOORE.—On 1st March, 1963, Robert Foster Moore, O.B.E., F.R.C.S., J.P., aged 85. Qualified 1904.
- NICHOLSON.—On 9th March, 1963, Dr. Guy Bernard Nicholson, M.R.C.S., I.R.C.P., aged 92. Qualified 1898.
- SLATER.—On 22nd March, 1963, Dr. George Nathan Oscroft Slater, M.D., M.R.C.S., M.R.C.P., D.P.M., aged 94. Qualified 1894.
- SMITH.—On 11th March, 1963, William Smith, M.D., aged 66. Qualified 1928.

## Appointments

### Institute of Ophthalmology

Mr. E. S. Perkins has been appointed to the newly created Sembal chair of experimental ophthalmology.

resources.

The Supplement has grown to 16 pages this second issue in order to accommodate two main articles, one from the Surgical Unit and one from the Department of Neurology.

**Mr. A. W. Badenoch is standing for election to the Council of the Royal College of Surgeons.**

### Royal College of Physicians

Dr. E. R. Cullinan has been elected Senior Censor of the Royal College of Physicians.

### University of London

Dr. E. M. Crook has been appointed to a chair of biochemistry at St. Bartholomew's Hospital Medical College.

## Changes of Address:

- Dr. F. G. L. Barnes, Belgravia Private Hotel, 2-12 Ulsterville Avenue, Belfast 9.
- Surgeon Commander G. A. Binns, R.N., R.N. Hospital, Malta, G.C.
- Mr. J. Beattie, Ivy Cottage, Reigate Heath, Surrey.
- Dr. R. C. Cook, Lenthorpe, Wennington, Near Rainham, Essex.
- Dr. A. Maples, Bramshott, Craneswater Park, Southsea, Hants.
- Dr. H. E. Milligan, 6, Brookside Close, Runcton, Chichester, Sussex.
- Dr. E. W. Morgan, c/o T. D. Jones and Co., 80, Fleet Street, E.C.1.
- Dr. W. D. Nicol, Halcyon, Boyneswood Road, Four Marks, Alton, Hants.
- Dr. W. Norman-Taylor, Highworth House, Highworth, Wiltshire.
- Dr. B. R. Whittard, 25, Derwent Close, Cambridge.

## WESSEX RAHERE CLUB

The Spring Dinner of the above club will take place at the Cleve Park Hotel, Washford, Somerset, on Saturday, 11th May. It is hoped that, as usual, a member of the Staff will be present as Guest of Honour. Further details will be circulated or can be obtained by any Bart's graduate who is not already a member from the Hon. Secretary, Mr. A. Daunt Bateman, F.R.C.S., 11 The Circus, Bath.

## Calendar

### MAY

- Thurs., 2 May: Abernethian Society: Gerald Gardiner, Q.C., *Medicine and the Law*, Physiology Lecture Theatre, 5.45 p.m.
- Sat. & Sun., 4 & 5: Dr. Graham Hayward  
Mr. A. W. Badenoch  
Mr. J. N. Aston  
Mr. G. H. Ellis
- Wed., 8 May: VIEW DAY.
- Wed., 8 May - Fri., 10 May: Bart's Sailing Club Regatta at Burnham-on-Crouch.
- Thurs., 9 May: Abernethian Society: Symposium on *Therapeutic Abortion*, 5.45 p.m.
- Fri. 10 May: Prof. M. Dolivo, M.D., *Metabolism of the Superior Cervical Ganglion in Relation to Drug Action and Sensitivity to Acetyl Choline*. Physiology Theatre, 5.30 p.m.  
Prof. Jawitz, Ph.D., M.D., *Problems and Prospects of Antibiotics after two Decades*. London School of Hygiene and Tropical Medicine, 5.30 p.m.
- Sat. & Sun., 11 & 12: Dr. A. W. Spence  
Mr. E. G. Tuckwell  
Mr. W. D. Coltart  
Dr. R. Ballantine
- Mon., 13 May: Augustine Society: Rev. D. M. Paton, *Council for Ecumenical Co-operation*, 5.45 p.m.
- Sat. & Sun., 18 & 19: Prof. E. F. Scowen  
Prof. G. W. Taylor  
Mr. H. Jackson  
BURTOWS  
Dr. Ian Jackson
- Thurs., 23 May: Abernethian Society: Dr. W. Ritchie Russell, *Neurological Aspects of Amnesia*, 5.45 p.m.
- Sat. & Sun., 25 & 26: Dr. R. Bodley Scott  
Mr. Alan Hunt  
Mr. J. N. Aston  
Dr. T. B. Boulton
- Tues., 28 May: Dr. L. V. Gimson, of Canterbury, *Diagnosis in General Practice*. 4.45 p.m.
- Wednesday, 29 May: SPORTS DAY.

Physician Accoucheur on duty for the month of May is Mr. J. Beattie.

## DEMONSTRATIONS

### Bacteriology:

- Wed., 8 May: General demonstration of Virological technique, 10 a.m. - 1 p.m.
- Thurs., 16 May: Film on the Human Blood Fluke, 5.30 p.m.
- Thurs., 30 May: Demonstration of Cultures.

### Pathology (in the Museum):

- 16-23 April: Heart.
- 23-30 April: Blood vessels.
- 30 April-7 May: Urinary system.
- 7-14 May: Alimentary system.
- 14-21 May: Bones and Joints.
- 21-28 May: Respiratory system.
- 28 May-4 June: Liver, Gall Bladder, Pancreas.
- 4-11 June: Reticulo endothelial system.
- 11-18 June: Nervous system.
- 18-25 June: Generative system.
- 25 June-2 July: Ductless glands.

## PHOTOGRAPHIC SOCIETY

The View Day Exhibition will be held on View Day in the Hospital Library.

The Exhibition will be divided into two main groups: colour work and monochrome work. The Colour section will be divided into two classes:

1. Colour Prints.
2. Colour Transparencies.

The black and white section will be divided into four classes:

1. Pictorial.
2. Portrait.
3. Action.
4. Record.

All black and white prints must be at least whole plate (6 in. by 8 in. size), mounted, and entirely the work of the exhibitor. Colour entries may be processed commercially.

All entries must be handed into Mr. Thornton, the Hospital Librarian, by Friday, 3rd May.

FRIDAY, 17th May—Matter for the June Journal should be sent to the Editor by this date.

## ART EXHIBITION

An Art Exhibition is to be held in the Great Hall during the first week of July this year. Contributions are welcomed from past and present members of the Hospital and Medical College Staff (both lay and medical), the Nursing Staff and Students.

The Exhibition will be on similar lines to the one held in 1958. In addition, it may be possible to include a section devoted to Medical Art, and it is hoped also to have one or two Memorial exhibits.

The proceeds from the sale of the cata-

logue will be given to OXFAM.

Anyone who is interested in exhibiting should contact either Dr. J. H. Coulson, Student Health Service, Charterhouse Square, or John Challis (Secretary to the Art Exhibition Committee), c/o Students' Union, St. Bartholomew's Hospital.

It is hoped that the response will be good. Anyone with active past and present connections with Bart's, in whatever capacity, is warmly encouraged to send in their work.

## OBITUARY

ROBERT FOSTER MOORE, O.B.E. (Mil.), J.P., M.A., B.Ch., F.R.C.S.



ROBERT FOSTER MOORE, consulting Eye surgeon to St. Bartholomew's Hospital and Moorfields Hospital, died at his home at Bemerton on 1st March, aged 85. "Foster" will always be remembered with deep affection and high regard by his contemporaries and by generations of young men he taught. He was a man of absolute integrity in all he did. His scorn for showmanship, humbug and matters which were not scientifically true was uninhibited and amusing. Foster had a wholesome scepticism for some popularly acclaimed therapeutic measures. He would say, "You

ask me my opinion about vaccines, it is this. Taken in sufficiently large quantities over a very long period of time they may have some small nutrient value". Foster Moore's Medical Ophthalmology was a classic in its time. This and his many contributions to ophthalmic medicine and surgery and to anatomy won him an international reputation. He was a scholar of Christ's College, Cambridge, graduated with 1st Class honours in Part I of the Natural Sciences Tripos in 1900 and gained a 2nd in Part II in 1901. Whilst at Cambridge he did research work in the Anthropological Laboratories on the head of the Australian native. He always had a great love of Cambridge. Whilst an undergraduate he saved two ladies from drowning in the frozen Cam and for this was awarded the Humane Society's Medal.

From Cambridge he entered St. Bartholomew's Hospital as a scholar. He became Sir D'Arcy Power's house surgeon. In 1905 he passed the F.R.C.S. and from 1907-13 was Demonstrator of Anatomy at St. Bartholomew's Hospital. His writings and his teaching were expressed lucidly and with characteristic incisiveness. He retained to the end of his career a profound knowledge of anatomical details, a feat which gave him some mischievous pleasure in teaching students and assistants.

In 1913 he was elected Lang Research Scholar and in 1914 won the Middlemore Prize. The 1914-18 war came during his early struggles in practice. He served in France as a Captain in the R.A.M.C. and was made Officer in Charge of the Ophthalmic Centre at

Etaples. For his services to the Army he was awarded the O.B.E. and was mentioned in despatches. It was in times of military tranquillity that he acquired considerable skill as a water colour artist. I think that one of his best paintings of land and sea was done at the age of 83.

In 1916 he was appointed to the Consultant Staff of St. Bartholomew's Hospital and in 1917 to Moorfields. He became surgeon in charge of the Eye Department at Bart's in 1924. In 1936 he was elected President of the Ophthalmological Society of the United Kingdom and his address gave an account of the pioneer work he had done in treating intra-ocular neoplasms with radon seeds. In 1949 he delivered the Middlemore Lecture in Birmingham. He served on committees at the Ministry of Health and was Ophthalmic Consultant to the Ministry of Supply and Ministry of Pensions. Foster Moore kept a wide interest in scientific matters. He possessed the finest qualities of a surgeon, exquisite craftsmanship, imperturbability, ingenuity and re-

source. Early in his career he acquired perfect ambidexterity in dissecting, surgery, drawing and water colour painting.

A whimsical sense of humour enriched his dealings with people in diverse walks of life. When the writer was a house surgeon there came to the Eye O.P.D. a dishevelled tramp wearing two pairs of dark glasses, an eye-shade, a slouch hat and the soiled medals of some minor Imperial wars of the last century. To an experienced glance the diagnosis of malingering was clearly evident. I asked Foster if he would see this patient with a view to taking him in. The immediate reply was, "Are you quite sure that he is not taking you in?"

On his retirement from St. Bartholomew's Hospital the Foster Moore Club was founded by his old house-surgeons who met annually to dine their Chief, a tribute to the genuine affection and high regard in which he was held. His memory will endure with all who knew and admired his many fine qualities as a man and a surgeon.

H.B.S.

## BRITISH MEDICAL STUDENTS ASSOCIATION

### Foreign Clerkships

The following countries have now accepted their full quota of British students and consequently will refuse applications from now on:—

North America,  
Norway,  
Israel and  
Switzerland.

### B.M.S.A. Yugoslavian Study Tour. July 16th - Aug. 2nd.

A full programme of visits, hospital tours and parties has been arranged by the Yugoslavian medical students. Cost, £33.

### B.M.S.A. Russian Medico-Social Tour. Sept. 5th-20th.

A full programme of visits to hospitals, museums. Visits to Moscow, Leningrad and Warsaw. Cost, £70 approx., probably less.

### B.M.S.A. Polish Study Tour. Aug. 12th-28th.

Modelled on the same lines as last year's highly successful tour. Visits: Warsaw, Chopin's birthplace, Polish Forest, Gdansk, beach at Sopot and Malbork, former seat of the Teutonic knights. Also hospital visits, parties in students' Club and a visit to a theatre. Cost, £32.

### International Clinical Film Course. Gothenburg. July 28th - Aug. 4th.

Films on: Internal Medicine, Endoscopy, Psychiatry, Neurology, Surgery, Obstetrics, Gynaecology, Ophthalmology and others.

Language of course—English.

No. of participants—120 clinical students.

Cost—£10 (does not include travel).

Deadline for application—May 1st.

I.V.B.



*“ Le corps humain  
est un arbre dont  
l'automne est  
perpétuel ”*

A. Claude.

## CLINICAL APPLICATIONS OF EXFOLIATIVE CYTOLOGY

by G. CANTI.

St. B.H.J., April, 1963

71

WHILE MOST PEOPLE are familiar with the deciduous nature of skin, few outside clinical pathology appreciate the extent of the continual exfoliation from all epithelial surfaces. This exfoliation increases when a malignant change occurs in the epithelium, owing to a loss of mutual adhesiveness which is a characteristic of malignant cells. Exfoliative Cytology is founded on this basic concept. By microscopic examination of the secretions from various organs it is possible to detect carcinoma at an early stage of the disease even before there are any clinical manifestations, but there are three obstacles to success: the first, about which nothing can be done, is the failure of the cells to appear in the secretion owing to necrosis, obstruction of the lumen, etc.; the second is the labour involved in finding the cells among the quantity of other material collected, a sufficient number of trained technicians is at present the only answer to this problem; the third is the difficulty of identifying the cells as malignant when they are found, this becomes less of a problem as experience is gained, and there is a good chance that selective techniques will improve the situation still further.

As Exfoliative Cytology is relatively expensive (in man-hours) and available facilities are limited, the purpose of this article is to show how the method can be most economically applied in hospital practice and to give some guidance in the collection of specimens for the best results.

### Uterus

Of all organs, the uterus and particularly the cervix uteri is the most suitable for cytological investigation; it is one of the commonest sites for carcinoma, it is readily accessible so that a direct smear can be made from the cancer bearing area (the squamocolumnar junction), there are few cell types present so that malignant changes are easily spotted (Fig. 1) and, owing to the relatively small amount of material in the specimen, search time is minimal; because of its accessibility for biopsy there is really no need for the cytologist to establish the diagnosis, but merely to indicate which cases should be investigated further.

The report is therefore often made by classifying the cells, according to Papanicolaou:—

- Class I No abnormal cells seen.
- Class II Atypical cells but no evidence of malignancy.
- Class III Cytology suggestive but not conclusive for malignancy.

- Class IV Cytology strongly suggestive of malignancy.
- Class V Cytology conclusive for malignancy.

The finding of malignant cells is, of course, no indication of invasion though Class V cells will usually, though not necessarily, have come from an invasive lesion.

The extreme sensitivity of the test might be considered to be one of its disadvantages, as it not only discloses unsuspected carcinomas, but it brings to light a number of epithelial dysplasias short of frank malignancy which raise new problems in management; however, the simplicity of the test, which is no discomfort to the patient and does not require admission, facilitates continued observation and in cases of doubt the organ is after all, in most of the patients (who will be in the older age group), disposable.

Many of these lesions are in fact early carcinomas at the pre-invasive stage (Stage 0)—the so-called carcinoma-in-situ (Fig. 2)—and it is the discovery of these as well as the early, symptomless, and clinically undetectable cases, at a stage when the disease can be completely eliminated, which justifies the use of Papanicolaou Test for screening purposes.

Very occasionally an exceptionally well differentiated or necrotic carcinoma of the cervix might be missed, but on the whole it is a very sensitive test though not necessarily specific for the reasons already stated; it is less sensitive for detecting carcinoma of the corpus uteri as it is then dependent on cells that have pooled in the posterior fornix where they are likely to be rather degenerate.

In addition to the early detection of cancer, an assessment of the patient's hormonal state can be made from vaginal smears. The various stages of the menstrual cycle, menopause, pregnancy and abortion are all reflected by morphological changes in the epithelial cells, but the subject is a complex one; apart from the simple assessment of oestrogenic activity the clinical applications of hormonal cytology have not yet been fully explored.

Two smears should be made from each patient: one of the secretion from the posterior fornix and the other of a scraping of the external os. The specimens are taken with an Ayre spatula—a disposable wooden spatula shaped to facilitate the scraping of the os. As in all Papanicolaou preparations the smears should be fixed quickly, while still wet, in equal parts of Ether and 95 per cent. alcohol;

drying before fixation impairs morphological detail.

### Lung

Of all the cytological investigations requested, examination of the sputum is the most time-consuming, owing to the bulk of the material which has to be searched, and the irregularity of expectoration of the malignant cells. It is nevertheless an important branch of cytology because of the high incidence of bronchogenic carcinoma in this country and the frequency of unexplained pulmonary lesions.

A recent survey showed that 90 per cent. of all cases of carcinoma of the bronchus admitted to the Thoracic Unit for investigation and treatment had malignant cells in the sputum, but this high positive extraction rate was achieved only at the cost of a quite uneconomical expenditure of time—as much as three hours in a few cases. As about 60 per cent. of the patients were diagnosable by bronchial biopsy or bronchoscopy (which is an essential pre-operative procedure anyway), it is obviously more economical to reserve cytology for those cases where bronchoscopy is contra-indicated or likely to be negative, e.g., patients with X-ray evidence of peripheral or upper lobe lesions. The situation is slightly complicated by the fact that post-bronchoscopic sputum is not so suitable for cytology owing to the bleeding and artefacts produced by the inevitable trauma. It is a wise precaution, therefore, when the outcome of the bronchoscopy is in doubt to keep a pre-bronchoscopic specimen of sputum (in the refrigerator) for cytology, in the event of a negative result. There are, however, occasions when it is desirable to avoid subjecting a patient to bronchoscopy, such as when confirmation of a suspicious X-ray shadow is needed in an inoperable case in order to save an admission, or when it is necessary to establish the histological type (Figs. 3 and 4) with a view to Deep X-ray Therapy; on these occasions the simplicity of the cytological method from the patient's point of view commends itself.

The time required for accurate sputum cytology precludes its use as a screening test, but sometimes it is prudent to take some steps to exclude malignancy short of bronchoscopy, e.g., cases of haemoptysis, unresolved pneumonia and unexplained neuropathies; such cases should be carefully selected for cytology bearing in mind that at least one hour's microscopy is required on every negative case if a

reasonable standard of reliability is to be maintained.

It is useful to have some idea of the reliability of the test, but this is bound to vary considerably, as the percentage of positive sputa is dependent upon the type of case selected for cytology. It is unreasonable to spend more than one hour (3 specimens) on any one case, and this will bring the positive extraction rate down to 80 per cent. on all cases, but if all the bronchoscopic positive cases were excluded, the rate would theoretically fall to 50 per cent., because this group accounts for the majority of the positive sputa. In practice, the selected cases will include quite a number of bronchoscopic positives; and the extraction rate will probably vary between 60 per cent. and 70 per cent.

The "False Positive" rate is likely to be under 1 per cent., but the term is a relative one, because, apart from the very occasional mistake by the cytologist, the majority of "false positives" are caused by squamous metaplasia, and carcinoma-in-situ. "Malignant cells" may appear in the sputum months or even years before there is any clinical evidence of tumour. An equivocal report is sometimes unavoidable in these cases, but in the great majority a specific diagnosis is possible, and obligatory if it is going to be of clinical value.

Fig. 1. Poorly differentiated malignant squamous cells in cervical smear; compare with the normal superficial squamous cell with pyknotic nucleus in the centre of the field.  $\times 500$

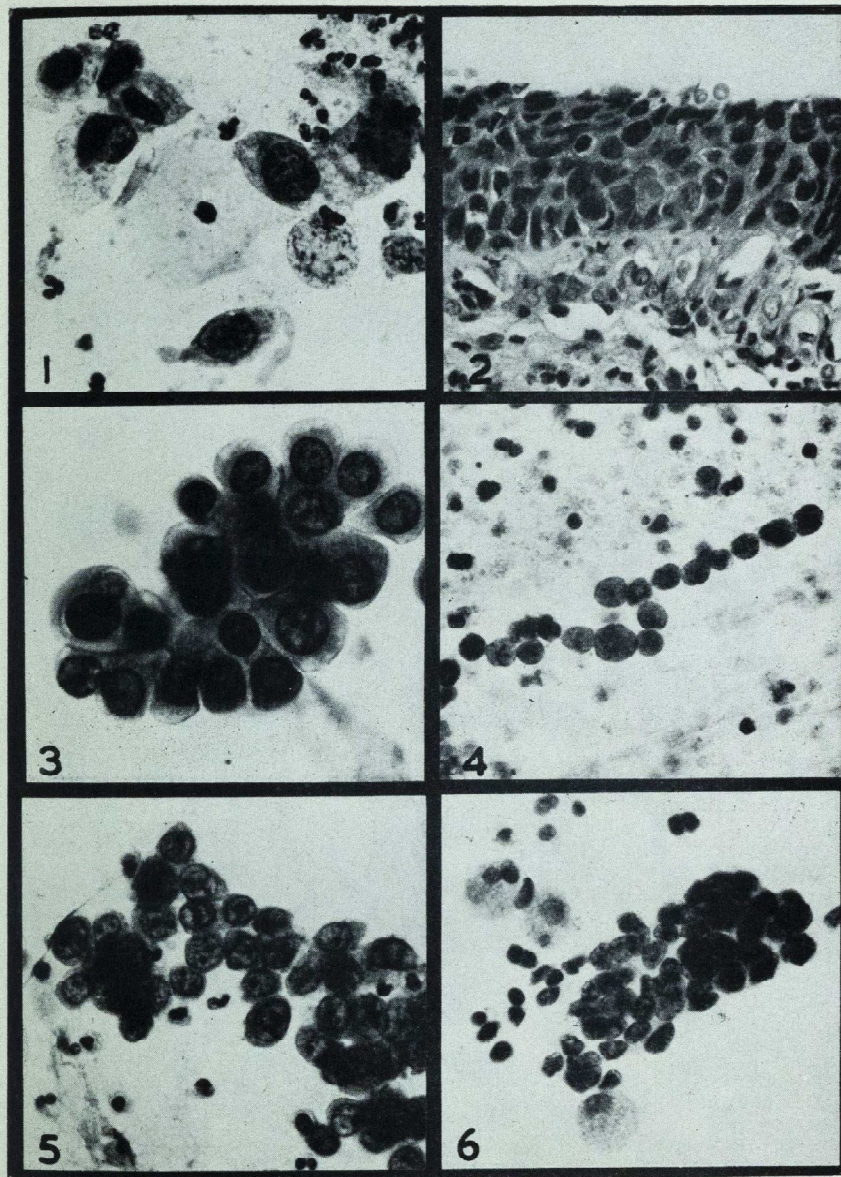
Fig. 2. Biopsy from same patient as Fig. 1 showing carcinoma-in-situ; note loss of normal stratification, poorly differentiated basal type malignant cells reaching the surface, and intact basement membrane.  $\times 300$

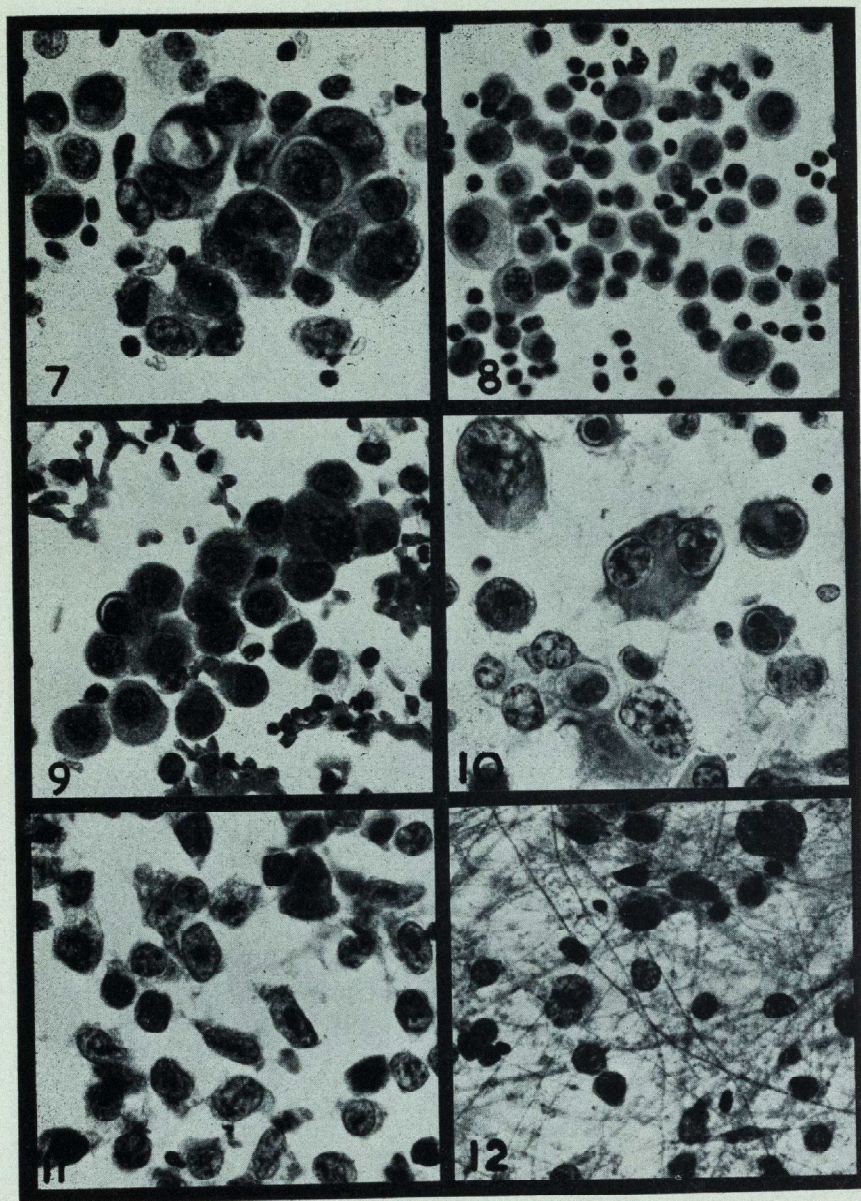
Fig. 3. Adenocarcinoma cells of bronchogenic type in the sputum; the tendency to form an epithelial surface is apparent.  $\times 500$

Fig. 4. Undifferentiated malignant cells (Oat cell type) in sputum; the small pleomorphic nuclei, scanty cytoplasm, and tendency to spread in lines are characteristic.  $\times 500$

Fig. 5. Adenocarcinoma cells in stomach washings; pleomorphic cells with scanty cytoplasm and prominent nucleoli are features.  $\times 500$

Fig. 6. Malignant cells in blood-stained nipple discharge; the three foamy cells are histiocytes; from a case of early duct carcinoma which proved to have a 3 mm. diameter area of infiltration outside the duct.  $\times 500$





Sputum should be collected on three consecutive days and despatched to the laboratory on the day of collection. Specimens more than 24-hours old are of little value especially if purulent; but refrigeration will delay autolysis to some extent. Specimens collected in the early morning before admixture with food are preferable, and blood-stained specimens are especially valuable. When three specimens have proved negative or when the patient is unable to produce sputum and a suspicious lesion is present, postural drainage and some assistance from a physiotherapist will sometimes produce the desired result.

#### Oesophagus and Stomach

Both X-ray and oesophagoscopy are capable of demonstrating oesophageal growths at quite an early stage, and cytology will rarely be necessary, but early and high growths of the stomach are not so easily seen on X-ray or by gastroscopy. Cytology offers the best hope of early diagnosis but has the disadvantage that the obtaining of the specimen is a somewhat laborious procedure.

Complete emptying of the stomach is a prerequisite to a successful test; for most patients 8 hours' preliminary starvation is sufficient; for those with obstruction, a preliminary period on a fluid diet may suffice, but if this fails it will be necessary to aspirate the night before the test; the forty-eight hours following a barium meal should be avoided.

Fig. 7. Large bizarre malignant cells in ascitic fluid from a case of carcinoma of the colon.  $\times 500$

Fig. 8. Pleural fluid from a patient who had been treated for carcinoma of the breast 8 years previously; the smallest cells are lymphocytes, all the rest are malignant cells growing free in the fluid.  $\times 500$

Fig. 9. Mesothelial cells in pleural fluid from a case of pulmonary infarction; one cell in mitosis.  $\times 500$

Fig. 10. Highly pleomorphic malignant cells in C.S.F. from a case of "sterile meningitis"; the patient had had a "pigmented mole" removed from his back 3 years previously.  $\times 500$

Fig. 11. Seminoma cells in haematocele fluid; the pleomorphic nuclei with irregular chromatin clumping and the ragged cytoplasm are characteristic.  $\times 500$

Fig. 12. Smear of an Astrocytoma; the irregular nuclei are enmeshed in a felt work of glial fibre.  $\times 500$

The patient is instructed to clear nose and throat and refrain from swallowing sputum during the test if possible; with glycerin for lubricant a Kyle's or similar tube is passed to the appropriate mark and the resting juice is aspirated; 300-500 ml. of normal saline is injected, and then the fluid should be aspirated and vigorously re-injected several times with the tube at varying levels and the patient in different positions; introduction of air, to increase turbulence, and massage of the upper abdomen will increase the yield of exfoliated cells. If the first specimen contains more than a trace of food it should be withdrawn and lavage repeated with fresh saline. All specimens should be conveyed to the laboratory immediately for processing, as digestion of the cells can be very rapid; in the event of unforeseen delay neutralisation and refrigeration will slow digestion, but the specimen is unlikely to be of much value after two hours.

The same principles apply to collection from the oesophagus. With the tube passed to 45 cms. the tip should be just projecting into the cardia of the stomach; aspiration is performed while the patient slowly swallows about 100 ml. of saline. Further sampling can be obtained by the quick injection and withdrawal of small quantities of saline with the tube at different levels.

The accuracy of the test depends a great deal on the skill and experience of the operator collecting the specimen. Submucosal and large necrotic growths are least likely to yield positive results, but these cases are easily diagnosed by conventional methods; fortunately the early growths have been found to yield the most cells. The cytology is not difficult in the majority of cases (Fig. 5). Over 80 per cent. accuracy in the malignant cases has been achieved by some investigators, but occasional false positives do occur owing to the remarkable variety of cells that can be exfoliated under different benign conditions. The chief problem is the clinical one of selecting the right group of patients for the test from among the numerous possible candidates.

#### Duodenum, Pancreas, Colon

The difficulties of preparing the patient, collecting the specimen, and recognising the malignant cells which are often scanty and part digested, preclude the use of cytology for these organs at the present time.

### Kidneys and Bladder

Carcinoma of the kidney tends to compress the calyces rather than infiltrate, and rarely exfoliates at an early stage. Tumours of the renal pelvis on the other hand are readily diagnosed by cytology.

The bladder offers considerable scope for cytological investigation, but cystoscopy is usually to be preferred as it affords a direct assessment of the size and nature of the tumour and biopsies can be taken from selected sites. Moreover, treatment is dictated more by clinical evidence of infiltration of the bladder wall than by the cytological classification of exfoliated cells.

However, cytology is a relatively quick procedure which does not require the admission of the patient, there is no risk of infection in the male patient and the result is a reflection of the epithelium of the whole urinary tract. These advantages can be applied in the screening of populations at risk (e.g., dye and chemical workers); there is probably also a place for cytology in the follow up of treated cases and occasionally in the primary diagnosis when cystoscopy has failed or is contra-indicated.

The whole of one specimen or a large aliquot is required; the early morning specimen is best as this is likely to contain the highest concentration of cells. Catheterisation is unnecessary in the male but preferable in the female.

### Prostate

It has been claimed that up to 40 per cent. of all males over sixty have histological evidence of a malignant focus in the prostate, but the significance of this finding is not known. Certainly the prostate frequently presents a histological problem; it is not surprising, therefore, that diagnosis by cytology is not an easy subject, and the significance of a positive is often doubtful. Moreover, the collection of a satisfactory specimen by prostatic massage is not always achieved and many people have misgivings about the wisdom of this manoeuvre.

Smears should be made directly on to slides and fixed wet; a specimen of urine should also be taken immediately after the prostatic massage.

### Breast

A minority of breast carcinomas originate within the duct and may give rise to a blood-stained discharge from the nipple. Cytological

examination of this discharge gives a good chance of a really early diagnosis (Fig. 6).

The fluid should be expressed into a small rubber stoppered tube to prevent drying as quantities may be small; if there is insufficient for collection in this way, smears should be made directly on to slides and fixed wet.

### Buccal Cavity, Nasopharynx and Larynx

Early malignant change can be detected in scrapings from the upper respiratory tract; this is especially true of early symptomless lesions in the mouth, which may not be considered sufficiently suspicious clinically to warrant a biopsy. Dental surgeons have a good opportunity of picking up early carcinomas by this means.

Scraping with a firm slightly edged instrument should be smeared on to slides and fixed wet.

### Skin

Diagnosis of basal cell carcinoma can be quickly and simply confirmed from scrapings, but cytology is of little value in more sophisticated lesions; it is useful, however, for confirming the diagnosis of Pemphigus by the finding of acantholytic cells in the fluid of the bullae (Tzanck Test).

Scrapings should be smeared on to a slide with gentle pressure and fixed wet. Fluid from bullae should be taken with a pipette or wire loop and filmed as for blood but fixed rapidly before drying.

The investigations so far described are literally *exfoliative* cytology and are designed with a view to early detection of a malignant change in an epithelium; but a cytological diagnosis can also be made from aspirated material.

Though rarely contributing to an early diagnosis, aspiration cytology is the only method for fluids, and it is sometimes the method of choice for soft tumours as an alternative to open biopsy.

### Serous Fluids

Unexplained ascites and pleural effusions are not uncommon in hospital practice; the demonstration of malignant cells in the fluid will sometimes save the expense of many other investigations and may even save the patient from an exploratory operation.

Cytological diagnosis from serous fluids is often quite simple but it can be extremely difficult and on rare occasions perhaps im-

possible. Effusions can, of course, be caused by malignant disease without any direct involvement of the serous membrane; the situation can also occur where the membrane is involved but no malignant cells appear in the fluid; the easiest to diagnose are those cases where fragments of the growth, either primary or metastatic, are shed into the fluid (Fig. 7). There are also occasions when the cells grow independently in the fluid as in tissue culture and lose their epithelial character (Fig. 8); these can be particularly difficult to diagnose especially as histiocytes and mesothelial cells can also grow independently in the fluid and undergo mitosis and other morphological changes, which can be confused with malignancy (Fig. 9).

Some malignant cells can be classified (e.g. bronchogenic oat cell carcinoma) and some well differentiated clumps of cells may give a clue as to the probable site of the primary, but often characteristic features are lost in a fluid environment.

Generous (200-500 ml.) specimens should be sent to the laboratory when possible; about one-third by volume of 3.8 per cent. Sod. Citrate should be added at the time of collection to prevent clotting, and any contact with cotton wool should be avoided. Obvious clumps of malignant cells may still be recognisable after 24 hours, but in the difficult fluids a delay of even a few hours may make all the difference between success and failure.

### Cerebro-Spinal Fluid

Surprisingly few intracranial or spinal tumours shed neoplastic cells into the cerebro-spinal fluid, but when protein or cell content is raised it is sometimes worth while examining the centrifuged deposit; particularly is this so in the rare and diagnostically baffling cases of malignant meningitis when demonstration of the cells in the cerebro-spinal fluid is the only way of establishing the diagnosis (Fig. 10).

As much fluid as can be safely withdrawn should be collected in a rubber stoppered tube; cotton wool plugs must be avoided as the fibres interfere with the spreading and examination of the centrifuge deposit.

### Miscellaneous Fluids

Hydroceles (Fig. 11), breast cysts, joint fluids, breaking down lymph nodes and fluctuating swellings of all types are suitable for examination when association with malignancy is suspected. If there is any risk of clotting 3.8 per cent. Sod. Citrate should be added.

### Solid Tumours

Malignant tissue in life is softer and more friable than might be supposed from examination of post-mortem and fixed material and there are few malignant tumours that cannot be aspirated through a wide bore needle. Aspirations will often yield sufficient material for histological sections, but if only minute fragments or semi-fluid material is obtained it can be used for cytological diagnosis. The minimal trauma to the patient and the rapidity (5-7 minutes) with which the diagnosis can be made are of advantage in certain situations.

This technique is particularly suitable for cerebral tumours as they are usually soft and make good smears (Fig. 12); it can be used for rapid diagnosis during the course of an operation.

Though primary bone tumours can be diagnosed cytologically, they are difficult as the diagnosis often rests on the histological pattern of the tumour rather than the types of cell present, and in view of the vital decisions which sometimes hang on the diagnosis, open biopsy is obviously preferable; but when a metastasis is suspected, confirmation by cytology of the aspirate is a relatively simple procedure. Now that the X-ray Image Intensifier is available, the needle can be accurately guided into the tumour. In the event of success there is no delay waiting for the wound to heal before DXR therapy can begin, and in the event of failure, little harm has been done and open biopsy can be proceeded with.

### Conclusion

Great Britain lags behind the rest of the civilised world in the clinical application of cytology. This is partly due to innate British conservatism and partly to a lack of momentum inherent in the financing of the National Health Service. It is difficult for clinicians to recommend the appointment of a cytologist before experiencing the possibilities of the method, yet they are precluded from realising its capabilities until properly staffed cytology departments have been set up. In consequence the majority of cytology in this country is being done rather grudgingly, as a side line, by histologists trained in a different discipline—more different than most people imagine—and it is not surprising that results may sometimes fail to come up to expectations and lead to violent attacks on cytology as a method.<sup>1</sup>

Opposition on economic grounds is more rational, but the cost of diagnosing a case of

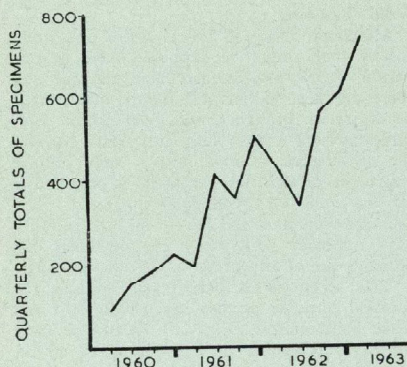


Fig. 13. To show the rate of increase in the number of specimens submitted for cytology since the department was opened in Jan., 1960.

## LAST MONTH

Exams are on at Charterhouse at the moment; the faces of those who have clearly passed are puckered and worried; there is an air of diligence about the place, chiefly due to the fact that the other preclinicals have gone home. Soon it will all be over and late examinees, whatever the result, will be imbibing with their tutors at a party at which, in very British style, hatchets are generally buried. At times like this students are heard wishing the exams were over; yet when they are over it's somewhat of an anti-climax. No more Summer Vacs., only six weeks' holiday a year; the county grant is increased disproportionately to the amount of extra time spent at the Hospital. Instead of being a student of the University, one becomes a medical student proper, the junior member of a team, regarded as the lowest form of human nature. Of course, the advantages offset the disadvantages, but why is it that the medical student has such a low reputation? How much truth is there in stories that tell of the amorality and promiscuity of this student? Why is it that the medical student car owner is quoted the highest insurance premium? And, moreover, what is the nature of the miraculous change that

comes over the student the day he qualifies?

Does the answer lie in publicity? Students in general, and ourselves in particular, seem to be slow in jumping onto the publicity bandwagon. Smooth official statements must be issued at regular intervals from a smooth Central Office for Medical Student Publicity. Official spokesmen must be nominated (any offers Broadsheet?) who can give an opinion to the public on any subject not concerned with medicine. Perhaps a fund could be started for our well-being, maybe with the assistance of the R.S.P.C.A. Away with these rumours of medical student behaviour; in their place a story of charity and kindness to animals.

I have to report the conquest of the crane. "It was there, so it had to be climbed", and it was on 2nd April. One woman and three men (all students?) found the effects of alcohol at 250 feet up much the same as at ground level.

Next month I have a short story to tell entitled, "What one Roman Catholic brought another from America; what would the Pope say?"

I am indebted to Mr. P. Crocker for the photography.

<sup>1</sup> H. E. Vickers, "The Fallacy of Exfoliative Cytology", *Lancet* II, 1962, p. 139.

## FIFTY YEARS AGO

From "A Note on Tobacco-Smoking" by Adolphe Abrahams, B.A., M.B., B.C.

"The smoker can afford to laugh when a more or less direct connection is traced between Sir Walter Raleigh's discovery and his disastrous termination; when quoted cases of 'poisoning' include influenza, tabes and dilation of the heart as sequelæ of each other and of tobacco-smoking; when the soothing weed is given as a prominent cause of sterility; and it is stated that even the perspiration of a smoker being absorbed by his wife can poison the ovum and lead to abortion; whilst the opinion is added that the only women who suffer from cancer are the wives or daughters of men who have indulged to excess in tobacco.

"To the smoker with the habit fully established, tobacco has the following virtues.

"It is a digestive—there is a well-known saying to the effect that you lose half your dinner without the cigar at the end of it—an obvious hyperbole, but it illustrates the great regard in which the after-dinner smoke is held. It is a laxative of a particularly efficacious nature, and it is an intelligent laxative, for it induces a regular matutinal evacuation and does not act outside regulation hours.

"It is a mental stimulant; it is a soporific. And finally it possesses a great many advantages which cannot be directly analysed in the same way as the preceding. Thus a peculiar sense of satisfaction is produced which cannot be referred to any particular sensation, and the sociability that is afforded by indulgence in a common habit is also an advantage which cannot be expressed in a definite formula.

"Perhaps the advantage the smoker would put first if he really believed in it is the antiseptic action of tobacco smoke. Exposure to infection at least provides a good excuse for indulgence, but I very much doubt if any considerable disinfection is afforded save on the lines suggested by an enthusiast—that tobacco is really the best antiseptic in the world, being the finest preservative of the milk of human kindness.

"Certainly tobacco-smoke is a good deodorant, and the unpleasant consciousness of a bad smell may be avoided. It is unnecessary to point out that tobacco may in this way be a two-edged weapon if indifference to a smell exposes one to the influence underlying the smell."

## LETTER TO THE EDITOR

Dear Sir,

I saw with nostalgic regret the not wholly unexpected obituary notice of Foster Moore in the B.M.J. last week. He taught me how to use an ophthalmoscope, and his charming personality, anatomical knowledge, ambidextrous hands and sartorial neatness with his white waistcoats made a lasting impression on me. I did a locum for him as house surgeon to the Eye department while he was convalescing at Hunstanton from what proved to be a renal calculus, under Jessop and Holmes Spicer. I well remember the latter operating in white cotton gloves on account of some

skin trouble.

For many years after that my ways and Foster Moore's lay apart. I next saw him two or three years ago in his beautiful old "Red House" and garden with the Salisbury Avon flowing past. I admired his water-colours and compared experiences of the water-colour game. He was then about and active, and I found him layering carnations in the garden. He told me he still occasionally caught a trout in the river at its foot.

Yours sincerely,

H. E. Quick.

## THE WELL WOMEN'S CLINIC AT ST. BARTHOLOMEW'S HOSPITAL

by BRIAN MEASDAY

Resident Assistant Accoucheur and Senior Lecturer in Obstetrics and Gynaecology

THE CITY OF LONDON CANCER DIAGNOSIS CLINIC or "Well Women's Clinic" was set up in this Hospital in January, 1960. The original aim was a pilot study of the value of exfoliative cytology of the cervix on a voluntary population living or working within the City boundaries. It is hoped that some of the lessons learnt in the present clinic will have an application in a nation-wide prophylactic Public Health service if this comes about.

The present clinic at St. Bartholomew's Hospital sets out to offer cervical cytology and gynaecological examination to women over the age of 35 years working or living in London. It has had relatively little advertisement, yet there seems to be a demand for its services. Leaflets offering the scheme are exhibited in the rest rooms of business houses and companies with a reasonable number of female employees who, if they wish to attend, may telephone for an appointment. Their reason for attending and a brief menstrual history are elicited, and the breasts, abdomen, and pelvis are then examined together with the collection of material from cervix and posterior fornix to provide cytological smears.

The fundamental basis of cytology is that epithelial surfaces desquamate cells which can be recognised in suitably stained preparations, and in fact malignant epithelial surfaces desquamate generally to a greater extent than do normal epithelia. Thus cast-off malignant cells can be recognised in the preparation if they are there.

The present-day concept of the earliest recognisable origin of carcinoma is the intra-epithelial, or in situ lesion which, whilst it may persist as such before invasion of the underlying stroma for a long time, perhaps up to 15 years, will almost certainly become invasive eventually.

The results of treatment by whatever means of invasive carcinoma of the cervix are roughly proportional to the extent of the disease at the time treatment is begun. However, there is an enormous difference in prognosis in early

stages of this disease depending upon whether diagnosis precedes penetration of the basement membrane or not, and with the aid of cytological tests advantage could be taken at once to effect the vital early diagnosis. The condition can then be cured by extirpation, which should have negligible mortality and morbidity.

Diagnosis in Stage 0, when the condition is clinically inapparent, must be made by a diagnostic aid such as is offered at present by exfoliative cytology or possibly in the future by enzyme tests. Such tests detect the presence of atypical cells and they must be followed up by cone biopsy of the cervix and careful histological examination to determine whether the lesion is in situ or invasive. Definitive treatment can then be planned and in the case of intraepithelial lesions, heroic surgery and radiotherapy can be avoided. The outcome of present-day knowledge and opinion is that carcinoma of the cervix could become a virtually 100 per cent. curable condition given early diagnosis at the in situ stage.

There is now ample evidence of the value and accuracy of exfoliative cytology, but largely owing to the cost of providing such services they have been slow to evolve in this country. McLaren and Attwood report the use of the technique in gynaecological outpatients in Birmingham over the past 10 years but such facilities are uncommon and particularly backward in London. In gynaecological outpatients McLaren expects to pick up 3 or 4 cases of carcinoma in situ per 1,000 patients screened, together with one case of clinically inapparent but actually invasive carcinoma of the cervix. The numbers from our clinic at St. Bartholomew's Hospital are still too small to have any significance. We have so far seen just over 1,000 patients, 72 per cent. of whom came for a "check up" and were symptom free. Yet there have been 5 positive smears. Subsequent investigation by cone biopsy and serial section of the material removed has shown that 3 were associated with

carcinoma in situ, one with microscopically invasive carcinoma, and one with a frank clinical carcinoma—no credit this last to cytology, but perhaps a credit to the existence of a clinic which the patient attended, because of its impersonality, in preference to her own doctor.

If such screening could be applied to a population there should be an associated decrease in the incidence of actual invasive carcinoma, as the pre-invasive cases are removed and cured. This is exactly what is suggested by the British Columbia experiment in which about one-third of the female population over 20 years old had smears taken over a 12-year period. There was an associated fall in incidence of invasive carcinoma of the cervix from 28.4 cases per 100,000 women in 1955, to 19.7 in 1960.

The clinic at St. Bartholomew's Hospital does not set itself up as a model for the future. The essential need is for expansion of pathological facilities so that anyone in practice can obtain expert opinion on smears they themselves have taken—the general practitioner in his surgery just as much as the consultant in out-patients; although, admittedly, it would be pleasant as a first step to see the average gynaecological clinic capable of this additional investigation.

Stanley Way reports a survey made by 2 general practitioners with his collaboration in which personal approach by the family doctor produced a high response and of a total of 626 patients examined 2 invasive and 4 intra-epithelial carcinomata were discovered. If, as Way suggests, after an initial negative smear it is unnecessary to take further smears for several years, surely this volume of work could come within the bounds of an expanded pathological service, and surely too, any prophylactic public health scheme must employ the family practitioner as its central pivot. The practitioner who wishes to employ this test can learn the essential technique very quickly and easily. If there is to be selection of cases it should be towards those without symptoms, particularly gynaecological ones. It must be remembered that a negative smear does not exclude carcinoma of the genital tract and in particular that this diagnostic test is not nearly so reliable in cases of carcinoma of the uterine body as it is in cervical cancer. Thus cases of post-menopausal bleeding will continue to require diagnostic curettage.

However, the test can usefully be directed towards selected groups, for example, the diabetic, and the woman who has already suffered a carcinoma elsewhere in her body.

### The Reward of Routine Gynaecological Examination alone

The work of the Well Women's Clinic has not been solely concerned with taking cervical smears. The opportunity of making a pelvic examination has been taken and a variety of pathology, both benign and malignant, has been disclosed. This clinic therefore has had a secondary reward which rivals that of cytology itself and which is solely due to a routine examination of the supposedly healthy without employing any special diagnostic tests.

Briefly, 12 patients with postmenopausal bleeding presented in the first 1,000 cases seen, and, emphasising an earlier point, were all advised to undergo curettage. One patient who had had negative smears taken on one occasion before curettage was found to have an adenocarcinoma of the corpus uteri and this was subsequently treated by extended hysterectomy. Like the patient with a clinical cervical carcinoma she preferred to attend a clinic rather than her own doctor, and this may have resulted in her attending earlier than she would otherwise have done.

Four ovarian tumours were diagnosed, usually in patients without symptoms, and one of these was of "borderline" malignancy. Exfoliative cytology is not going to assist the early diagnosis of carcinoma of the ovary which, although less common than carcinoma of the uterus, is even more insidious. Gynaecology badly needs a means of diagnosing ovarian carcinoma at an early stage, but at present such diagnosis must rely upon clinical judgment; the woman whose ovarian tumour is found almost accidentally at an examination, routine or otherwise, is indeed fortunate.

Fibromyomata were detected on 70 occasions and were either of such size or else associated with sufficient symptoms to warrant advice to undergo hysterectomy in 21 cases.

Cervical polypus was noted and removed in 71 patients. 47 had no symptoms, and all the polypi were benign, but it is likely that these polypi would eventually produce symptoms and require treatment.

Cervical erosion was noted on 94 occasions, 73 times in the absence of symptoms. Trichomonas vaginitis (17 cases), atrophic vaginitis (16 cases) and candidal vaginitis (3

cases) have been diagnosed clinically and confirmed bacteriologically. One case of **diabetic vulvitis** and one of **leukoplakic vulvitis** have been seen together with miscellaneous other gynaecological conditions. So far we have only seen one florid case of carcinoma of the breast.

If it were possible for the family doctor to examine his "healthy" female patients there would be a similar worthwhile result, and the impetus for him to do so might well come through the advent of a national cytology service. Alternatively, the possibility of diagnostic clinics attached to gynaecological units and run in existing departments by general practitioner clinical assistants able to take cytological smears, would be worth investigating.

Routine ante-natal and dental care, together with mass radiography, have become accepted as of obvious benefit to the community, yet

they were in a position similar to that of cytology to-day when they first began. In McLennan's opinion, with careful propaganda, many women would come to regard prophylactic cytology and a routine examination as little different from an annual visit to the dentist.

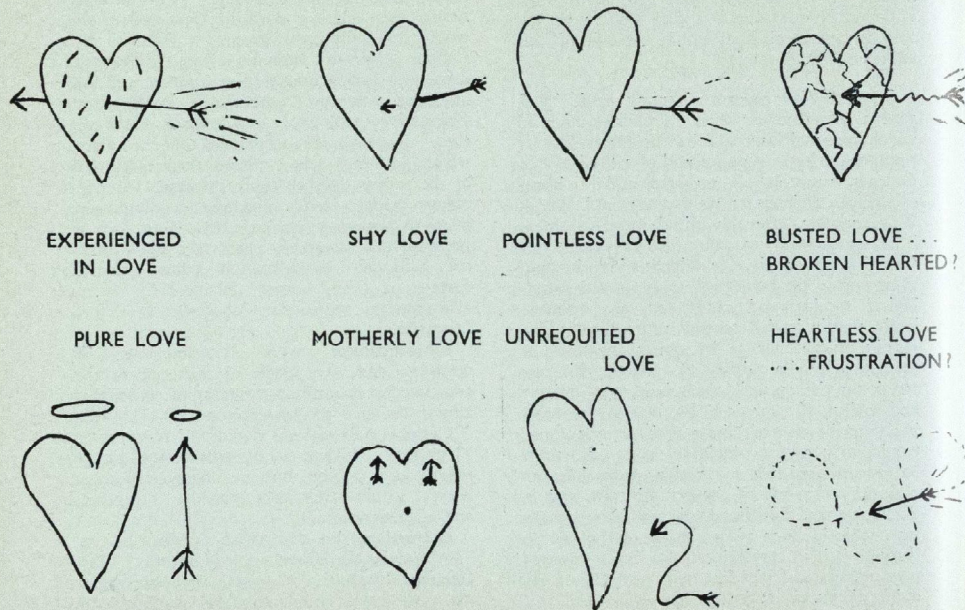
This could surely be done without raising the incidence of cancerophobia, which is the argument generally proposed for doing absolutely nothing in the matter to-day.

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## AFFLICTIONS OF THE HEART

(according to D. Lloyd)



## THE NEW CHARTERHOUSE BRANCH LIBRARY



(photo by the Photographic Department)

A **PRE-CLINICAL LIBRARY** existed in Charterhouse before the war, and was growing into a useful collection when, in 1941, it was completely destroyed by fire. After the war the nucleus of a new library was housed in temporary quarters, at first in the Department of Anatomy, and later in a prefabricated hut which was originally planned to last for five years, but in actual fact functioned for considerably longer. Accommodation for books and readers has been quite inadequate for many years, but after patient planning and re-planning, the premises opened in December, 1962, should suffice for a lengthy period.

The Reading Room on the ground floor seats 92 readers, and is well-lit by a combination of tungsten and strip lighting. The ten alcoves contain suspended shelving, with tables and chairs for four readers in each bay. Forty individual tables and chairs, and twelve easy chairs around "occasional" tables complete the seating. Clinical and pre-clinical textbooks and a selection of periodicals

are provided in the 74 cases, and there are small reference and historical collections. Heating is supplied by full-length radiators situated along the two sides where full-length windows provide the natural lighting; warm air is also wafted through ventilators in the pillars. Cork composition tiles cover the floor, and venetian blinds are provided for all the windows.

The Librarian's Room is situated at the end of the Reading Room opposite the issue desk, and is suitably furnished with desks, chairs and shelving. Internal and external telephones are provided, maintaining contact with the Store and the Staff Room, the latter being situated between the Reading Room and the Research Library now being erected.

The sub-basement beneath the entire length of the library premises is devoted to two Stores for library purposes, separated by a corridor. One is connected to the Reading Room by means of a narrow spiral staircase situated behind the issue desk, which is also

equipped with an electric book-lift terminating in the Store. This also houses a Bandavolop Photocopier, an electric duplicator and a microfilm reader. Both stores contain steel shelving, there being a total of 231 cases with 1,595 shelves. One store will be used to relieve pressure on the Main Library in the Hospital, which is being reorganised. The Charterhouse Branch Library can house approximately 50,000 books, about double the present stock of the two libraries.

This Library is now open in the evenings, Monday to Friday, until 10 p.m. and is well-used both by pre-clinical and clinical students. Clinical textbooks have been purchased, the stock has been brought up-to-date, and the collection is being re-catalogued and re-organised. The most-used books are arranged by subject at one end of the Reading Room, and the general periodicals, bibliographies and abstracts are situated at the far end, while journals devoted to special subjects are shelved in the alcoves. A guide to the location of journals and a key to the arrangement of the room, will be found on the notice board above the catalogue. Current journals are also temporarily displayed near the catalogue.

Current textbooks and reference books are not available for loan, as readers are encouraged to use the library during the evening. There is no point in opening the library if books are not available to readers. Former editions of textbooks, and journals, together with certain other material not marked as reference books, can be borrowed. Readers are reminded that they have access to both the Charterhouse Branch Library and the Main

Library in the Hospital. The latter is particularly well-equipped bibliographically and historically. Both libraries are adequately staffed, and students and staff are invited to use the information services available for queries relating to the library, bibliographical tools and research, the preparation of papers, proof-reading, and for general information.

Material can be photocopied in each of the libraries, and details of this service are provided in a leaflet obtainable from the library staff. Books can be obtained from certain other libraries by means of co-operative lending schemes, but it must be appreciated that the postal charges (both ways) must be borne by the individual or by his department. We can assist in the compilation of bibliographies; we can trace the location of periodicals not housed in the Hospital and College; in many cases we can obtain books and journals from other libraries. But this latter does depend, of course, upon our being able to find a library that stocks the required item, and is also willing and able to lend it. Certain large medical libraries, depending upon the subscriptions of members for their existence, will not lend to other libraries. In actual fact, few items cannot be procured from one source or another, but tracing certain references, and locating libraries that will lend them, does take time. Readers can sometimes gain access quite readily, for reference purposes, to other libraries, and the Patent Office, Science Museum Library and the University of London, for example, house extensive collections of scientific literature.

## ABERNETHIAN SOCIETY

On 14th February, Dr. Felix Mann addressed the Society on "Acupuncture". I will not write anything on this intriguing lecture since the Editor hopes to print an article on Acupuncture by Dr. Mann in a future edition of the Journal.

On 21st February, Professor O. L. Zangwill, an experimental psychologist, gave a very high powered lecture on "The Problem of Cerebral Dominance". After discussing the classical work on laterality, hemiplegia and aphasia and disabusing his audience of the

belief that left-handed people usually have a "dominant" right hemisphere (apparently less than half of them do), he described work that he had done himself on people suffering from brain injuries sustained during the war.

This work seemed to show that the right side of the brain was more important for higher visual function and the recognition of spatial relationships whereas the left temporal region seemed more involved with speech and memory.

Professor Zangwill described the difficulties

of reconciling this modern work with the older concept of cerebral dominance and the difficulties for any theory of the demonstration of the relatively slight disability produced by hemispherectomy in the first year of life.

On 21st March, Professor Woodruff of Edinburgh University addressed a large audience on "Transplantation of the Human Kidney".

Professor Woodruff pointed out that 7,000 people die in Britain each year from renal failure, consequent on glomerulonephritis, pyelonephritis, hydronephrosis or polycystic disease. Many of these lives could be saved by renal transplantation but there are many problems which limit the application of this method.

These problems are technical, immunological, the difficulty of storing kidneys in a viable state until required for grafting, and the legal and ethical problems raised by the procedure.

The surgical technique consists of placing the donor's left kidney (which has a longer renal vein) in the recipient's right iliac fossa, the renal artery being anastomosed end-to-end to the divided internal iliac artery or end-to-side to the external or common iliac artery, the renal vein end-to-end to the external iliac vein and the ureter to the bladder. The mastery of this technique was shown by the fact that there had been 26 out of 27 successful renal transplants between identical twins.

Professor Woodruff devoted most of his lecture to the problems of immunological intolerance (graft rejection). This arises because tissues grafted from one person to another provoke the formation in the recipient of antibodies which eventually effect the destruction of the transferred tissue. However, this does not occur when:—

- (a) The donor and recipient are antigenically similar (as in identical twins).
- (b) When the transplanted tissue is avascular, e.g., cornea.
- (c) When the transplant is inaccessible to recipient cells.
- (d) When the capacity of the recipient to reject the transplant is modified by constitutional abnormalities, such as uraemia, or by experimental and therapeutic procedures—these include the use of ionising radiation, steroids, alkylating agents and antimetabolites.

Professor Woodruff then described a series of his cases, not involving identical twins, in

which attempts were made to overcome the immunological difficulties.

The ABO, Rh, MN, S, P, Kell, Duffy, RS and Lutheran blood groups of the potential donors were compared with those of the future recipient. The donor was chosen who had the greatest degree of compatibility of blood groups, provided that he also was in good health, and had excellent renal function which was shared equally between two kidneys of normal size and form.

The great liability of irradiated patients to infection was combated by complete isolation of the patient and extremely stringent aseptic precautions for from four to six weeks after operation.

His first patient was prepared with 150 rads of whole body irradiation with a later dose of 50 rads, combined with local irradiation of the spleen and graft site prior to transplantation. This resulted in gross leucopaemia and such severe thrombocytopenia that she was transfused with platelets from more than 160 donors in the course of 10 days. The graft began to function and the patient was doing reasonably well, when she suddenly developed enterococcal septicaemia and died 30 days after the transplantation operation.

Professor Woodruff decided that whole body irradiation was too dangerous even with the aseptic precautions and later cases were prepared by local irradiation of the spleen, graft site and regional lymph glands and administration of an anti-metabolite Imuran (6-[(1-methyl-4-nitro-5-imidazolyl)thio]purine) starting on the morning of the operation and with a daily dose which after the first week was varied with the leucocyte and platelet counts and the transplant function. A large number of haematological, biochemical and serological tests were performed at frequent intervals and if there was any evidence of graft rejection, e.g., a sustained fall in urinary output, an increase in blood urea nitrogen, a decrease in creatinine clearance or an increased urinary excretion of albumen, the dose of Imuran was increased or supplemented by intravenous Actinomycin C or Prednisone in high dosage. (The latter drug Professor Woodruff found very useful in one case in which the grafted kidney became swollen and tender and the patient was febrile and had proteinuria. All these symptoms and signs disappeared within 24 hours of the administration of prednisone.)

Professor Woodruff has had two failures. One, already mentioned, died from septi-

caemia from a gut bacterium, consequent on a radiation-induced leucopaenia, the other from the toxic effects of Imuran which produced gross ulceration of the gastro-intestinal tract eight weeks after operation. At autopsy the two transplanted kidneys showed no sign of graft rejection. Thus both patients died of over-treatment although the second was grossly debilitated before the operation. However, he has also had four successes, some of them still

on a maintenance dose of Imuran, and one who remained hypertensive, alive and well after a bilateral nephrectomy. Since no patient is considered for operation until they are virtually moribund, these four successes demonstrate the true value of the technique.

Professor G. W. Taylor gave the vote of thanks following this enthralling lecture.

D.S.T.P.

## GENETICS IN THE MEDICAL CURRICULUM

by MICHAEL HOLLINGSWORTH

Lecturer in Zoology, St. Bartholomew's Hospital Medical College

**S**TUDENTS reading for the M.B. B.S. Degree of the University of London are not required to have a knowledge of medical genetics. Any knowledge they do have is acquired through their own and their teacher's interests in the subject. Yet it is not unreasonable to expect a practising physician to be able to tell anxious parents what the probability is that a second child will have retinoblastoma, when their first-born has already had its eyes removed in order to save its life; to understand why massive doses of antibiotics are more and more frequently being found unable to cope with bacterial infections; and to be able to recognise the significance of aberrations in the dermatoglyphic patterns of new-born infants.

An Expert Committee on Human Genetics of the World Health Organisation has considered\* the present status of human genetics, its importance to the practising physician and its role in the modern concept of public health. It found that the average medical graduate's knowledge of medical genetics in all countries of the world was seriously incomplete. It pointed out that owing to the popularisation of science in the press, on radio and on television, the medical graduate is in danger of knowing less about certain medical topics than his more intelligent patients. This would be a disturbing state of affairs, and, if not prevented, may result in a loss of confidence in physicians by their patients.

\* *Wld. Hlth. Org. tech. Rep. Ser.* 1962, 238

More time is now being devoted than a generation ago to the study and treatment of diseases that are directly or indirectly genetically determined. This is because the proportion of patients with acquired diseases has abruptly decreased. Few people die as a result of infections in the technically advanced countries owing to the discovery and application of anti-bacterial drugs. The infant mortality rate is low and the expectation of long life is high. Yet many become ill with psychiatric disorders, diseases of the vascular system and with cancers. It is becoming generally realised that differences in susceptibility to these diseases is partly, at least, owing to inborn differences between individuals, that is, to genetic differences.

Genetics is advancing with an ever-increasing velocity, many of the recent discoveries being of direct importance in medicine.

It is now known that the chromosomes—the bearers of the hereditary material—contain a genetic code, and that this code is responsible for the production in cells of the many thousands of different kinds of enzymes essential for the normal functioning of the body. Errors in the code result in abnormal functioning and possibly disease. For example, sickle cell anaemia occurs in individuals who have an error in the code responsible for the production of just one of the 300-odd amino acids that constitute the haemoglobin molecule.

The consequence of errors in the genetic

code can frequently be detected in a patient by means of biochemical tests. Several new discoveries of this kind are described every year. Investigations are aimed at discovering which metabolic pathway has been blocked by the non-production of the normal enzyme. In some cases the consequences of this blockage can be overcome and the patient "cured" of his disease by adjusting his environment. For example, damage to the brain and the consequent mental deficiency in phenylketonurics can be lessened by prescribing a diet low in phenylalanine. This disease is caused by an error in the genetic code which results in the non-production of the enzyme that normally metabolises phenylalanine to tyrosine. The phenylalanine which accumulates in the blood is de-aminated by the kidneys and the product, phenylpyruvic acid, can be detected in the urine. Further, phenylpyruvic acid can also be detected in the urine of individuals heterozygous for this error in the genetic code. This means that physicians are in the position of being able to advise parents, both of whom are carriers of this trait, of the consequences of having children.

Eight years ago a new technique, which enabled chromosomes to be seen widely separated from each other and not clumped together as had previously been the case, revolutionised human cytology. It was discovered that man had a diploid number of 46 and not 48. Since this initial fundamental discovery deviations from the normal complement of chromosomes have been identified as the cause of a seemingly ever-increasing number of syndromes, the aetiology of which had previously been a mystery.

The cytological aberrations concern both the autosomes and the sex-chromosomes. Of the abnormalities of the autosomes, trisomy for chromosome 21 is the best known. It is the cause of mongolism, or Down's syndrome, as it is now frequently called in deference to our Asian colleagues. Trisomy for other autosomes is the cause of other well-characterised syndromes. The sex-chromosome abnormalities have been of interest because they have demonstrated the important role of the Y chromosome in human sex-determination. Individuals with a normal complement of autosomes, but with only a single X chromosome and no Y chromosome are abnormal females (Turner's syndrome), and individuals with two X chromosomes plus a Y chromosome are abnormal males (Klinefelter's syndrome). Mosaic individuals have been known in other

animals for some time, but their discovery in man was something of a surprise. Human sex chromosome and autosome mosaic individuals, who frequently exhibit only a partial manifestation of the syndromes, are being discovered with increasing frequency. Readers of the *Lancet* will have noticed that hardly a week goes by without a report of these and of other important discoveries in the field of human cytology.

The study of the effects of the use and misuse of ionising radiations has been the concern of man ever since Muller discovered in 1927 that X-rays can produce lethal mutations. A recent report of the United Nations\* states that the risk of hereditary defects from medical irradiation for diagnostic and therapeutic purposes in technically advanced countries is about three times as great as the risk from the fall-out from atomic tests. Any dose of radiation, however small, causes genetic damage, and the Report expresses the view that all unnecessary radiation exposure should be minimised or avoided entirely. It believes that the dosage of radiation in medical diagnosis and treatment could be considerably reduced by the use of improved techniques without loss of medically important information.

Immunogenetics, which began with the problems associated with blood transfusion, haemolytic disease of the newborn, and with skin-grafting, has come to the fore with the recent well-publicised attempts at organ grafting between genetically different individuals, a technique which, until now, had only been possible between identical twins.

The interaction between nature, or heredity, and nurture, or environment, in the development of almost all human traits is now recognised. Exceptions, where the environment has no modifying effect on expression of heritable traits are the blood group antigens, the haemoglobins and the specific enzyme defects. The value of studies on identical twins, which necessarily have identical genotypes, in elucidating the problem of the interaction between heredity and environment has been fully exploited. But even here there is a possibility of confusion, for identical twins are frequently exposed to a more uniform environment than are genetically different individuals.

Confusion about the respective roles of heredity and environment is mostly with respect to

\* Report of the U.N. Scientific Committee on the Effects of Atomic Radiations, 1962. Official Records of the General Assembly of the U.N., 17th Session Supp. 16 (A/5216).

characteristics determined, in part, by many genes, each of which has a similar effect but which cannot be individually identified. These are the so-called quantitative or metric characteristics. For example, some argue that the observed differences between individuals in human intelligence and in body constitution are almost completely determined genetically. Whereas others believe that intelligence and body constitution of all but the mentally defective and the deformed can be increased at will, given an adequate educational system and nutrition. This controversy is clearly expressed in the modern eugenics movement. Eugenists are very concerned about the current increase in the rate of growth of the human world population and also with the supposed consequence that the average intelligence of the future human population will steadily decline. They infer this from two observations; firstly, intelligence is a heritable trait, and secondly, the less intelligent people are more fertile, that is, they have larger families than do the more intelligent people. However, many geneticists believe this argument to be fallacious. Positive eugenics, as well as negative eugenics, has been proposed as a means of avoiding catastrophe. Such measures include selective human breeding and artificial insemination with semen from selected genetically desirable human males. The arguments against eugenics are as strong as those for. Medical practitioners will be able to make extremely valuable contributions to this discussion when they are better equipped to do so.

The teaching of genetics to medical students should be in two parts; the first covering the elementary or general aspects of genetics as applicable to all living organisms, but with particular reference to man; the second covering the advanced or specialised clinical aspects.

The elementary course should consist of lectures, demonstrations and practical work on:—

- (a) The nature of the genetic code and the mechanism of protein (enzyme) synthesis. Their relationship to inherited characteristics. The study of human pedigrees.
- (b) The physical and chemical structure of chromosomes. Chromosome behaviour. Normal and abnormal human cytology.
- (c) The interaction between genotype and environment and the development of normal traits. Normal variation between individuals with

respect to both continuously and discontinuously variable characteristics.

- (d) Gene and chromosome mutations, and the genetics of populations.
- (e) The genetics of bacteria and viruses, in particular in relation to the development of resistance to antibiotics by the former, and the possible relationship between infection by the latter and the development of cancers.

Effective use of this knowledge can only be made by incorporating it into the curriculum of medical students.

The elementary genetics given at school is a totally inadequate substitute, for not only is the teaching of genetics in schools out-dated, being restricted to a consideration of Mendel's "two laws", and also not being medically orientated, but there is as yet no adequate elementary text-book on modern genetics, and, further, modern genetics is not always in the curriculum of biology teachers.

Students entering medical schools through a first-year course are, in some respects, in a more advantageous position than those entering direct into 2nd M.B., for they are more likely to have received a good grounding in the elements of modern genetics. However, this advantage is offset by the disadvantage of requiring these students to reach an "A" level standard in biology in three terms from nothing, for many have had no previous training in biology, or in any science for that matter, before entry to a Medical College. This task is almost impossible for both teacher and student.

Thus modern genetics cannot at present be effectively included in the medical curriculum before entry to 2nd M.B. Perhaps the best solution to this difficulty is to extend the 2nd M.B. course by not less than one term. This additional term could also accommodate the other recent advances in the biological sciences, for example, in cell physiology and in anthropology, to name but two, that are close to modern genetics and therefore relevant to modern medicine, which could with benefit be included in the medical curriculum. The curriculum in this additional term should, of course, be subject to examination.

The more advanced course would consist of lectures and particularly demonstrations of the applications of genetics to human diseases and of genetic counselling. It would be carried out in close collaboration with the clinical depart-

ments. Use would be made of special clinics where clinicians and geneticists could discuss with groups of students the several aspects of the disease in question. Such a course would best occur late in a student's clinical years.

However, it is not possible to include genetics in the curriculum of medical students at present for there is a lack of qualified teachers, that is, medical graduates with post-graduate experience in genetics. This difficulty could be partially and temporarily removed by employing non-medical geneticists from outside

institutions on a part-time basis to give the pre-clinical course. The clinical course could be given by existing members of the staff of the medical school who have a practical interest in genetics. In the years to come, when the necessity for the inclusion of genetics in the medical curriculum becomes generally recognised, we shall see the establishment of Departments of Medical Genetics in all Medical Schools, not only in this country, but also abroad.

## SPORTS NEWS

29th MAY

One of the most pleasant events in the Bart's calendar is the occasion on which members of the staff, students, girl-friends and nurses all enjoy the amenities of Chislehurst on a summer's afternoon. Sports Day is one of those rare occasions when everyone can happily indulge their own whims whether by running a three-mile race, leaving a tankard to putt the shot or just airing a new summer frock. Chislehurst with its pleasant turf and surrounding trees provides the ideal setting. An excellent tea is served in a marquee and the pavilion is an admirable venue for the Dance in the evening.

It is indeed unfortunate that as more and more social events are crowded into June, Sports Day should suffer from lack of support. Last year, the View Day Ball on the previous night, a regatta and two Bart's weddings prevented many people from getting down to Chislehurst, and it was decided that it was time a big effort was made to restore Sports Day to its former popularity. Therefore the Athletics Club and the Students' Union have combined to run Sports Day. The Dean has consented to preside over the Sports and Matron is being asked to present the prizes. The date has been arranged for WEDNESDAY, 29th MAY, and efforts have been made to prevent it conflicting with other activities. There is no teaching normally on a Wednesday afternoon so a full turnout of students can be expected. Besides the programme of athletic events less serious events will be arranged. It is hoped that a Croquet Tournament or Match will be staged as well as a skittle alley and darts competition. In the evening there will be a dance in the pavilion to Ted Carden and the Cambridge Five. Transport to and from Chislehurst will be provided.

The success of Sports Day depends on the attendance, so come and support the efforts of the organisers and enjoy yourselves at Chislehurst on Wednesday, 29th May.

### THE CHESS CLUB

The five matches this year have been attended with more success as far as points are concerned. We were conceded a walk over in both the 2nd team match against Woolwich and the first team match against the Northern Polytechnic which were arranged for January. Having beaten Royal Free Hospital 2nd team 4-2 in February, we lost our first team match

against King's College and were conceded a further 2nd team walk-over against Royal Hall.

Arrangements are now under way for the inter-hospital Championship Cup which we shall do our utmost to retain.

We are most grateful to the enthusiastic response that we have received from a large number of preclinical members.

### CROSS COUNTRY

#### St. Bartholomew's Hospital Cross Country Club Visit to Dublin

To conclude their exceptional season Bart's Cross Country Team arranged to go to Dublin as a separate team from United Hospitals to race with them against Trinity College (Dublin University), Belfast University, Bangor University and Aberystwyth University. We approached this match with high hopes, but in the week before the race N. Pott had to withdraw owing to unfortunate family circumstances, R. Thompson was rendered athletically ineffective by a recurrent attack of gastric 'flu and D. Tunstall-Pedoe was swallowing Broxil and nursing a septic toe.

This "almost Welsh and Irish Universities Championship race" produced a field of 55 runners. The course was 6 miles of fast parkland, a joy to run on after the frozen plough and three-foot snowdrifts cross country runners have had to contend with this season.

After a very fast start Whittonne of Dublin went into an early lead, followed by Napier and Brotherhood (U.H.) and Foxton (Bart's) with Littlewood and Tunstall-Pedoe (Bart's) gradually working their way up the field.

Foxton and Brotherhood both faded slightly and after about one mile Whittonne had a hundred yard lead over Littlewood, Napier and Tunstall-Pedoe.

Whittonne, who runs 70 miles a week, seemed to have an impregnable lead at 3 miles since he then led Littlewood by nearly 200 yards. Littlewood, in chasing him, opened up a gap on Napier (U.H.) and Tunstall-Pedoe.

Littlewood closed gradually and at 5 miles passed Whittonne, running into a strong wind, and went on to win by 9 seconds, although Whittonne tried desperately to catch him over the final half mile. Behind them Napier, the U.H. captain, found he could not hold Tunstall-Pedoe, who finished very fast on the final mile of road, so that Bart's had the first and third men home.

Foxton, in finishing tenth, had for him a poor run and was beaten for the first time this season by Brotherhood (U.H.) who was eighth. Roger Sanders (31st), Fred Hardy (39th) and Robert Hale (44th) completed the Bart's scoring six.

#### Results

	mins.	secs.
1. P. Littlewood (Bart's) ...	31	59
2. Whittonne (Dublin) ...	32	08
3. D. Tunstall-Pedoe (Bart's) ...	32	38
4. Napier (U.H.) ...	32	50
10. T. Foxton (Bart's) ...	33	35

	mins.	secs.
31. R. Sanders (Bart's) ...	35	21
39. F. Hardy (Bart's) ...	36	14
44. R. Hale (Bart's) ...	37	14

#### Teams

1. Dublin ...	76
2. U.H. ...	109
3. Aberystwyth ...	109
4. Belfast ...	121
5. St. Bartholomew's Hospital ...	128
6. Bangor University ...	171

(Scoring a full U.H. team, including Bart's men: 43 pts., a winning score.)

Thus Bart's did not do as well as they had anticipated. However, it should be said that had Nick Pott been able to come and even finished only 10th, Bart's would have scored 94 points and come second to Dublin University (the vanquishers of both Oxford and Cambridge at rugby football).

However, nothing can detract from P. Littlewood's magnificent run, possibly his last for Bart's Cross Country team, in which he pulled Whittonne to within 2 seconds of the Dublin University Undergraduate Course record, and Tunstall-Pedoe, in finishing third, demonstrated that he has the necessary strength for a very successful season on the track.

20th February, 1963. London University Cross Country League Division I. Run over 5½ miles of frozen ground at Peter-sham.

	mins.	secs.
1. J. Farrington (U.C.) ...	27	45
{ P. Yates (U.C.) ...	27	45
3. T. Foxton (Bart's) ...	28	24
4. N. Pott (Bart's) ...	28	28
5. P. Littlewood (Bart's) ...	28	48
6. D. Tunstall-Pedoe (Bart's) ...	29	03
7. 8. 9. (University College)		
27. F. Hardy (Bart's) ...	31	25
31. R. Sanders (Bart's) ...	31	54
51. R. Pickard (Bart's) ...	34	43

#### Teams

1. University College ...	328
2. St. Bartholomew's Hospital ...	310
3. King's College ...	270

This was the last league race of the season and the final positions were:

1. University College ...	1588
2. St. Bartholomew's Hospital ...	1486
3. King's College ...	1393
4. Imperial College ...	1318
5. L.S.E. ...	957
6. Guy's Hospital ...	918

Bart's have now finished second in the University League Division I for the second year in succession, but this time to University College rather than Imperial College.

This will probably be the vintage year in Bart's cross country running with P. Littlewood, N. Pott, T. Foxton, and D. Tunstall-Pedoe all running in the London University 1st Team in a year when London University has been stronger than for many years. P. Littlewood, N. Pott and R. Pickard will be hard to replace, but if the team manages to retain its enthusiasm it should do just as well in U.H., if not University circles, next year.

During the season R. Pickard and D. S. Tunstall-Pedoe have been awarded their United Hospitals Colours, and T. Foxton is to be congratulated on the award of a London University Half Purple and D. S. Tunstall-Pedoe on the award of a Team Purple.

### MOTOR RACING CLUB

In the past month five events have been entered. Jim Robinson, with his Lotus XI, competed in a sprint at Brands Hatch

on 17th March, in which he finished a very creditable 4th. Ted Carden has competed in 3 sprints and one race meeting in his Turner. On 17th March, at a sprint at Blackbushe Aerodrome, after setting the fastest time in practice it rained and he was then pushed into third place by 2 cars fitted with special "Rain Tyres". On 24th March, the Turner was entered in its first race, The John Davy Trophy race at Brands Hatch, where it finished 5th in its class despite many bugs occurring in the car. A sprint at Sealand Aerodrome on 30th March brought its first class win and a third place was attained on 31st March at a National Sprint Meeting at Debden Aerodrome.

### LACROSSE CLUB

London University Inter-Collegiate Tournament.

St. Bart's v. Q.E.L. Won 2-1.

St. Bart's v. Goldsmith's. Won 7-1.

St. Bart's v. Westfield. Won 4-3.

Unfortunately only four colleges entered the tournament this year. Owing to weather conditions, this was our first match since Christ-

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mas. Everyone was badly out of training and therefore extremely pleased that we won the Cup for the second time running.

**Bart's v. Q.E.L.** By half-time in the first match the team was feeling exhausted, but the defences continued to play well and Bart's just managed to win.

**Bart's v. Goldsmith's.** We were on top throughout this game, most of the work being done by the attacks.

**Bart's v. Westfield.** After winning two matches we only had to beat Westfield to win back the cup again. The final was a slow gruelling game. Three minutes before time Bart's led 3-2, but Westfield equalised one minute later. Determined to win, Bart's won the draw and the attacks made a final effort. Luck was with us and the winning goal was shot seconds before the whistle.

Team: B. Anderson, E. Bohn, J. Clarke, G. Darch, A. Glew, A. Grieg, D. Leyton, U. Onians, J. Pitt (capt.), R. Sutton, S. Williams.

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# ST. BARTHOLOMEW'S HOSPITAL JOURNAL



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### EDITORIAL

The occasion on which Gordon Watson and Frherington Smith were able to race their new cars round the Square while they were on the House must seem to many to belong to the uncluttered and nearly forgotten past, but in fact is within living memory of some Bart's men. In those days it was the custom for members of the staff, arriving in carriage and pair, to make one majestic sweep round the fountain before finally drawing up at the entrance to their wards. The introduction of parking meters round the Hospital has led to such a pressure on space within the precinct that for a while it seemed that this custom was about to be re-introduced; but, through necessity, for although the square was now filled with cars, their owners were frequently seen driving round and round—this time in search of a few square feet of parking space which, if found, was usually far from their destination. The situation was not helped by the invasion of frustrated motorists who had little connection with the Hospital—it has been known that travelling salesmen used the Hospital as an excuse for free parking while they went their rounds on foot or that a Bummarree could show a bleeding finger as an excuse for parking safely on the site, avoiding the hazardous business of paying sixpences to meters, or larger fines to the coffers of the local Borough.

A search for alternative arrangements for increasing the available space by making use of part of the redundant Smithfield Goods Depot revealed that Fleet Street had unfortunately thought of it first. Thus the only relief to the limitation of parking within the precinct to one hundred cars is the opening of the new park at Charterhouse. This will help temporarily those affected by the new arrangements who do not want an even longer walk to street-parking in an area which is so far free from meters. However, the long-term provision of facilities under the new Out-patient block and in the Cock Lane site will probably come after the present relief is made unusable by building and new parking restrictions. The problem is one which affects in one way and another all residents in Central London and which requires early solution, remembering the mistakes of the brave new L.C.C. estates which sometimes appear to have been designed without realising the gradual and inevitable approach on the universal "family-car" age—these blocks even now stand surrounded by a tightly-packed mass of motor-cars.

The posts of Assistant Editor and Assistant Manager to the Journal fall vacant in June. Applications should be sent to the Editor by 14th June. Candidates for the post of Assistant Editor should include a specimen Editorial.