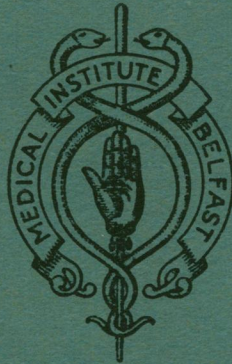


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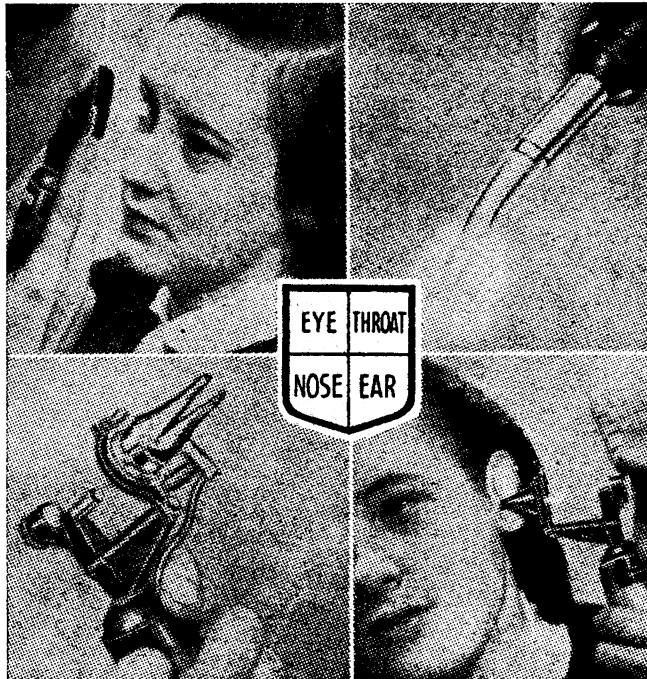
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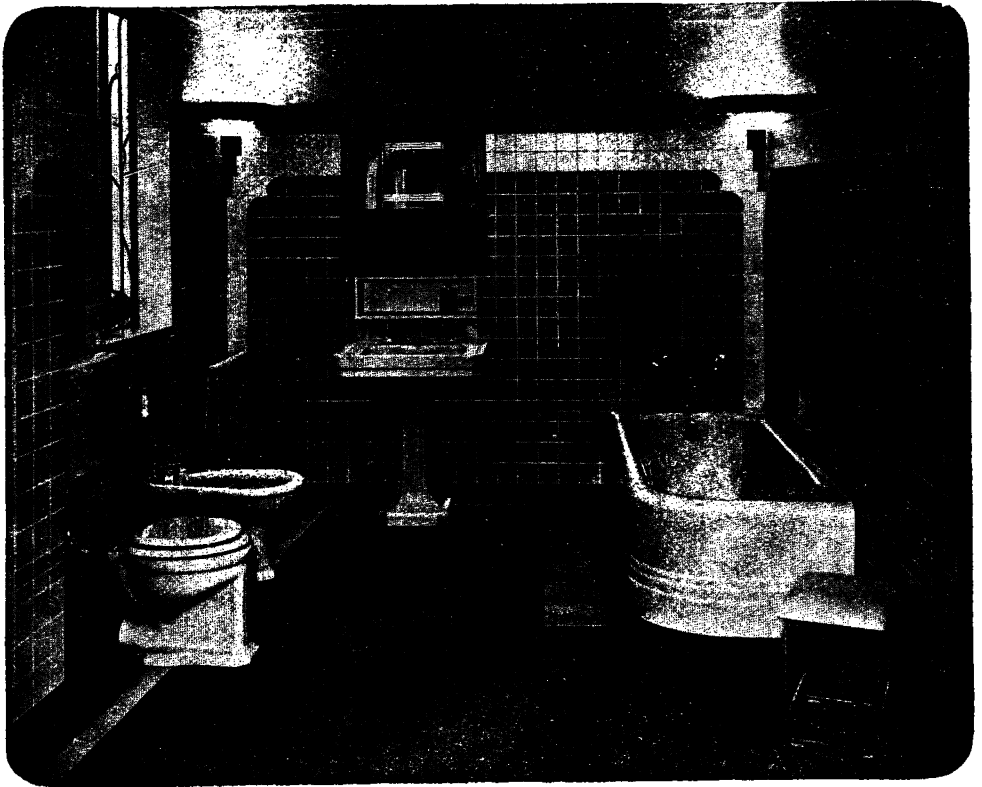
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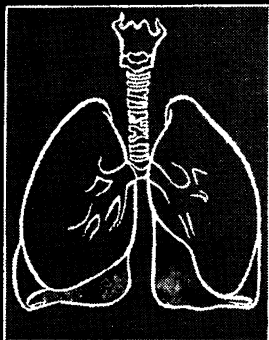
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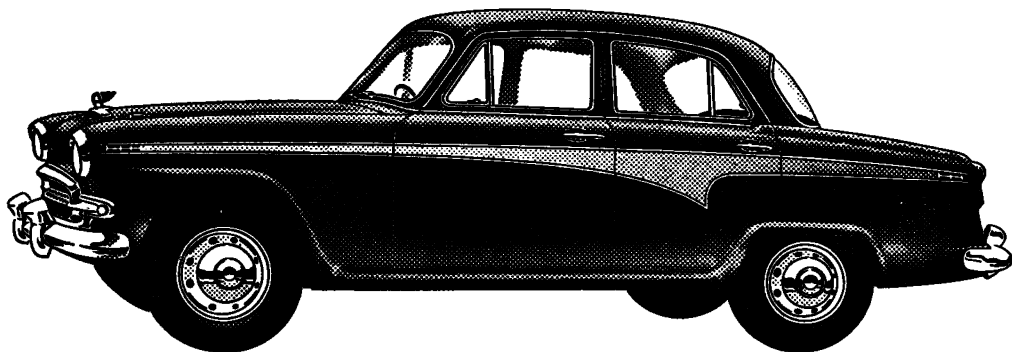
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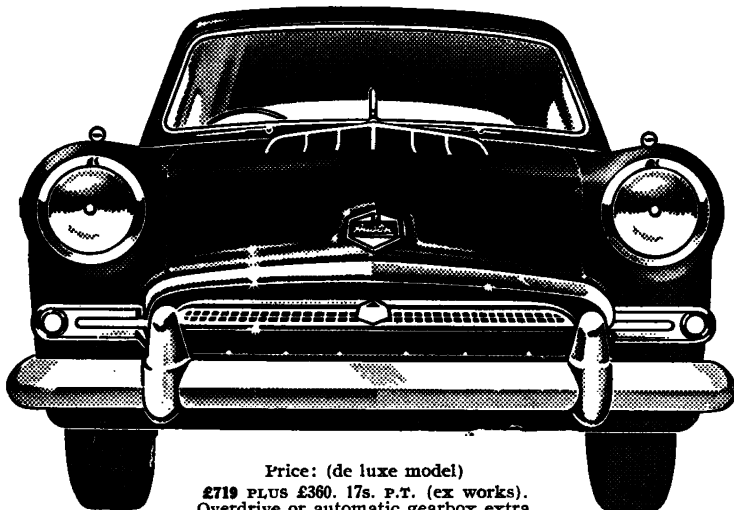
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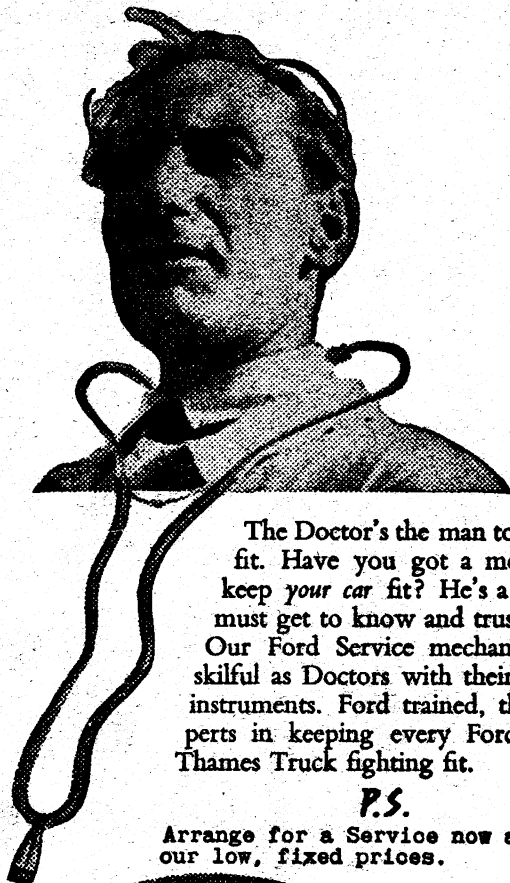
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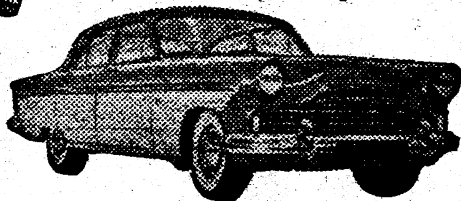


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CONTENTS

No. 1 : May, 1958

	PAGE
PÆDIATRICS IN THIS CHANGING WORLD. Kenneth H. Tallerman, M.C., M.D., F.R.C.P. - - - - -	1
DIAGNOSIS AND TREATMENT OF ADRENOCORTICAL INSUFFICIENCY. D. A. D. Montgomery, M.B.E., M.D., M.R.C.P. - - -	12
WILLIAM SMELLIE. Gavin Boyd, M.B., F.R.C.S.(ED.), F.R.C.O.G. - -	29
POST-TRAUMATIC EPILEPSY AND BRAIN-STEM SIGNS. J. H. D. Millar, M.D., M.R.C.P.(LOND.) - - - -	37
THE LEUCOCYTE COUNT IN WEIL'S DISEASE. C. Cotton Kennedy, M.A., D.M.(OXON) - - - - -	43
THE VIRUS REFERENCE LABORATORY. G. W. A. Dick, M.D., D.SC., F.R.C.P.E., and D. S. Dane, B.A., M.B.(CANTAB.) - - - -	47
THE VIRUS REFERENCE LABORATORY (REPORT). H. G. S. Murray, M.B.(BELF.), D. S. Dane, M.B.(CANTAB.), and G. W. A. Dick, M.D.(EDIN.) - - - - -	53
SUPERIOR VENA CAVAL OBSTRUCTION COMPLICATING CARCINOMA OF BRONCHUS. S. D. Killough, M.B., B.CH., D.(OBST.)R.C.O.G., and J. H. Jones, M.B., B.CH. - - - - -	61
HOSPITAL BED ACCOMMODATION REQUIREMENTS OF A REGION. A. T. Elder, M.D., PH.D., D.P.H. - - - - -	64
PITUITARY CHORISTOMA: A SURVEY OF THIRTY CASES. David L. Freedman, M.B., B.CH., B.A.O. - - - -	73
CLINICAL TRIAL OF BUTYLPHENAMIDE IN THE TREATMENT OF CERTAIN VARIETIES OF RINGWORM. J. Martin Beare, M.D.(BELF.), M.R.C.P.(LOND.) - - - - -	79
AN EVALUATION OF DEXTROTEST METHOD OF BLOOD SUGAR ESTIMATION. R. Armstrong, M.B. - - - - -	86
REVIEWS - - - - -	11, 28, 42, 52, 85, 89-100

No. 2 : November, 1958

BURDEN'S GHOST. C. H. G. Macafee, M.B., F.R.C.S.(ENG.), F.R.C.S.I., F.R.C.O.G.	101
REST AND EXERCISE. R. J. W. Withers, M.D., M.CH., F.R.C.S.E. - -	117
6-METHYL PREDNISOLONE IN THE TREATMENT OF RHEUMATOID ARTHRITIS. D. A. D. Montgomery, M.B.E., M.D., M.R.C.P. - - -	130
RECENT ADVANCES IN CARDIOVASCULAR DISEASE. A. Schott, M.D. (HEIDELBERG), M.R.C.S. - - - - -	137
MILIARY AND MENINGEAL TUBERCULOSIS. Lilian V. Reilly, B.SC., M.D., D.P.H. - - - - -	146
TUBERCULIN SENSITIVITY IN CO. FERMANAGH, N. IRELAND, 1952-55. W. T. Warmington, M.D. - - - - -	158
SIMULTANEOUS ADMISSION OF TWO SISTERS. Edward S. Lamont, M.B., D.P.M. - - - - -	162
SEROLOGICAL INVESTIGATION OF UNIVERSITY STUDENTS. H. G. S. Murray, M.B.(BELF.), and J. J. McAlister, A.I.M.L.T. - - -	165
REVIEWS - - - - -	129, 161, 168-180

CONTENTS

	PAGE
BURDEN'S GHOST. C. H. G. Macafee, M.B., F.R.C.S.(ENG.), F.R.C.S.I., F.R.C.O.G.	101
REST AND EXERCISE. R. J. W. Withers, M.D., M.CH., F.R.C.S.E. - -	117
6-METHYL PREDNISOLONE IN THE TREATMENT OF RHEUMATOID ARTHRITIS. D. A. D. Montgomery, M.B.E., M.D., M.R.C.P. - - -	130
RECENT ADVANCES IN CARDIOVASCULAR DISEASE. A. Schott, M.D. (HEIDELBERG), M.R.C.S. - - - - -	137
MILIARY AND MENINGEAL TUBERCULOSIS. Lilian V. Reilly, B.SC., M.D., D.P.H. - - - - -	146
TUBERCULIN SENSITIVITY IN CO. FERMANAGH, N. IRELAND, 1952-55. W. T. Warmington, M.D. - - - - -	158
SIMULTANEOUS ADMISSION OF TWO SISTERS. Edward S. Lamont, M.B., D.P.M. - - - - -	162
SEROLOGICAL INVESTIGATION OF UNIVERSITY STUDENTS. H. G. S. Murray, M.B.(BELF.), and J. J. McAlister, A.I.M.L.T. - - -	165
REVIEWS - - - - -	129, 161, 168-180

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CONTENTS

	PAGE
BURDEN'S GHOST. C. H. G. Macafee, M.B., F.R.C.S.(ENG.), F.R.C.S.I., F.R.C.O.G.	101
REST AND EXERCISE. R. J. W. Withers, M.D., M.CH., F.R.C.S.E. - -	117
6-METHYL PREDNISOLONE IN THE TREATMENT OF RHEUMATOID ARTHRITIS. D. A. D. Montgomery, M.B.E., M.D., M.R.C.P. - - -	130
RECENT ADVANCES IN CARDIOVASCULAR DISEASE. A. Schott, M.D. (HEIDELBERG), M.R.C.S. - - - - -	137
MILIARY AND MENINGEAL TUBERCULOSIS. Lilian V. Reilly, B.SC., M.D., D.P.H. - - - - -	146
TUBERCULIN SENSITIVITY IN CO. FERMANAGH, N. IRELAND, 1952-55. W. T. Warmington, M.D. - - - - -	158
SIMULTANEOUS ADMISSION OF TWO SISTERS. Edward S. Lamont, M.B., D.P.M. - - - - -	162
SEROLOGICAL INVESTIGATION OF UNIVERSITY STUDENTS. H. G. S. Murray, M.B.(BELF.), and J. J. McAlister, A.I.M.L.T. - - -	165
REVIEWS - - - - -	129, 161, 168-180

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Burden's Ghost

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Professor of Obstetrics and Gynaecology, The Queen's University, Belfast

Presidential Address to the Ulster Medical Society, 16th October, 1958

IN 1906 the founder of antenatal care, Dr. J. W. Ballantyne, read a valedictory address to the Edinburgh Obstetric Society. It took the form of a hypothetical, highly imaginative telephone conversation with the unknown President who should occupy the Chair thirty-four years later, in 1940. As it happened the normal activities of the Edinburgh Society were suspended during the war years. But in 1946, Professor R. W. Johnstone, then Professor of Obstetrics at Edinburgh, was the President and delivered a valedictory address. In it "evoking," to quote his own words, "Ballantyne's spirit without unduly disturbing his rest," he conducted his predecessor's ghost round the Edinburgh Medical School of 1946.

"Of the altruistic instincts," Osler once said, "veneration is not the most highly developed at the present day; but I hold strongly with the statement that it is the sign of a dry age when the great men of the past are held in light esteem."

Sharing this view, I should like to follow Professor Johnstone's example and evoke the spirit of my predecessor, William Burden, the first professor of Midwifery in the Queen's College of Belfast, and show him how the seeds he had sown had grown into flourishing trees.

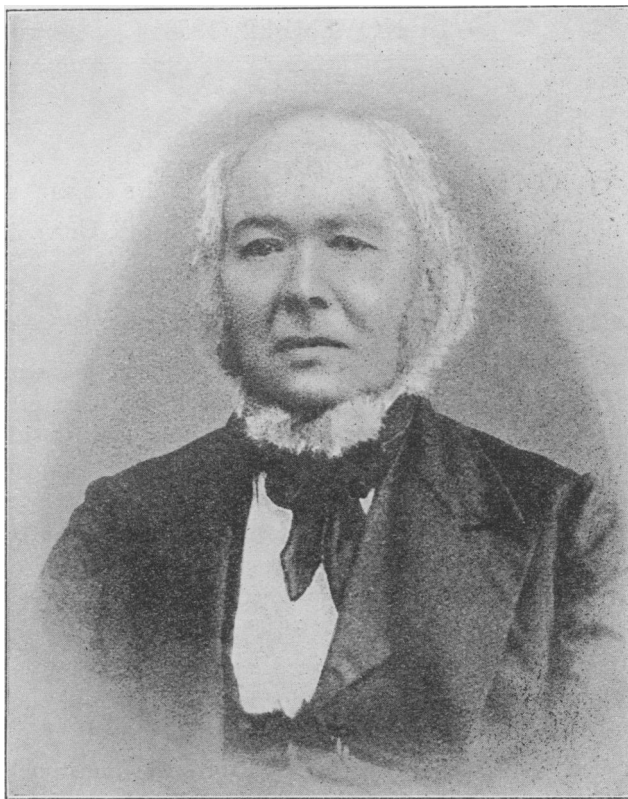
To most of our Fellows and Members the name of William Burden perhaps conveys little. The only child of Dr. Henry Burden, he was born in India in 1798. On the death of his father and mother when he was 12 years old, he came to Belfast to live with his three aunts, the Misses Burden. After being apprenticed to business, he studied medicine under Dr. James McDonnell in the old General Hospital, and then proceeded to Glasgow where he gained his M.D.

Returning to Belfast about 1830, he was elected a member of the Belfast Medical Society, the forerunner of this Society. For a short time he practised in Newry, In

1833, however, he settled in Belfast and in 1838 was appointed physician to the Belfast Maternity Hospital, a position he retained until 1870.

From 1840 to 1849 he lectured on midwifery and the diseases of women and children in connection with the Faculty of Medicine of the Belfast Academical Institution, and in 1848 he was elected President of that Faculty.

In 1849 he was translated to the newly-established Queen's College to be the first occupant of the Chair of Midwifery, which he occupied with distinction for eighteen years. He died in 1879 when he was 81 years of age.



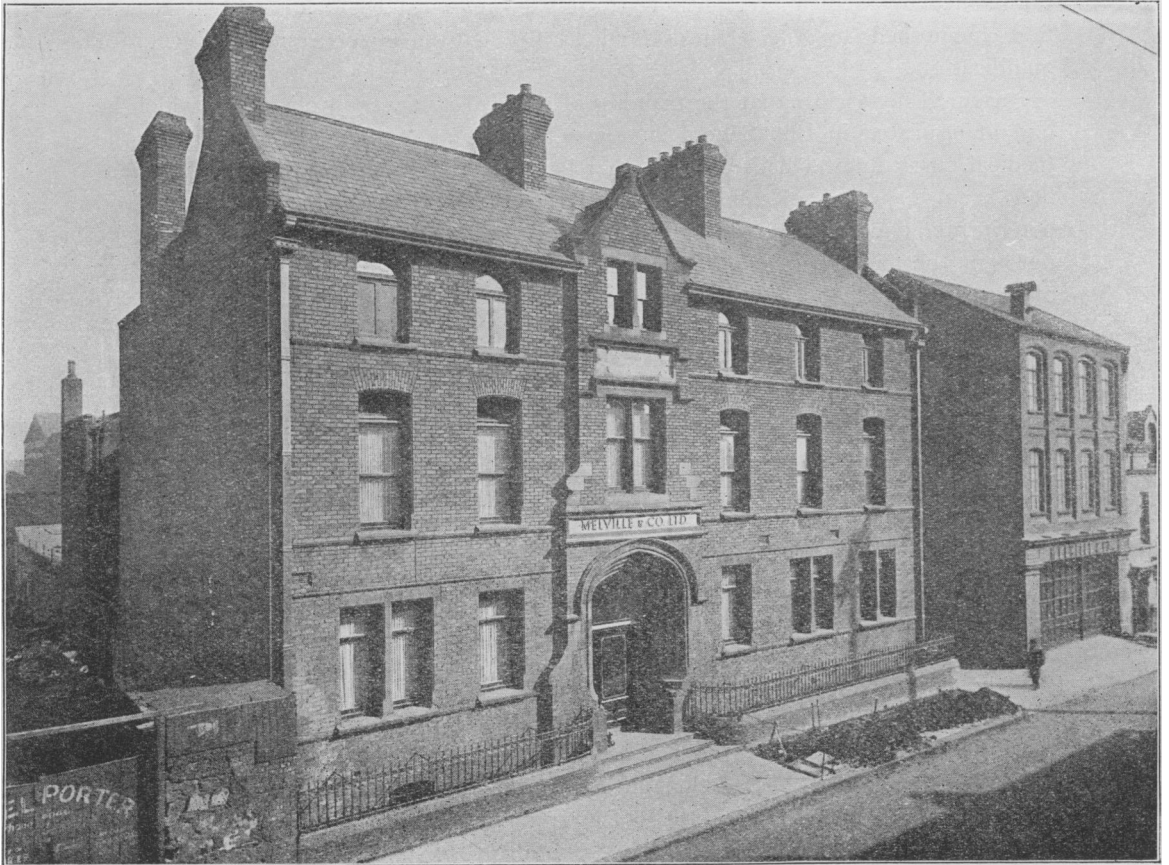
Professor WILLIAM BURDEN, M.D.
Professor of Midwifery 1849-1867

Evoking Burden's spirit—I trust “without unduly disturbing his rest,” I conducted my predecessor's ghost from Clifton Street via Townsend Street to the present site of the Royal Maternity Hospital.

The site of the old hospital in Clifton Street is now occupied by business premises and therefore my visitor could not orientate himself immediately. However, glancing at the other side of the street, he recognised the Charitable Institute. Ghostly visitors probably do not have the capacity of turning purple with rage or

they have realised the futility of doing so. "The Committee that ran that place in my time gave me a lot of trouble," was his only comment. To understand the reason for his comment we must look at the state of affairs in Burden's time.

The Medical Faculty at Queen's College had been founded in 1849, and after much trouble Professor Burden obtained permission in 1852 from the Ladies' Committee of the Hospital to admit medical students to the practice of the



Incorporated Belfast Maternity Hospital

Hospital. In 1854 three students were courageous enough to defy the difficulties associated with obtaining instruction in practical midwifery.

To-day the training of medical students in any branch of medicine is taken for granted and it is therefore hard for us to appreciate the difficulties Professor Burden had to overcome.

In the first place, the Charitable Society, the ground landlords of the Hospital, claimed an increased rent because the Hospital, having been converted into a

training school for medical students, was being used for a different purpose than that for which it had been founded. After a bitter and rather acrimonious struggle, Professor Burden managed to defeat the far from charitable Society.

Secondly, it was in 1852 that an ordinance of the Queen's University of Ireland was passed governing the curriculum for the teaching of obstetrics. With the compiling of this ordinance Burden probably played a great part, but there was no statutory body in existence to enforce the ordinance, as the G.M.C. was not established by Medical Act until 1858. It was not until 1886 that midwifery was first mentioned by the Genral Medical Council as a necessary subject for qualification.

I assured my visitor that the training of medical students in obstetrics which he had inaugurated in this School is now a flourishing and important part of the medical curriculum. I had to admit that between 1867 and the present time there had been a period of thirty-four years when the teaching of students had deteriorated and had almost ceased; one of his successors in the Chair of Midwifery not being on the staff of the Hospital, and another being prevented by the jealousy of his colleagues from doing his full duties.

It was not until the years from 1921 to 1945, when the late Professor C. G. Lowry occupied the Chair, that teaching as we know it to-day was, or could be, revived.

Passing from Clifton Street to Townsend Street I drew my visitor's attention to the building which housed the hospital from 1904 to 1933. "Why did the Committee move from Clifton Street to this crowded site?" he asked. "It was against the wishes of the medical staff," I said, "but largely because the Charitable Society wished to remove them from Clifton Street." "That Society again interfering?" said Burden's ghost.

"With the passage of time and the development of the teaching school," I added, "this Hospital in Townsend Street proved to be unsuitable in every respect. My immediate predecessor, Professor Lowry, aided by the then Professor of Medicine, Professor Lindsay, worked hard to remove the Hospital and amalgamate it with the main teaching hospital, which they succeeded in doing in 1930." "Did you say that the Professor of Medicine helped?" said my visitor. "The physicians were obstructionists in my time." "Professor Lindsay," I said, "was a man of long vision for which I and my successors must ever be grateful."

If I may say so to this Society, I feel that Professor Lindsay never received the credit which was his due, but I look forward to hearing some future president correct this omission.

Arriving at the Royal Maternity Hospital I felt that my visitor required some explanation of the location of the Hospital. "In 1903," I said, "the old General Hospital, which you knew in Frederick Street, was closed, the patients and staff being moved to the hospital which you now see in front of you. The name of the Hospital was also changed to the Royal Victoria Hospital."

Taking him to the roof of Bostock House, the new Nurses' Home, I showed him the geographical arrangement of the Royal Victoria Hospital, the Children's Hospital and the University Departments. "I could never have believed," he said,



Royal Maternity Hospital, Belfast

“that such a close association would have been possible. It must be the envy of other teaching schools.”

As we entered the Royal Maternity Hospital he was astonished at the number of nurses to be seen in the corridors and wards. He reminded me of his difficulty in getting nurses trained and that he had had to admit the first one with the status of a medical student against the wishes of the Committee.

The first nurse trained under this scheme was a Mrs. Hamill, who was charged a student's fee, and she had to be instructed alone as she was not allowed to attend lectures given to medical students. It has to be remembered that at this time there were no lady medical students. To have mixed the sexes in a class would really have been too much for an early Victorian committee to have permitted. Smiling, my visitor said, “Do you remember what the Ladies' Committee had to say about this?” The Ladies' Committee had objected to Professor Burden's action and had written: “It was with considerable reluctance that the ladies revived the old

custom of admitting nurses into the hospital, as it had generally been productive of great annoyance." In the second place, they regarded the charging of a student's fee as an imposition and the tuition as unnecessary. "They know it is impossible a woman could require or would be capable of receiving so much instruction."

At the period to which I refer the training of midwives was in chaos. The fully qualified midwife as we know her to-day was non-existent, and to gather some idea of what the midwife of Professor Burden's time was like it is necessary to refer to Charles Dickens' description of Sarah Gamp. It was not until 1858, that is, about the time Professor Burden was training Mrs. Hamill, that the Obstetrical Society of London was founded. This Society in 1870 pressed for the compulsory examination of midwives and for legislation to restrain practice by untrained women. From 1872 to 1905 the Obstetrical Society of London conducted voluntary examinations and issued certificates of proficiency. Then in 1905 the Central Midwives' Board was established, and the midwives' roll at that time contained 22,308 names of whom 12,521 were so-called *bona fide* midwives holding no certificate. It is hard to believe that the last of these *bona fide* midwives disappeared from the practising Roll as recently as 1947. Therefore, in training midwives when he did, William Burden was indeed a man of foresight.

At this stage we approached the antenatal ward and I reminded my visitor of his own instructions to his Practical Midwifery class :

"To visit his patient once a week, or as often as necessary, and to mark the date of each visit on the recommendation paper."

I pointed out to him that had he detailed his reasons for advising his students to visit their patients once a week he should have been regarded as the inaugurator of antenatal care in the British Isles. "What is antenatal care?" he asked. "From my knowledge of Latin I know what 'ante-natal' means, but your use of the term seems to indicate that you are referring to an established system."

"For the past forty years," I replied, "it has been recognised that the expectant mother requires supervision from the earliest weeks of pregnancy. Nowadays she attends either her family doctor, a hospital or public health antenatal clinic where she has routine regularly spaced examinations." "Is this really necessary?" he asked. "Most certainly," I said. It is a most important branch of preventive medicine because it permits us to recognise and correct at an early stage some of the complications of pregnancy and establishes an atmosphere of confidence between the patient and her attendants."

I told him that while the antenatal outpatients is an important function of any maternity hospital, the provision of antenatal in-patient accommodation is now regarded as a most vital part of the hospital work.

The first hospital bed to be set apart for the antenatal investigation and treatment of disease in the expectant mother was in Edinburgh in 1901 in response to the plea of Dr. J. W. Ballantyne. The first antenatal clinic to be established in 1910 was by Dr. T. G. Wilson, later Sir George Wilson, in Adelaide, South Australia, closely followed by one at Boston, U.S.A. I was glad to be able to tell

my visitor that the first antenatal clinic in Ireland was started by Professor C. G. Lowry and Mr. H. L. Hardy Greer in 1921 in the old hospital at Townsend Street.

Ballantyne instituted antenatal care with the object of improving the prognosis for the unborn and newborn child. Since Ballantyne's time the scope of antenatal care has widened enormously, and to give my ghostly visitor some idea of the problems facing every obstetric department I took him round the antenatal ward.

As we passed from bed to bed I showed him cases of diabetes, cardiac disease, antepartum hæmorrhage, patients with hypertension and, of course, the ever present pre-eclamptic toxæmia. "But what of eclampsia?" enquired Burden's ghost. I had to admit that while it had been hoped that antenatal care would eliminate this dread complication it is still an important cause of maternal mortality. I told him that even now we do not know the cause of pre-eclamptic toxæmia, and yet eclampsia can be prevented by rigid prenatal supervision. In view of this fact it was depressing to have to add that in England and Wales between 1952-1954, 110 women died from eclampsia, a preventable disease.

I had also to admit to my visitor that in Northern Ireland in 1957 39 women died from diseases due to pregnancy or childbirth, of which 10 died from toxæmia. "It is depressing," I said, "to think that since your time we have advanced such a short distance towards discovering the cause of this complication."

I next took him to the bed of a patient aged 25 who had been a diabetic for ten years. This patient interested him immensely. "Why," he asked, "is she still alive, and how did she manage to conceive?" "I presume she must be a very mild case or that she and her baby will die before fullterm." "She certainly should not die," I said, "because we now have got the hormone insulin which was discovered by Banting and Best in 1921." "What is a hormone?" he asked. "A hormone," I explained, "is a chemical substance secreted by an endocrine gland into the blood stream, and insulin is the hormone secreted by cells in the pancreas which controls the metabolism of starch and sugar." "We rarely saw diabetics who were pregnant," said my visitor.

In Burden's time pregnancy in a diabetic patient was rare either because the patient died before the child-bearing period of life or because she was sterile as the result of genital atrophy. In 1882 Matthews Duncan reported a maternal mortality rate of 60 per cent. among diabetic mothers. In 1909 Whitridge Williams in America reported a maternal mortality of 27 per cent. in such patients, while to-day this figure would be infinitesimal.

Unfortunately, the results for the baby have not improved in the same way. I told him that nowadays one terminates the pregnancy somewhere between the 35th and 38th week, frequently by Cæsarean section, to avoid the risk of an intrauterine death in the latter weeks of pregnancy. Even with insulin therapy and a well stabilised patient the foetal mortality is still about 25 to 30 per cent.

He was surprised to see so many cases of cardiac disease lying in the antenatal ward. "You seem to be running a medical ward in a maternity hospital," he remarked. I astonished him still further when I explained that in severe cases of

mitral stenosis the pregnant patient can be operated on and have the stenosed valve stretched even when presenting signs of cardiac failure (2.7 per cent.). By this time he appreciated the close co-operation necessary between physicians, surgeons and obstetricians in the treatment of medical complications associated with pregnancy, and how this co-operation is facilitated by various departments being close together.

TABLE 1.
PLACENTA PRAEVIA.

AUTHOR			Date	Maternal Mortality %		Foetal Mortality %	
Simpson	-	-	1844	...	30	...	60
Berkeley	-	-	1936	...	7	...	59
Browne	-	-	1939	...	5	...	54
Grant (R. M. H.)	-	-	1955	...	0	...	12

He was surprised to see a number of cases of antepartum hæmorrhage lying in the antenatal ward. In some of these cases the cause of the hæmorrhage was a placenta prævia, and he wondered if it was safe to leave them undelivered. We have to remember that in 1844 Simpson stated that the maternal mortality associated with this complication was 30 per cent. and the foetal mortality 60 per cent. It is possible that in Burden's time, when the treatment was bipolar version, the maternal and foetal mortality was probably the same. In 1936, Berkeley showed that the position had changed to the extent that the maternal mortality was only 7 per cent. with a foetal loss of 59 per cent. Three years later Professor F. J. Browne showed that the situation was much the same, with a 5 per cent. maternal and a 54 per cent. foetal loss.

"To-day," I said, "by postponing any treatment to as near full term as possible, and delivering a large percentage of cases by Cæsarean section, the foetal loss is about 10 to 12 per cent., while the maternal loss is under one per cent."

Time did not permit us to discuss many of the other patients when we passed on our way upstairs to the Lying-in Ward. He was delighted with the cheery sunlit wards and with the babies lying in the cots at the side of the mothers' beds. Although none of the mothers was walking about, he was surprised to hear that normally the patient gets up on the second or third day, but was astonished to find that only 50 per cent. of the mothers were breast-feeding. "How do you manage to get wet nurses for all the babies?" he said. In his curriculum for medical students the importance of the wet nurse is stressed. For example, the following appeared as a subject for one of his lectures :

"The management of children after birth, washing, dressing, food, etc., and the choice of a wet nurse, and the treatment of such accidents as take place at this period, or soon after."

Indeed, a question on the choice of a wet nurse frequently appeared on the midwifery paper of that time. During Professor Burden's regime the following

announcement appeared for several years in the Annual Report of the Maternity Hospital :

“A register of wet and monthly nurses is also kept for the convenience of the public and is open to the inspection of subscribers for the payment of one shilling and to all others on payment of half a crown.”

It is hard to appreciate to-day the difficulties encountered if the mother died or could not breast feed her baby. The many proprietary foods on the market to-day were not available in Burden's time and even later. Even feeding bottles are a relatively modern invention. Reading the opening chapters of *Dombey & Son* may make us realise that many babies must have died of starvation or gastro-enteritis from infected milk if a wet nurse could not be secured or afforded.

TABLE 2.

			Per 1000 Total Births		Per 1000 Live Births
1730 - 1749	-	-	600*	...	—
1838 - 1839	-	-	159	...	—
1871	-	-	153	...	—
1951	-	-	—	...	30
1956	-	-	—	...	24

*Died before 2 years.

That this was so is reflected in the infant mortality figures in various epochs. At the period 1730 - 1749, 600 out of every 1,000 children born died before reaching the age of two years. In 1871, 53 babies of every 1,000 died in the first year of life, whereas in 1956 the mortality was 24 per 1,000 live births.

Informing him that we no longer employ wet nurses, and promising to show him the milk preparation room, I pointed out a baby who had had an exchange transfusion. “What do you mean by that?” he asked. I briefly explained to him the importance of the Rhesus factor. He was amazed to hear that icterus gravis, hydrops foetalis and hæmolytic anæmia of the newborn are all related to the same factor. “We used to think that hydrops foetalis was due to syphilis,” he said. I told him that by removing a large proportion of the erythroblastotic baby's blood and replacing it with suitably typed blood, most of the cases of icterus gravis and almost all of the cases suffering from hæmolytic anæmia can be saved.

From the Lying-in ward we passed to the Labour suite and he was amazed to find that it was relatively quiet. This feature made him wonder if all the patients in labour had been given morphia. He was intensely interested to learn that the duration of labour had shortened considerably and that nowadays any patient in labour for much over 12 to 14 hours must be reviewed as she has to be regarded as abnormal.

“Why is the duration of labour reduced?” he asked. “There are probably many factors,” I replied. “There is a different psychological approach to pregnancy and

labour to-day as compared with earlier times, and improved antenatal care, nutrition and anæsthesia have all contributed towards this reduction."

By this time he appreciated the value of antenatal care in helping one to anticipate or avoid complications, and was delighted to hear that the destructive operations, so frequently required in his day, are rarely necessary. He was surprised at the extensive use of Cæsarean section in cases such as placenta prævia and disproportion, cases that in his time were dealt with by podalic or internal version.

"What of the forceps operation?" he asked. "I am not sure that I approved of those instruments, as they often damaged the baby," he remarked. "Forceps are still frequently used," I said, "in fact, the forceps rate in this hospital is about 15 per cent., but they are only used when the head is deep in the pelvic cavity or actually on the perineum." I told him that the high forceps operation had been abandoned and for the very low application small forceps of the Wrigley type are used to expedite the second stage.

He regarded the anæsthetic apparatus in the Labour Ward almost as an infernal machine. Of course, Burden had experience of chloroform anæsthesia, as Sir James Young Simpson used chloroform in obstetrics for the first time in November 1847, two years before Burden was appointed to the Chair, and on April 7, 1853, John Snow had administered chloroform to Queen Victoria at the birth of Prince Leopold. It was hard for my ghostly visitor to realise that apart from domiciliary midwifery chloroform is now rarely used. It was also impossible for him to appreciate the deep debt of gratitude the obstetricians owe to the anæsthetists for having made possible and safe many obstetric manœuvres and operations carried out to-day. For having put at the disposal of all obstetric patients many pain-relieving drugs or gases the anæsthetists can claim to have helped in the reduction of both maternal and neonatal mortality and to have removed a great deal of the dread of childbirth so common until recent times.

Obstetric anæsthesia is now a highly specialised and most difficult branch of anæsthesia, and only those of us who can look back on the anxieties of the "rag and bottle" era can fully appreciate the service we receive to-day. We have, however, to pay a tribute to many family doctors who became skilled anæsthetists as the result of years of experience. There were, however, episodes which, while amusing in retrospect, gave one serious anxiety at the time.

"Why are the nurses and doctors wearing those white pieces of cloth over their faces?" he said. Before answering his question I had to remember that it was not until 1879, the year that Burden died, that Pasteur described the finding of microbes in the lochia of women suffering from puerperal sepsis.

I said to him, "Those pieces of cloth are masks which prevent the microbes normally present in the noses and throats of doctors and nurses being conveyed to the patients delivered in the Labour Wards or Theatres." He was horrified to think that in his time he might in this manner have infected patients whom he had delivered. I comforted him by pointing out that it was not until the late 1920's that Lancefield in New York and Dora and Leonard Colebrook in London, showed

that many cases of fatal puerperal sepsis were the result of the transfer of hæmolytic streptococci from the nose and throat of the attendant to the patient. "Has the wearing of masks made any difference to the incidence of puerperal sepsis?" Before replying I took my visitor upstairs to the Rea Ward, the isolation unit of the hospital. "This unit," I said, "was incorporated in this Hospital when it was built in 1933 to accommodate cases of puerperal sepsis. Until about 1939 it was used solely for this purpose, but to-day there is not a single case of puerperal sepsis in the unit. It is now used for cardiac cases or patients suffering from pulmonary T.B." "Do you mean to say that there are no cases of puerperal sepsis in this hospital," asked my ghostly visitor. "That is so," I replied. "You will remember the work of Alexander Gordon of Aberdeen in 1789, Oliver Wendell Holmes in 1843, and Semmelweis in 1846. Since your time, Pasteur in 1879, Koch in 1882 and the Colebrooks in this century completed our knowledge of the cause of puerperal sepsis and some of the ways of preventing it."

I told him also of the additional important factors such as the discovery of Prontosil by Domagk in 1935 and of Penicillin by Fleming in 1929, with its development by Florey and his colleagues during the years 1939 - 1940. These powerful chemotherapeutic and antibiotic agents revolutionised the treatment of puerperal sepsis due to the hæmolytic streptococcus. It was with regret that I had to admit to my visitor that the misuse by the medical profession of the antibiotic agent Penicillin and the many others discovered since is likely to make the treatment of many types of infection very difficult or impossible in the future.

"The virtual abolition of puerperal sepsis must have reduced the maternal mortality," suggested Burden's ghost. "This is quite true," I said, "because even a quarter of a century ago sepsis was responsible for more than one-third of the maternal deaths. We have, however, some way to go before the figure for maternal mortality rate is entirely satisfactory." For his information I elaborated this point.

In England and Wales in 1928 there were 2,920 women who died as the result of pregnancy or from causes directly associated with it, an incidence of 1 in 226. This appalling figure stirred the public conscience and a Departmental Committee on Maternal Mortality and Morbidity was appointed. This Committee attempted to assess the primary avoidable factor in each case and since that time each maternal death has thus been analysed. In the years 1952, 1953 and 1954, approximately 1,800 women died as a result of pregnancy or associated causes such as cardiac disease. If the mortality rate which was a feature of 1928 had persisted throughout these three years, then approximately 9,000 women would have died.

While conditions have obviously improved, we are still short of the ideal, especially when we read in the recent Wrigley Report that the four largest groups of deaths which together account for two-thirds of the total were due to toxæmia, hæmorrhage, abortion and pulmonary embolus. Two additional groups have been considered, namely, deaths after Cæsarean section, which accounted for 183 deaths, and complications of anæsthesia. Puerperal sepsis accounted for only 3.8 per cent. of deaths and this remarkable decrease is the most outstanding factor in the reduction of maternal mortality.

The fact that toxæmia of pregnancy and hæmorrhage account for a large proportion of the maternal deaths is a grave reflection on those practising obstetrics. As already mentioned, in 1952 to 1954, 110 mothers died from eclampsia, a disease which is preventable with close supervision, and in the toxæmic group as a whole, avoidable factors were considered to be present in over 50 per cent. of the cases.

In referring to hæmorrhage the assessors in the Wrigley Report were of the opinion that where the hæmorrhage was antepartum half the deaths could have been prevented, and in the postpartum group 90 per cent. of the mothers should not have died.

In 1928 the risk of the expectant mother dying from her pregnancy or associated causes was 1 in 226. In 1955 this risk was 1 in 1,500 which signifies considerable progress, but there are still some aspects of our maternity services that are black; to quote from the Wrigley Report—"Avoidable factors were considered to be certainly present in 40 per cent. of the deaths directly due to pregnancy and childbirth."

How have we progressed in Northern Ireland? An investigation similar to that carried out in England and Wales is proceeding here, and I am indebted to the Ministry of Health and Local Government, and Mr. Greer, for supplying me with some of the relevant details.

TABLE 3.
NORTHERN IRELAND.

Year				Infant Mortality		Maternal Mortality
1926	-	-	-	86	...	6.21
1936	-	-	-	77	...	7.30
1946	-	-	-	54	...	2.92
1956	-	-	-	29	...	0.85
1957	-	-	-	-	...	1.3 (estimated)

If one looks at the Table for Infant and Maternal Mortality there is an improvement up to 1956, but then we see that the Maternal Mortality rate has again risen above one per 1,000. In 1956 and 1957, 64 women died from childbirth and diseases associated with pregnancy. From a preliminary review of these patients it would appear that, as in England and Wales, the percentage of avoidable factors is high.

Obviously there is no room for complacency, indeed there is need for anxiety—anxiety on the part of everyone concerned to see that all avoidable factors are eliminated.

As we passed from Rea Ward I showed him the resident doctors' and pupils' quarters. When he found that between the University and the Hospitals Authority (a body which I had to explain later) I am allowed in the Department seven qualified doctors of which at least three are likely to be at consultant level, he said, "You do not know how lucky you are to have all those assistants." I fully agreed with him and took the opportunity of explaining to him that many former residents are now holding important consultant appointments in Northern Ireland or

in teaching departments in other parts of the world. He viewed the accommodation for medical students, and when I said that it is not ideal he was very caustic. "My poor students had nothing like this," he said, and I had to admit that until 1925 there was no proper accommodation for students doing their practical training.

The history of residential accommodation for students is interesting. In Professor Burden's time, and for a long time afterwards, the student tried to get lodgings as near the hospital as possible. At one stage, the late Dr. J. S. Morrow told me, the lodgings were in Upper Townsend Street which was some distance from Clifton Street. The students were warned that a patient was in labour by the nurse placing a white card in the window of the Labour Ward which looked on to Stanhope Street at the side of the hospital. To obviate the necessity for a student having to stand all the time in Stanhope Street a 'Tele' boy was employed to keep a watch on the window. When he notified the presence of the card to the students in Upper Townsend Street he received the sum of six pence. The penalty for false notification was the threat of an operation which plays a large part in the Jewish ritual.

At a later stage the lodging house was in 20 Regent Street, quite close to the hospital, and then in 1925 the University bought the two houses in Townsend Street.

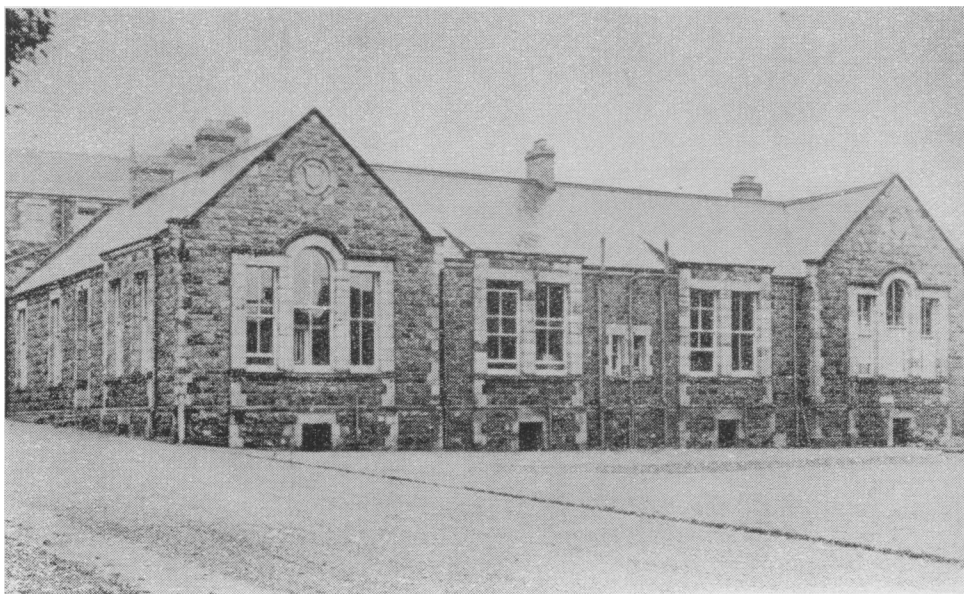
As we passed the door of Johnstone House I explained to him that there are 15 private beds available in this wing. He was amazed to find that roughly 50 per cent. of all confinements now occur in institutions, and that if sufficient beds were available this figure would be in the region of 70 to 80 per cent. In one area in Northern Ireland 85 per cent. of births take place in public or private obstetric beds. "This is a revolution," he said, "but must be much safer and easier for all concerned." I admitted that it is easier for both consultant and patient, but could not entirely agree that it is always safer. Hospital confinements where so many mothers and babies are collected together can only be safer than a confinement at home if a most rigorous standard of asepsis is maintained to avoid the ever present danger of cross infection.

From Johnstone House we went to the Nursery which, as the result of the work of Professor Allen, is one of the most up-to-date establishments in the United Kingdom. My visitor had seen the babies in the Lying-in Wards, and I explained that the Nursery is for complicated or ill babies. "Do you resign all responsibility for the newborn baby?" said my rather surprised guest. "No indeed," I said, "but we have close co-operation with the pædiatrician in the care of the child." I explained that nowadays the care of the premature baby has become an almost specialised field, and in addition we are indebted to the pædiatrician for the early recognition of certain anatomical abnormalities, e.g., tracheo-oesophageal fistulæ, for all exchange transfusions in babies with erythroblastosis and for the treatment of the potentially infected baby.

As I had promised, I showed him the Milk Room on the opposite side of the corridor, where we not only sterilise and prepare the bottle feeds for the babies, but also maintain a bank of mothers' milk for use by premature babies. The

modern milk bottle and the care taken to sterilise it astonished my visitor and was in complete contrast to what he might have seen 100 years ago.

As we walked up the corridor I pointed out to him the near-by Department of Gynæcology. "I did not do any gynæcology," he said, "but I am interested to learn that now the two subjects are combined in the one Chair." Gynæcology (the term was first used in 1847) as a subject, apart from surgery, really did not exist until after 1845 when Marion Simms became the pioneer of the subject by operating on patients suffering from vesico-vaginal fistula and later treating such a condition in the Empress Eugene. Ephraim McDowell of Kentucky had done the first ovariectomy in 1809, but it was not until after Listerian principles were accepted



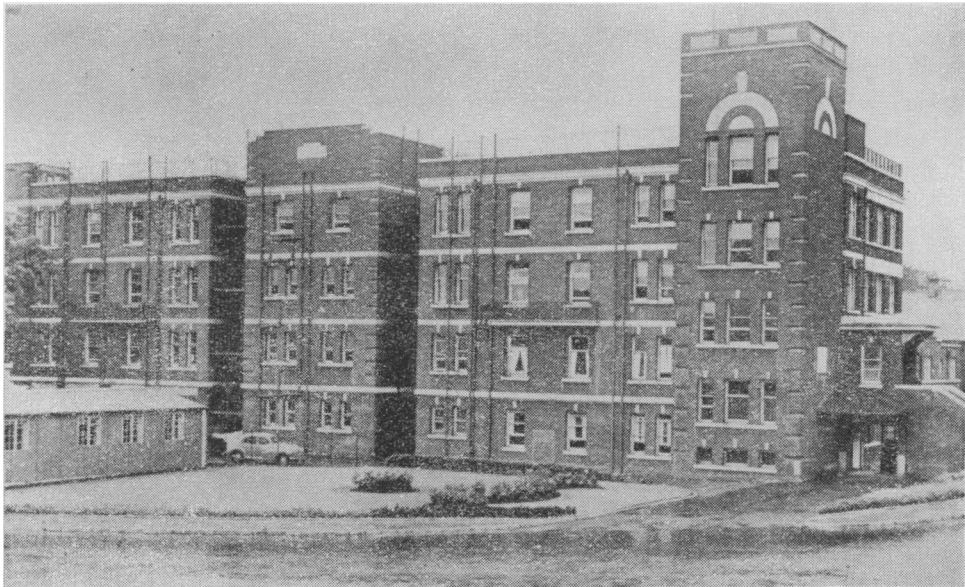
Ivy Building, City Hospital

in 1870, and anaesthesia became safer, that abdominal gynæcology began to develop. I explained to my guest that the great attraction of gynæcology is that it forces us to be partly physician, partly surgeon, and most times a psychologist.

He listened astounded as I explained briefly the relationship of the anterior pituitary gland to the ovaries, the adrenals, thyroid, etc. I told him as well as I could of the ovarian and pituitary hormones, of which, of course, he was completely ignorant. He was astounded when I told him that now we refer with assurance our doubts as to the existence of an early pregnancy to the arbitrament of a toad, thereby elevating those despised animals to the rank of obstetric consultant.

From the Hospital I took him to the Institute of Clinical Science and showed my University Department. He was amazed at the facilities of the beautiful building, the lecture theatres, the proximity of all the University clinical departments and

the teaching hospitals. Most of all did he wonder at the provision of laboratories in the clinical departments. "What point have these?" he asked. "What have laboratories to do with maternity work? Surely any physician can test urine." So I told him something of erythroblastosis, of blood oxygens, and of the rapid advances which had resulted in the publication of more papers in the last ten years than in the previous one hundred in the history of the School. "Someone put a lot of thought and work into the layout of these buildings," said my visitor. "Yes," I replied, "one of your successors in the Deanship, Professor Biggart, was behind the idea that the building should be on this site and was responsible for the layout of the various departments."



Jubilee Maternity Hospital, City Hospital

My conducted tour would have been incomplete had I failed to show my visitor the Jubilee Maternity Hospital. He had, of course, remembered the establishment of the parent building in 1840, but had never seen the Ivy building, the original maternity block, to which the Jubilee Maternity Hospital is attached. (The Ivy building was not opened until 1893.) He was again impressed with the developments that had taken place on this hospital site. When he had viewed the two hospital groups a thought suddenly struck him. "Where do you get all the money to run these hospitals?" You surely cannot depend on voluntary subscriptions to maintain the services I have seen to-day."

I explained to him that in July, 1948, all the medical services in the United Kingdom were taken over by the Government. In Northern Ireland the administration of the hospital service is vested in a body called the Hospitals Authority. I

added that the Governments, both in Great Britain and Northern Ireland, had underestimated the cost of the Health Service and that this, in my opinion, was partly due to the fact that neither Government had appreciated the proportion of gratuitous medical advice and treatment given prior to 1948.

I told my visitor that the hospitals he had seen at the Royal Victoria Hospital site had been built and equipped by voluntary subscriptions and donations. The hospitals in association with the Jubilee Maternity Hospital had originally been provided by the Ratepayers of the City, but now both hospitals are financed by the Taxpayers through the Hospitals Authority. The first budget of the Hospitals Authority was in the region of £5 million, the budget for 1958 - 1959 is in the region of £12 millions. These figures horrified my visitor, but I told him that this much-criticised body had revolutionised the hospital services in Northern Ireland. Now consultant and improved hospital services are available to the most remote resident in the area.

The hospitals in Northern Ireland were structurally twenty-five years behind those in Great Britain, but since 1948 this disparity has been gradually removed.

At this stage he showed signs of weariness, and said, "Mr. President, what you call time is passing and I must return to my rest. You need make no excuse for disturbing it. The development of the medical school amazes me and makes one proud to have been associated with its early days. To have received recognition of what at the time seemed to me to be a small contribution but which you assure me was the foundation stone well laid, has indeed been gratifying. I am happy to think that I had in my time a share in sowing the grain which you are now reaping. What I have seen and heard of the triumphs over disease and death will make my rest the sweeter. To see puerperal sepsis apparently defeated, to see the quest for the relief of pain so effectively pursued, to see the co-operation between all branches of the profession in combating the diseases associated with pregnancy, and to note the amazing improvement in foetal and maternal mortality which is partly the result of improved teaching and practice, makes me proud to have played even a small part on this great stage."

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Rest and Exercise

By R. J. W. WITHERS, M.D., M.Ch., F.R.C.S.E.

*Opening Address of the Winter Session,
Royal Victoria Hospital, 7th October, 1958*

LADIES AND GENTLEMEN,

It is my privilege and my pleasure to welcome you on behalf of the Medical Staff to the practice and the teaching of the Royal Victoria Hospital on this the opening of a new session.

You have chosen Medicine as your life's work. Let me congratulate you on your choice of career though I would remind you that Medicine is not an easy calling. It demands—over and above factual knowledge—judgment, concentration, good humour, tolerance, kindness and tenderness towards human beings and, above all, a deep consciousness of one's obligations and responsibilities to the sick. These are aspects of human behaviour which you must try to cultivate for without them you can never hope to become really good doctors no matter how great your scientific knowledge. Reading textbooks and listening to lectures is not enough. Only by direct contact with human suffering can your pity and charity be stimulated and the virtues I have just mentioned be germinated and in time brought to full growth. If you are interested in humanity you will become good, possibly even a few of you will become great, doctors. Our hospital offers you in the wards and the out-patient departments the opportunity to become so.

During your years of attendance at the hospital you will learn a little about many things unheard of when I was a student. In my time we were taught that the saving of life and the easing of pain were two of the chief functions of a doctor. In those days the doctor saved life now and then. Today life saving is a commonplace, thanks to the development of anti-biotic drugs, excellent methods of anæsthesia and with them safe surgery to mention only a few of many advances. In spite of the changes over the past thirty years, and they have indeed been great, relief of pain still chiefly interests the patient, and skill in this direction forms an important part of a doctor's life. The sufferer wants action, he is uninterested in theories for, to him, there is no virtue in needless suffering or in submission to misery because the means of succour are withheld through carelessness, lack of knowledge, or for any other reason. I would advise you, therefore, to think a lot about pain, its causes, its significance and the measures both medical and surgical necessary for its relief, for you will find as you mature that the ability of a really good doctor can be measured by his capacity to distinguish between the trivial and the serious and who knows when to wait and when to act swiftly.

Up to the present you have been chiefly concerned with the study of the structure and functions of the human body. From now on you will be learning how this functioning body reacts to injury and to disease and what methods of treatment can be adopted to help to restore it to health.

Medicine is the aggregate of all knowledge to do with the human body and so I must remind you that the study of anatomy, physiology and pathology, far from being a passing phase in your education, must continue along with clinical medicine and surgery. Indeed, the association of clinical and non-clinical subjects is one we cannot, we dare not, break throughout our whole medical lives. We can subdue Nature only by obeying her, i.e., by understanding her. Recognition of the inescapable framework which hems in every biological process is the first essential to the sane conduct of treatment. You must, therefore, remember your Anatomy, your Physiology and your Pathology and revise them yearly throughout your lives. The rules of the game are to be found in these three subjects and only a thorough knowledge of these rules allows the game to be played freely for its own sake without waste of futile and hazardous effort.

When Blaise Pascal wrote "*Il ne faut pas juger de la Nature selon nous, mais selon elle,*" that is to say we mustn't judge Nature according to our lights but according to hers, he was condemning a mistake which I fear some of us make when we try to explain to our patients, and indeed to ourselves, the reactions of the body to disease by likening it to a machine, a motor car for example. How wrong this is! The body, unlike any machine, has a brain through which has developed a mind and, being activated by cellular processes, it possesses intrinsic powers of self repair, something a machine can never acquire. Whatever part, therefore, we, the medical mechanics, may play, the final restoration from the ravages of injury and disease is effected by powers inherent in the living tissues of the patient. Let's never forget either the part the human mind has to play for who can tell what man, that is the whole man, really is.

Nature is the master, the doctor, the assistant. This was the final conclusion which John Hunter came to in the latter years of his life and when he was recognised by his professional colleagues, as well as by the public, as the leading British surgeon in the latter half of the eighteenth century.

This lesson of Hunter's is needed at all times and I dare to think in none more than the present. The doctor can, if he will, assist these powers of repair. He must always see to it that he makes Nature's job easier if possible but must be certain that he never stands in her way or frustrates her by unnecessary meddling, for the power to heal lies not in his hands. By the nature of things the surgeon is more liable to fall into this trap than is the physician. Here I would like to quote from Florence Nightingale. "It may seem a strange principle to enunciate," she says, "as the very first requirement of a hospital that it should do the sick no harm even if it does them no good." Students, therefore, must appreciate early in their careers that the glamour of the operating theatre and the intricacies of surgical technique are mere adjuncts to, not replacements of, the healing powers of Nature. In modern operative surgery the doctor's share in effecting a cure is unquestionably

great, but whether what he sets out to achieve at his operation is to become a permanent feature or not depends entirely on biological processes—that is the power to heal—over which he has no real control. In limb surgery there is another factor—the power to recover function. This is a property of the patient's will and brain and it is the doctor's business to direct, encourage, interest and if need be cajole that will and brain. If he would only do this he would never make the mistake of supposing that elaborate batteries of gymnastic apparatus can take the place of his own thinking brain and the willing response of his patient.

Nature in her efforts to effect cure has two powerful natural allies. I refer to Rest and Exercise and I would now direct your thoughts to these two principles in relationship to that branch of medicine which interests me most, namely Orthopædics. This speciality has to do with injury and disease of the locomotor system—those parts of the body by which we move, namely the arms, the legs and the spine and their associated muscular, nervous and vascular elements.

It is probable that man from early times cared for his broken bones and diseased limbs in much the same way as do the higher animals, that is by instinctive rather than judicious application of rest and movement. In the words of Annie of musical comedy fame, early man probably did what comes naturally. Since then we have learnt how to augment rest by support and splintage and how to increase the benefits of motion by assisted movements and physical measures. With our increased knowledge, however, has come the big question. Is it to be rest or is it to be exercise? The answer depends on many factors including the cause, the reaction of the tissues, and the physiological effects of the injury or disease under consideration. Even when these are known, however, it is sometimes difficult to decide. In early times the choice was probably simple. To survive early man was forced to be active, since the whole structure of primitive life was dependent upon strength and speed. The family had to defend itself, kill game and always be ready for prolonged endurance, instant retreat and spells of famine. A man crippled by injury or disease was consequently an unreasonable burden for the tribe to support. Possibly an occasional chieftain or warrior injured heroically was honoured for his disability but there could be no other logical excuse for his maintenance in the perpetual struggle for existence. One suspects that those who were inactive were simply left behind to die or to be killed by the marauding beasts of the field. This policy of destruction reached its zenith in the rational ethics of the Spartans who destroyed the imperfect for racial supremacy where the primitive code had annihilated the infirm for survival.

During the long period of Greek influence on medicine the controversy on rest versus activity was already an old one. Greek philosophic thought boldly condemned all forms of exercise as not only of no advantage but even prejudicial to health, and recommended rest as the chief preserver of it. On the other hand there was Hippocrates who taught that "exercise strengthens whilst inactivity wastes." Here in a few words is all our scientific knowledge of the physiology of the atrophy of disuse. Early movement of injured limbs is one of the principles recognised by

the ancients, ignored for almost two thousand years and, in the past two hundred, almost perennially rediscovered.

I will not bore you, however, with the beliefs of the ancients, hemmed in as they were by their theories of the body humours and the wrath of God. Rather I will follow Voltaire who once remarked that he would advise a young man to acquire a slight knowledge of remote ages but would have him begin the serious study of history at that period where it becomes truly of value to him.

In searching for useful knowledge on rest and exercise we need only go back to the 18th century, to France and to Dr. Nicolas André. In 1741 he published a treatise entitled "*Orthopædia*," a term which he coined from the Greek and which signifies a child upright or free from deformity. André lived in a period when men were convinced that they could improve upon Nature. Nature, they believed, had to be tamed, disciplined and trimmed and so they applied to the human body the same pruning, training and shaping as they did to their fantastic garden shrubs and bushes. André taught that the methods of orthopædics were within the grasp of parents since he could not conceive of a time when a mother would not take pains to secure for her daughter a properly shaped waist line—one which was perfectly flat in front but full, prominent and curved in the region of the buttocks. This was to be obtained by the early and proper use of stays. Within the scope of orthopædics André included not only the fashioning of the waist but the care of the nails and hair, the shaping of the hands and nose, the arching of the eyebrows and also much of what today has become the stock in trade of the beauty specialist and the mistress of deportment. A lot of his teaching was connected with uprightness though not what today we would call orthopædics. He did develop, however, one important truth—muscles are the chief instruments in shaping a child's body and it is upon these instruments that a physician may play his orthopædic tune. He learnt about muscles not by dissecting room study but by ordinary common-sense observation. For example, the corpulent man and the pregnant woman walk with a straight back, even an over extended one, because they are overloaded in front. If a youth stoops then the natural way to bring the muscles of his spine into play and give him an erect carriage is to make him carry a burden in front of his body or hang a weight from his neck. André encouraged exercises to the appropriate muscles, even to the stage of over-correction of the deformity, for he knew that with a crooked body, as with a crooked stick, you have to over-correct the deformity if you would aim at obtaining the just mean. He included as exercise the toil of ordinary everyday work as well as the play and games of children and the fencing, dancing, riding and even billiards of adults. Work and exercise were to him the best medicines of health but they had to be taken in proper dosage and at times required their proper antidote, namely rest. We see, therefore, that the founder of orthopædics recognised that rest as well as action had its own particular merit but, of the two, exercise was that to which he attached the higher value.

From André in France our search now brings us to London where in the year 1823 we find Dr. John Shaw of the Middlesex Hospital concerning himself with

the problems of spinal curvature. He soon became convinced that the curvatures were evidences of weakness of the spinal muscles. Why this weakness occurred he knew not though he observed that the deformities developed most frequently during spells of active growth. It is interesting to note that this study of his began in the anatomy department of the old Windmill Street Medical School tucked away in Soho a stone's throw from Piccadilly Circus. There is no medical school there now, though in the old building anatomy can still be studied which is both animated and animating. I refer to the Windmill Theatre which today remains as the joy and delight of older men who cling to the heretical faith of the triumph of hope over experience.

During Shaw's time rest and support was the treatment in vogue in England but Shaw rebelled against this and claimed support from what he called the "eternal law of disuse." The proper treatment for weak muscles was in his opinion not rest but graduated exercise. Impressed by the success which he saw attended the empirical efforts of rubbers, i.e., masseurs, and of the unqualified generally, he was led to formulate the principle of action. He embarked on all the tricks of the rubber: massage, shampooing, thumping, pinching, percussion and kneading. Set exercises were then given employing apparatus of various kinds where movements of the arms were used to influence the upper part of the spine and leg movements the lower part. Between doses of rubbing and exercises were spells of rest either by reclining or by the application of stays or spinal machines. Thus he realised that gymnastics and massage had a place in the therapeutics of surgery. Sad to relate, his influence on British thought disappeared rapidly after his death in 1827, in his 38th year, from typhoid fever.

About Shaw's time Jacques Delpech in France had reached similar conclusions about muscular exercise and its value in the treatment of deformities. He believed that the normal poise of the body is the result of a balanced action between opposed groups of muscles and if this balance is upset then deformity results. The surgeon's business was to cure deformities by restoring the muscular balance. He was convinced that this could only be done properly in a special institution. He therefore mortgaged his worldly wealth and, having purchased a plot of ground on the high road between Montpellier and Toulouse, he built there the world's first orthopædic hospital. He hoped in this institution to make his clinical cases yield up their physiological secrets. Inside its walls he gathered cases of deformity which he felt could be studied, treated and noted for the benefits of science. His hospital was to be a type of human menagerie or experimental garden, for Delpech was most surely the pioneer of physiological surgery in Europe. Here was on a great scale the first organised attempt to apply gymnastics to the treatment of deformities of the human body. Delpech, whilst an orthopædic missionary, was a realist and disciplinarian and he always warned the parents or guardians of those entering his institution that time, patience and perseverance would be necessary before cure could be effected. Many of his patients had to submit to fourteen out of twenty-four hours lying extended and stretched on various forms of apparatus though Delpech only regarded this as an accessory in treatment and eventually

periods of gymnastics were worked into the daily routine. He gave his imagination a free hand in designing a great variety of apparatus for he was well aware that only by trying a succession of changes could he maintain the patient's interest in the laborious efforts needed to bring about a cure. Unfortunately we do not know the degree of success which attended this great experiment since Delpèch died rather tragically before he could publish his results. He was shot dead by one of his patients upon whom he had operated for a varicocoele. After his death the Montpellier institution became forgotten and neglected and in a few years only a mass of weeds and crumbling masonry survived to mark the spot. We remember, however, that in the early decades of the 19th century and in the south of France one of the ablest surgeons of his time was convinced that gymnastic exercise constituted the best means of remedying certain deformities of the human body.

From the south of France our search now leads us to the south of Sweden and to the province of Skane. From this place there began a movement in the evolution of gymnastics which in its ultimate effects was destined to have a world-wide influence. Pehr Henrik Ling was born in 1776 and destined for the Church, indeed he actually studied at the University of Uppsala for this purpose. In his mature years, through his interest in gymnastics, he strayed into the outskirts of medicine. He gained his knowledge not by anatomical study but by observation of the ordinary movements we perform and the postures we assume in our daily duties. Ling was not only a scholar and a poet but was also a professional teacher of fencing in the University of Lund. In teaching the art of fencing he saw that all depended on the mastering of the muscles by the fencer's brain. When his pupils first came to him he observed that the special movements which he wished them to perform were impeded by other unnecessary movements which they employed from force of habit and past use. He therefore embarked on the production of an alphabet of simple movement and he developed a series of exercises covering the whole keyboard of bodily motion. Exercises and gymnastics had not only developed his own muscles but given him health and strength as well, for he had suffered from some form of multiple arthritis in his youth. Eventually he produced a system of medical gymnastics aimed at positive health and fitness and he included massage, kneading and all the various forms of manipulation by which friction and pressure can be brought to bear on the living body. Ambrose Paré humbly said "I dressed him, God cured him," but neither Ling nor his disciples took such a humble point of view. *They* wrought the cures and *they* made the converts. Ling's original methods were simple but the modern representatives of the Swedish school have added to muscle training a bewildering code of arbitrary and empirical practices and even a jargon of pseudo-pathology. All this can only be justified by the benefits which are said to attend their application. If we adopt empirical practices we have to make doubly sure that the results obtained are due to the means we have applied. We must ever remember that all living flesh is endowed with inherent powers of repair and of recovery so that in a large percentage of all our cases a cure would naturally occur without the intervention of any outside agency. If our practices have no known rational basis then it is our duty to determine by research

and controls how far the means we employ are accessory to the cure which has taken place and not to fall into the trap of thinking that we and our methods are replacing Nature. This was the trap into which the disciples of Ling fell; they continued a practice without first seeking a principle.

But I digress. Before Ling died he persuaded the Swedish government to found a central gymnastic institution and as a result he left behind him a permanent organisation and devoted band of pupils to carry on his work. From that centre in Stockholm his teaching has spread to the playgrounds of schools, barrack yards and hospitals of every civilised country in the world. That great benefit has resulted no one can reasonably doubt and Swedish drill is something that everyone in this room has indulged in at some time, whether voluntarily or as part of a school curriculum under the watchful eye of the "Gym" instructor, or as treatment in a physiotherapy department of a hospital.

But what of the *passive* measures of physiotherapy? What case can be made out for regarding them as constituting a scientific practice? The use of the elements and the simple physical phenomena of Nature is the oldest form of therapy known to man. The early temples of the healing gods of Egypt, Greece and Rome were invariably built round springs of curative waters. Bathing pools of hot and cold water were in common use throughout the Roman Empire. The application of heat and cold, as stoupes or compresses, was recognised therapy when mankind was in its infancy, and in all ages of recorded history the arthritic patient has found his greatest relief at the spas, either secular or religious.

The same is true of sunlight although the ancient civilisations, being situated in sub-tropical regions, did not recognise its value as distinctly as did the northern races somewhat later. The application to the body of electrical currents is not by any means new. In ancient Greece amber, subject to friction, was used as a source of stored electrical energy, and its curative powers were greatly sought after.

Friction of the muscles of the body by rubbing, kneading and pinching was established practice in the Gymnasia of the Greeks as a method of increasing the strength of young men undergoing training for the purposes of war or for competition in the public games.

All these practices have continued up to the present day though we have now introduced machines for the generation of heat, sunlight and electricity, thereby making us independent of Nature for our supply of these energies. We still use water and we still apply friction. Only the names and the sources of these physical measures have changed—we now talk of electro- and electrothermal therapy, heliotherapy, hydorthery and massage, and if we are thinking of the lot we speak of physiotherapy.

The practice has not changed, except in details and methods of organisation, but do we yet know how passive physical measures work and are we really sure what, if any, influence they have on the pathological and biological processes which we call disease and repair?

Ancient and accepted usage does not make any practice scientific nor does the cloaking of empiricism by pseudo-medical explanation further our search for reason

and truth. Lots of benefits have been claimed for the various physical measures which are today employed—they have a sedative effect and diminish pain, swelling is decreased and lymph and blood circulation improved, muscle spasm is relieved, the “pain pattern” is broken—but these are only expressions easy to put across to the patient who, in his ignorance, still accepts a sort of mechanistic view of his body and knows nothing of the elaborate and complex biological processes which underly repair from injury and disease.

In 1926 Titus of New York claimed that physiotherapeutic measures can be used in the treatment of *any* pathological process in an attempt to convert an inadequate reaction on the part of the patient into one that is adequate. This claim was not backed up by “controls” nor were his findings ever submitted to the constructive criticism of unbiased observers. The claim, therefore, makes no sense, as it is simply a statement of faith or hope, something which G. L. Mencken tells us, in another connection, is belief in the improbable.

Dr. Mennell—in his day a recognised exponent of physiotherapy—seeking an explanation for the effects claimed for passive measures, contended that they probably are obtained by “playing” upon the reflex mechanisms of the body. These are spinal and sympathetic reflexes which control the state of muscle tone and the degree of constriction or dilatation of the blood and lymphatic vessels. What the word “playing” means I do not understand.

In cases of injury the movements of massage, the application of heat, the stimulation of muscles by electrical currents apparently in some mysterious way effect restoration of the normal control mechanism. This is surely an enormous claim to make. Is it true? Again can you believe what Cyriax says in regard to chronic ligamentous sprains? Do his words even make sense? I quote from his book on orthopaedic medicine—“In chronic cases friction, i.e., deep massage, *thins* out the scar tissue by which the fibrous structures are held abnormally adherent and so *numbs* them that mobilisation becomes possible.” Are the explanations of Mennell and Cyriax simply words, or do they “make the punishment fit the crime.” I do not know, though by nature I am a doubting fellow.

Certain points are, however, beyond dispute—many patients say they are benefited by the measures which have been applied, some are certain that physiotherapeutic treatment has increased their discomfort, whilst others are like Sir Walter Scott’s Marmion, “uncertain, coy and hard to please.” In certain cases of chronic illness physiotherapy undoubtedly makes the patient feel that something important is being done for him. That it has a strong psychological effect no one will deny or will any deny the psychological benefits of physiotherapy nor, particularly in injured cases awaiting litigation, the psychological disadvantages. One thing is certain—we must never, never, consciously give the patient the impression that we have brought to the bedside the means of cure and all that is required of him is that he submit passively and allow a miracle to be performed.

When we come to the application of physical measures, and particularly heat and massage, in the later period of recovery from orthopaedic disorders we are

outside the realm of doubt or of dispute. To use a modern expression "we are in the clear" if we use physical measures only as a preparation to encourage the patient to be active, i.e., to exercise. This preparation is simply the production of muscle hyperæmia. The essential for success is that the patient must be an active and not a passive participant in the process. Ling was ever mindful of this and no one knew better than he that in recovery of movement, irrespective of the nature of the damage to the body, the active agent assisting in this recovery is the patient's will and brain.

During its long course of development, from early simple measures to the modern complex apparatus for the administration of a multiplicity of physical energies, physiotherapy has been the hand-maiden of every branch of Medicine. It is therefore the duty of Medicine, and I include all specialities, to submit these practices to modern scientific control and logical assessment, so that what is good, helpful and reasonable may be developed further, and what is unscientific and therapeutically useless be finally and without fear discarded.

Now we must return to Rest and Exercise.

John Hilton of Guy's Hospital published in 1862 a series of lectures in book form entitled "Rest and Pain." In his fourteenth lecture he states, "By regarding this subject of physiological and mechanical rest in what I conceive to be its proper light the surgeon will be compelled to admit that he has no power to repair directly any injury. It will induce him to acknowledge in all humility that it is the prerogative of Nature alone to repair the waste of any structure." Hilton believed that the surgeon's first duty was to give injured parts rest and in his scheme of therapeutics action found no part. Neither active nor passive movements were considered suitable in attempting to restore disorders of joints or muscles. Hilton, however, used the term "Rest" in a very wide sense. He did not mean pure passivity until Nature had effected a cure but he included also the removal of irritants which were preventing rest taking place. In the class of irritant he included a wide variety of lesions from stones in the bladder through abscesses in various parts even to painful scars, all of which were to be neutralised, i.e., removed before true rest could be effected. He considered rest a physiological state which was to be taken not in intermittent doses but through a long continuous course. The application of splints was his chief means for securing this desired physiological state when joints were the seat of the trouble.

His service to surgery lies not so much in the forms of splints which he recommended as in his insistence on their unremitted application. John Hilton preached the gospel of rest freshly and persuasively but Hugh Owen Thomas of Liverpool made it his religion and ritual and believed that an overdose of it was an impossibility. To use the expression that Thomas never tired of repeating—"Rest must be enforced, uninterrupted and prolonged." Thomas was a Welshman coming from a long line of unqualified bone-setters; but he was a doctor—his father saw to this, as he believed that medical training could give something to his son which he and his forebears had up to that time lacked. Hugh Owen flourished between 1834 and 1891. His field of experience was in the general practice of the

dock-land of Liverpool and his material the steady stream of accident cases which poured into his surgery from that great water-front. It was his greatest merit to have shown that a busy general practitioner can, by purely clinical methods, win for himself a permanent place among the great benefactors of Medicine. After each day's work Thomas was to be found in the attic room of his house, which he had converted into a workshop. Here, with expert hands, he produced the exact form a splint or appliance which he desired for the treatment of each particular case under his care. Thomas was a new kind of surgeon, one who could and did operate but whose eventual opinion was that the forge and the hammer, deftly used to produce the properly fitting instruments of rest—namely splints—were in most cases more powerful aids to reparation than the surgeon's knife. Towards the end of his life he wrote, "The crying evil of our art in these times is the fact that much of our surgery is too mechanical, our medicine too chemical, and there is a hankering to interfere which thwarts the inherent tendency to recovery possessed by all persons not actually dying." These words were written over seventy years ago. The more one thinks about them the more one finds them still wonderfully true.

Thomas has left us his splint, which is still in use the world over, unchanged in design from the original models made by his own hands in the attic room in Liverpool. I venture to suggest that his splints fitted his patients accurately and comfortably since each one was a tailor-made job. How unlike the modern splints, to be seen in a hospital splint cupboard, which occur in three sizes—Big, Bigger and Biggest—to quote from the late Professor McMurray who was a distinguished graduate of Queen's University.

In Nature there are two methods of giving limbs the degree of rigidity necessary for support and movement. In vertebrate animals there is an internal support—an endo-skeleton—whilst in invertebrates the support is external or ensheathing—an exo-skeleton. Thomas probably did not borrow any suggestions from the crab or the lobster and yet his knee splint is based on the ensheathing principle shown in these creatures' limbs. He cut away all unnecessary parts of the sheath leaving a basal ring round the inguinal region with two long bars extending one on either side of the limb from the ring to the foot. To this splint the limb was anchored by suitable bandaging or strapping. He thus furnished the limb with a new and temporary exo-skeleton which relieved its bones and muscles of work and stress. Thomas fashioned splints for all parts, but the example of his knee splint shows clearly that the principle of rest, which was his creed, depended on harnessing the affected parts of the locomotor system to a temporary exo-skeleton for the period which Nature would require to bring about a cure of the underlying disease.

Thomas holds an unique position in orthopædics since he is the only man who has grown in medical stature after his death. I venture to suggest that today surgeons know more of his work and believe more in the principles of his practice than his contemporaries did.

Long before the time of Thomas, immobilisation of diseased joints had become the accepted practice in Europe. The principle of rest appeared to have found a

permanent and undisputed place in surgical procedure throughout the whole world. There were, however, rebels, and how difficult their job was to convince their colleagues that action as a curative agent had a big role to play in restoring health to a part which had been injured by accident or put out of action by disease.

Among these was a Frenchman—Juste Lucas Championnière. He had no wish to bludgeon those who disagreed with him but nevertheless he persuaded his colleagues that his method was the proper one. In his opinion the right approach to locomotor disorder was the opposite to what had been taught for so long. He was honest, courteous and *saue* in the propagation of a heterodox doctrine and his colleagues could not but listen to him. He had the power of presenting his own views so lucidly and so convincingly that, after listening to him, no other view than his seemed to the hearer tenable or possible. Soon he was to advocate the treatment of all fractures in which joints were involved by the early application of movement. Soon he became known as the “ankylophobe.” In time so certain was he that splints rendered joints stiff that he gradually laid aside the whole armamentarium of splintage until ultimately it was only in cases of fracture of the thigh that he applied any means of restraint at all. It is interesting that he came to this belief shortly after the Franco-Prussian war when plaster of Paris was introduced by the untiring efforts of Mathijssen of Holland. It must surely have required a brave and forceful surgeon to deny the use of such a handy splint maker as plaster of Paris proved itself to be, or to deny himself the personal child-like delights of plaster paddling. In 1881 he introduced the use of massage in the treatment of fractures. Its application was not only to the neighbourhood of the fracture but to the actual fracture site itself and he claimed that massage allayed, almost instantly, the pain and that it accelerated the process of repair. Towards the end of his life he declared dogmatically that rest was a dangerous remedy and that action was life in the treatment of orthopaedic disease. When Championnière died his teaching died with him, at least for a while. The official manuals by the late Professor Leriche, published in 1916 for the guidance of French army surgeons, recommended still the methods of immobilisation. The sole trace of Championnière’s influence is to be detected in the early mobilisation of fractures involving joints, particularly those which occur in the neighbourhood of the elbow joint.

How then are we to explain the fact that opposite and irreconcilable methods have been recommended in the treatment of bone and joint injury? How are we to reconcile the teaching of Thomas of Liverpool who advocated rest and Championnière of France who advocated exercise.

The first inference to be drawn is surely that the tissues of the body have such a strong intrinsic power of repair that they will effect a cure even in the most disadvantageous circumstances. Inspiratory movements never leave a fractured rib or clavicle at rest for a moment yet healing is invariably accomplished. Fractures in wild animals and primitive people heal without medical intervention. Many it is true would have been better for surgical attention or, when one sees what can occasionally happen under so-called modern surgical adventure, would they? There are certain matters happily which do not admit of difference of

opinion. No one can doubt that the more accurately a surgeon re-apposes the ends of a fracture or keeps an inflamed joint at rest in the position of maximal function the easier he makes Nature's task. Common sense dictates rest during the early stages of orthopædic injury or infection or in cases where pain has for long been endured in chronic arthritic conditions. Yet it is clear that a stage will pretty rapidly be reached when rest can no longer be of service. One cannot operate on un-united fractures nor examine the conditions seen in limbs amputated after long periods of infection following severe compound fracture without being convinced that mobilisation, i.e., action, must play a part in the final stages of repair in the treatment of disabilities following bone injury. Muscles are bound down by inflammatory exudate so that their fibres are necessarily limited in their excursions. The whole connective tissue system of the limb has been swept by an inflammatory tide. Round the moving parts lie envelopes of newly organised inflammatory tissues. When such a stage of resolution has been reached rest can no longer be of help and its continuance must surely make the chances of eventual movement less and less likely. Can one conceive of any means which will lead to loosening of the plastic cellular bonds and thickenings which surround the muscles and joints except those implied under the all-embracing term mobilisation, i.e., massage, passive manipulation, and active or voluntary movement. Of these three there are many reasons for expecting the best results to follow voluntary activity. The voluntary impulse which sets a group of muscles into action exerts at the same time a regulating influence on the vasomotor connections of the part. Voluntary muscular movement therefore controls swelling of the limb by giving the maximum propelling impulse to venous and lymphatic return. The muscles of the damaged or diseased part are the agents by which increase of motion is to be obtained. The machinery which can set the muscles to work lies in the patient's own central nervous system and the only thing which can set this machinery going is the patient's own will. The sooner the patient realises that progress in movement depends on his own effort carried out in small doses many times daily, the quicker and better will be the ultimate result.

Each year, about this time, students are forced to listen to a member of staff delivering what is, with flattery to the speaker, called an Oration. The purpose of Oratory alone is not truth but persuasion, according to Macauley. It would be too much to hope that I have persuaded you to any point of view in the controversy on rest versus exercise. I should, however, be content if, the next time you put a patient to rest, order passive physical measures or impose a splint, you ask yourself this question—"Why am I prescribing this, what good will it do and what harm may it do?"

It is poetry that has made man look, through the mists which surround him, to the heights, so let the words of John Dryden express what I have been struggling so long to say :

"Better to hunt in fields for health unbought,
Than fee the doctor for a nauseous draught,
The wise for cure on *exercise* depend,
God never made his work for man to mend."

The following books and articles have been consulted in the preparation of this address—

BICK, EDGAR M. *Source Book of Orthopædics*.

CYRIAX, J. *Orthopædic Medicine*.

DAVID, J. P. "Dissertations sur les effets du mouvement et de repos dans les maladies chirurgicales."

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REVIEWS

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THIS is the third volume of this work of four volumes. The contributors are all specialists in the particular fields of surgery covered, and the approach is essentially clinical and practical.

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J. M. M.

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This theme is elaborated and extended throughout the text, which covers a wide variety of subjects—all of which are of fundamental importance. The authors consider the doctor's personal standards and his ultimate loyalties; his relationship to the disabled, incurable or dying patient; his relationship to the patient's family; and his relationship to his own colleagues.

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M. G. N.

6-Methyl Prednisolone in the Treatment of Rheumatoid Arthritis

By D. A. D. MONTGOMERY, M.B.E., M.D., M.R.C.P.
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IN recent years synthetic analogues of cortisone and hydrocortisone have been employed in the treatment of rheumatoid arthritis. Prednisone and prednisolone were first used by Bunim, Pechet, and Bollet in 1955, and since then further reports have followed (Dordick and Gluck, 1955; Margolis, Barr, Stolzer, Eisenbeis, and Martz, 1955; Hart, Clark, and Golding, 1955; Boland, 1956; and Montgomery, 1957). Although the greater anti-rheumatic effects and lessened risks of sodium retention in these compounds have been advantageous, most workers have been concerned by the increased incidence of dyspepsia and gastro-duodenal ulceration which attended their use. Because of this and other disadvantages, the search for newer compounds with fewer unpleasant side-effects has continued, and recently two new steroids, triamcinolone and 6 - methyl prednisolone have been discovered. 6 - Methyl prednisolone (Medrone Upjohn), which is the subject of this report, is 6 - methyl - Δ 1 - hydrocortisone and differs from prednisolone only in the substitution of a methyl group for an H atom in the 6 alpha position.

By means of animal experiments Lyster et al. (1957) have shown it to be three times as potent as prednisolone using the glycogen deposition assay, and twice as potent in anti-inflammatory activity by the granuloma pouch assay. No measurable sodium or water retention was found, and in fact, a sodium and water diuresis was observed in the experimental animal. 6 - Methyl prednisolone has also been shown to be less susceptible to enzymatic reduction by the liver than prednisolone (Glen et al., 1957).

In spite of these encouraging findings the earliest published report of the use of 6 - methyl prednisolone in rheumatoid arthritis was disappointing. Boland and Liddle (1957) stated that it possessed no obvious advantage over prednisolone and that both drugs exerted identical effects in equivalent doses. These findings are, however, at variance with the results of Bilka and Melby (1958), who believed that 6 - methyl prednisolone was 25 per cent. more effective than prednisolone, while Grater (1958) thought it was one and a half times more potent in the treatment of allergic disorders.

Because of these conflicting opinions it was decided to carry out a clinical trial of 6 - methyl prednisolone with the object of answering the following questions :—

1. What is the potency of 6 - methyl prednisolone in comparison with prednisolone?
2. Does 6 - methyl prednisolone possess any advantage over prednisolone in the treatment of rheumatoid arthritis?

METHOD.

Seven patients with severe rheumatoid arthritis were chosen for study and since the purpose of the trial was to compare 6 - methyl prednisolone with the results achieved by prednisolone, only patients who had received prednisolone previously and who were on a stable dose were selected. Before 6 - methyl prednisolone was administered joint function was assessed in accordance with the method described previously (Montgomery, 1957). Thereafter 6 - methyl prednisolone was substituted for prednisolone, and was given, for the first two months in almost equal doses. Owing, however, to the difference in the size of the two tablets (6 - methyl prednisolone is manufactured as a 4 milligramme tablet) exact matching doses could not be given easily and so were not attempted. Two months later a small reduction in the dose of 6 - methyl prednisolone was made and a clinical assessment was carried out then, and at 4 months, when the trial ended. For details of dosage employed see Table No. 1.

Because 6 - methyl prednisolone is an oval shaped tablet, patients were aware that a change had been made in their treatment. To avoid undue emphasis and comment, it was explained that the new tablets were almost identical with the old ones while no special enthusiasm was shown for them.

TABLE 1.

Dosage of prednisolone (P) and 6-methyl prednisolone (6 MP) in milligrammes.

CASE No.	P - BEFORE START OF TRIAL	6 - MP AT START OF TRIAL	TWO MONTHS LATER 6 - MP REDUCED	6 - MP AT END OF TRIAL
1	...	10	...	8
2	...	15	...	10
3	...	12.5	...	10
4	...	12.5	...	12
5	...	12.5	...	10
6	...	12.5	...	10
7	...	12.5	...	8 ³

1. Case 2 inadvertently failed to take an extra half-tablet which was ordered.
2. Owing to this patient's general condition a reduction in dose was not possible.
3. One month before completion of the trial the dose was further reduced because of her continued improvement.

RESULTS.

The results obtained at the various examinations are set out in tables 2, 3, 4, 5, 6 and 7. Although no special questions were directed towards the patients' subjective symptoms, all expressed the opinion that the 'new' tablets were superior to the old ones. While the trial was in progress, cases 2 and 4 had complicating illnesses which made assessment difficult. Case 2 had had a chronic peptic ulcer, resistant to treatment for many months, and when 6 - methyl prednisolone was started symptoms appeared to worsen. Since it was impossible to control the pain and as his arthritic condition necessitated the continuation of steroid therapy, a partial gastrectomy was successfully performed one month before the end of the

trial. Case 4 developed an ischio-rectal abscess three months after the commencement of 6 - methyl prednisolone treatment. This was drained and while he was in hospital the opportunity was taken to repair an inguinal hernia. Both patients were given additional amounts of Medrone to cover the stress imposed by their surgical treatment, but as soon as possible the dose was reduced to the previous level. In theory both should have improved with the enhanced dosage of 6 - methyl prednisolone, but if the tables are perused it will be seen that their response was, in fact, the poorest in the series. It is likely, therefore, that the complications altered their physical condition and accounted, to some extent, for their indifferent progress.

TABLE 2.
Percentage increase (+) or decrease (–) in strength of hand grip
over initial reading (both hands recorded together).

CASE No.		ONE WEEK AFTER STARTING 6 - MP		TWO MONTHS AFTER STARTING 6 - MP		TWO MONTHS AFTER REDUCTION IN 6 - MP
1	...	+ 28.3	...	+121.6	...	+ 135.8
2	...	+ 53.2	...	+117.7	...	+ 2.1
3	...	+ 28.9	...	+ 64.1	...	+ 75.9
4	...	+ 3.4	...	– 14.2	...	– 32.8
5	...	+ 15.8	...	+ 33.6	...	+ 38.6
6	...	+ 73.4	...	+100.1	...	+141.0
7	...	+181.0	...	+225.8	...	+152.8

Strength of Grip.—An increase in strength was seen in all patients at the end of one week's treatment, and in five the improvement was considerable. After two months there were further gains in all but one (4) where the grip had weakened. When the dose of 6 - methyl prednisolone was reduced, strength of grip remained approximately the same in four patients but declined considerably in two (2 and 4) and to a lesser extent in one (7). Nevertheless, at the end of the trial, strength exceeded the initial reading in five patients, very slightly in one (2) and was worse only in one (4).

TABLE 3.
Measurement of finger swelling with Jewellers' Rings.
Percentage increase (+) and decrease (–) both hands.

CASE No.		ONE WEEK AFTER STARTING 6 - MP		TWO MONTHS AFTER STARTING 6 - MP		TWO MONTHS AFTER REDUCTION IN 6 - MP
1	...	– 2.3	...	– 4.6	...	– 8.9
2	...	no change	...	– 3.7	...	– 5.2
3	...	– 4.1	...	–11.3	...	– 8.9
4	...	– 8.6	...	–10.9	...	–16.7
5	...	–12.2	...	–11.2	...	–13.8
6	...	– 3.1	...	– 8.7	...	–10.5
7	...	– 9.0	...	–13.5	...	–13.5

Proximal interphalangeal joints.—During the four months' treatment with 6 - methyl prednisolone, interphalangeal joint size decreased slightly in all, and none showed any increase over the initial reading. Even when the dose was reduced the joints continued to regress in five (1, 2, 4, 5, 6).

Joint mobility.—An increase in joint movement was noted in five patients after a week's treatment, but in two (1 and 5) it declined slightly. At two months, movement had continued to improve, being maintained on the reduced dose, although there were slight individual variations.

TABLE 4.

Measurement of joint mobility to show percentage increase (+) and decrease (−) in movement compared with initial reading (movement of wrists, elbows, knees and ankles recorded).

CASE No.		ONE WEEK AFTER STARTING 6 - MP		TWO MONTHS AFTER STARTING 6 - MP		TWO MONTHS AFTER REDUCTION IN 6 - MP
1	...	− 0.6	...	+ 5.2	...	+15.7
2	...	+18.6	...	+29.1	...	+26.1
3	...	+ 9.2	...	+12.4	...	+12.5
4	...	+ 7.7	...	+ 4.2	...	+ 8.7
5	...	− 5.7	...	+10.0	...	+ 4.2
6	...	+18.5	...	+24.9	...	+23.3
7	...	+20.8	...	+18.3	...	+17.1

Knee-joint circumference.—The changes in this measurement were minimal, but the majority of cases showed a decrease in joint circumference during the period of observation. The reduction in the dose of 6 - methyl prednisolone caused little overall change.

TABLE 5.

Circumference of knee-joints to show percentage increase (+) or decrease (−) in size

CASE No.		ONE WEEK AFTER STARTING 6 - MP		TWO MONTHS AFTER STARTING 6 - MP		TWO MONTHS AFTER REDUCTION IN 6 - MP
1	...	−1.6	...	−0.3	...	−2.0
2	...	+0.9	...	+1.8	...	−0.4
3	...	−1.1	...	−5.7	...	−8.4
4	...	−1.0	...	−1.7	...	+2.1
5	...	no change	...	−3.1	...	−0.3
6	...	−2.3	...	−1.0	...	−2.6
7	...	−1.6	...	−1.2	...	−2.4

Erythrocyte Sedimentation Rate.—The E.S.R. altered very little during the trial. In three (5, 6, 7) it was reduced at the end of the study, in three (2, 3, 4) it was increased and in one (1) it was unaltered.

TABLE 6.
Erythrocyte Sedimentation Rate.

CASE No.		WHILE ON PREDNISOLONE		ONE WEEK AFTER STARTING 6 - MP		TWO MONTHS AFTER STARTING 6 - MP		TWO MONTHS AFTER REDUCTION IN 6 - MP
1	...	4	...	4	..	8	...	4
2	...	66	...	75	...	63	...	76
3	...	14	...	20	...	16	...	24
4	...	50	...	36	...	65	...	58
5	...	18	...	15	...	10	...	12
6	...	28	...	12	...	13	...	12
7	...	54	...	41	...	24	...	26

Weight.—Only one patient (1) gained weight. If cases 2 and 4 who had surgical operations are excluded, the remaining patients showed a slight loss of weight in three (5, 6, 7) and a considerable loss in one (3). While these numbers are too small from which to draw definite conclusions, it seems that patients on 6 - methyl prednisolone are less prone to gain weight than those on prednisolone. It is of interest that case 3, who lost 15 lbs. while on 6 - methyl prednisolone, had gained weight excessively on prednisolone.

TABLE 7.
Weight (lbs.)

CASE No.		WHILE ON PREDNISOLONE		ONE WEEK AFTER STARTING 6 - MP		TWO MONTHS AFTER STARTING 6 - MP		TWO MONTHS AFTER REDUCTION IN 6 - MP		OVERALL INCREASE (+) OR DECREASE (-) IN WEIGHT (LBS.) DURING TREATMENT WITH 6 - MP
1	...	150	...	148	...	153	...	153	...	+ 3
2	...	150	...	151	...	154	...	144	...	- 6
3	...	146.5	...	145	...	134.5	...	131.5	...	-15
4	...	144.5	...	144.5	...	143	...	134	...	-10.5
5	...	180	...	178.5	...	176	...	179.5	...	- 0.5
6	...	176	...	175.5	...	175.5	...	174.5	...	- 1.5
7	...	122	...	119.5	...	121	...	120	...	- 2

Side-effects of 6 - methyl prednisolone treatment.—Because of their previous long-term steroid treatment all patients had already experienced some unpleasant side effects, and it was therefore difficult to know if 6 - methyl prednisolone lessened or increased these complications. Peptic ulceration is the most important hazard of synthetic steroid treatment, and the reputation of any new compound will be largely determined by the frequency of this complication. In this series one patient who had a chronic peptic ulcer continued to have disabling symptoms, and as already mentioned, a partial gastrectomy was carried out. It is unlikely that the 6 - methyl prednisolone made him much worse, for it seems virtually certain that

the severity and chronicity of the lesion would have necessitated surgery, whether steroids had been continued or not. One other patient (6) experienced mild epigastric heaviness after meals which he had not had during two and a half years' treatment with prednisolone. This symptom developed three months after 6 - methyl prednisolone was administered but cleared up quickly with a suitable dietary regime and antacids. A barium meal examination failed to show any ulcer or abnormality in the stomach or duodenum.

Two of the usual side-effects of prednisolone therapy seemed to be lessened when 6 - methyl prednisolone was substituted. The facial rounding or "Cushingoid" facies so characteristically seen in patients on long - term steroid treatment diminished appreciably in three patients and considerably in a fourth during the time they were taking 6 - methyl prednisolone. Similarly facial flushing and the accompanying burning sensation in the face was less pronounced in four patients, pleasing several to whom it had been an annoying feature of their previous treatment.

The tendency to bruise which had been observed in three patients was unchanged when 6 - methyl prednisolone was being taken. No alteration in electrolyte or water metabolism was seen during the period of observation, and no patient had glycosuria, hypertension or mental disturbances as the result of changing to 6 - methyl prednisolone. One patient (4) developed a severe complicating infection when on 6 - methyl prednisolone and it is probable that the treatment effectively masked the early symptoms allowing considerable spread of the infection before the patient sought advice.

DISCUSSION.

From the evidence gained in this short trial it appears that 6 - methyl prednisolone was more effective than prednisolone in relieving the symptoms of rheumatoid arthritis. When given in approximately equal doses joint performance and strength improved, and the patient felt better. Reducing the dose of 6-methyl prednisolone by between 17 and 20 per cent. still left the patient better off. The claim made by the manufacturers that medrone is approximately 25 per cent. more potent than prednisolone appears to be justified, and since the drug is marketed in a strength of 4 milligrammes, this allows a tablet of Medrone to be substituted satisfactorily for one of prednisolone.

The results achieved demonstrate clearly that 6 - methyl prednisolone is an effective suppressive agent in the treatment of rheumatoid arthritis. Whether it possesses any inherent advantage over prednisolone cannot be assessed from this short trial, but there are indications that some side-effects may be less pronounced. Nevertheless, these are among the least serious, and the more important problem of indigestion and peptic ulceration cannot yet be answered. It is obvious, however, that it is impossible to compare the extent and frequency of side-effects of a new steroid administered for a few months with older steroids given for protracted periods. All that can be done at present is to guess at trends, and an extended trial is required before the severity and frequency of side-effects can be accurately gauged.

SUMMARY.

A clinical trial in which 6 - methyl prednisolone was compared with prednisolone is described. Measurement of joint function was carried out at intervals to provide objective evidence of therapeutic response. The drug is an effective suppressive agent for the treatment of rheumatoid arthritis and is slightly more powerful than prednisolone. Side effects appeared to be similar to those occurring with prednisolone but facial rounding and flushing, and increases in weight were less pronounced. No opinion can be expressed about the effect of 6 - methyl prednisolone on gastro-duodenal function.

It is concluded that 6 - methyl prednisolone is a useful new steroid, and if additional experience confirms that the increase in therapeutic efficiency is matched by a reduced incidence of unpleasant side-effects, then it will probably become the steroid of choice for the treatment of rheumatoid arthritis.

I wish to thank Dr. A. R. H. Hicks and Mr. R. G. Kenny of Upjohn of England Ltd., who generously provided the Medrone for this trial, and for their continued help and co-operation. I am also indebted to Sister A. M. Wilson, S.R.N., for help with the clinical examination of the patients, and to Miss M. Gordon for typing the manuscript.

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Recent Advances in Cardiovascular Disease

Observations on Chest Pain and some Aspects of Digitalis Medication

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THAT a first description of an important clinical condition should be so complete and at once so concise that, for nearly two hundred years, no one has added anything material to it, or discarded anything from it as irrelevant, is indeed a great rarity. Yet this is true of Heberden's description of angina pectoris, as it is contained in the paper he read before the Royal College of Physicians in London on 21st July, 1768, and published in 1772. Nevertheless, it cannot be denied that in a certain proportion of patients complaining of pain in the chest, it is still far from easy to diagnose its origin with certainty. A diagnosis of "Pseudo-angina" is not more than a pseudodiagnosis. "? Pseudoangina," which was given in 1957 as a clinical diagnosis in no fewer than three cases where a cardiogram was requested, is even worse. While abandoning the term 'angina' altogether and replacing it by 'cardiac—or non-cardiac, as the case may be—pain due to . . .' would unquestionably make for clearer thinking, 'angina' has become too deeply rooted for this to be a practicable proposition. For the purposes of this discussion it is proposed to distinguish between angina of effort, angina of rest without evidence of myocardial infarction, and cardiac pain due to myocardial infarction, singling out for discussion a few aspects of each.

ANGINA OF EFFORT.

In most cases the diagnosis has to, and can easily be made from the history, attention to the well known precipitating factors being of particular importance. Difficulties tend to arise in patients with atypical distribution of pain. It used to be taught that radiation of pain into the upper jaw, as distinct from the lower jaw, does not occur in angina of effort, but the personal observation that this was present in three patients demonstrates that this rule is not absolute. In patients having a duodenal ulcer, anginal pain may be felt in the distribution of the ulcer pain and the anginal element therefore be overlooked. In one patient angina of effort was experienced in the right supraclavicular fossa, the diagnosis being subsequently corroborated when myocardial infarction occurred, with pain starting in the right supraclavicular fossa and thence radiating retrosternally. In another patient the unusual distribution of anginal pain in the right iliac fossa resulted in the removal of a healthy appendix (acute "remunerative" appendicitis, Wheelock, 1957). Of great importance for the understanding of referred pain are Cohen and Jones's (1943) observations of angina of effort in a phantom arm, which could be relieved or modified by anaesthesia of the brachial plexus or neuroma in the stump,

and Cohen's (1944) observation that pain of angina of effort could be elicited in a blister produced on the medial aspect of the right elbow though the patient had never had pain on the right before. These and similar observations are in accordance with the view that visceral pain is felt, either if the impulses arising from the viscus are sufficiently intense, or if, when reinforced by impulses normally arising from pain endings in homosegmental somatic structures, they exceed the threshold value. In other words, there is a summation of impulses arising from different structures with the same segmental nerve supply.

If the diagnosis of angina of effort is in doubt and, as is often the case, the resting cardiogram is normal, serial tracings after exercise may clinch the diagnosis by showing signs of temporary myocardial anoxia after exertion and thus supporting a clinical diagnosis of a cardiac origin of the pain.

In every patient a thorough clinical, cardiographic and radiological examination is necessary in order to ascertain the underlying condition. Of these, coronary sclerosis is, of course, by far the commonest, but by no means the only one. Two may be briefly discussed.

The recognition of an underlying aortic stenosis has become of paramount importance because of the increasing importance of surgery. While the symptoms and signs of this condition will not be discussed, attention should be drawn to Brock's recent findings (1957) that valvular aortic stenosis without demonstrable calcification of the aortic valves is rare in patients over 40. The demonstration of such calcification by the appropriate radiological technique is therefore a valuable diagnostic help. Brock has also described a functional subvalvular aortic stenosis, due to severe left ventricular hypertrophy and affecting the left outflow tract. This condition, as distinct from the analogous one in the right ventricle, is inoperable. If it co-exists with valvular stenosis, surgery of the valvular lesion may not relieve the condition.

Calcification of only the ascending aorta is practically pathognomonic for a syphilitic origin; this was first shown by Jackman and Lubert (1945).

Regarding treatment, a few points about drugs may be singled out. Trinitrin is, of course, the preparation of choice. In view of its transient effect it is unsound to give it a specified number of times a day. It should be taken at the onset of the pain, and also as a preventive whenever the patient is compelled to carry out an activity which he knows brings on the pain. Leaving home in the morning during the cold season is a case in point. The preparation should be of a specified make, as there are quite a number of ineffective tablets on the market, and should not be more than three months old. An attempt at increasing the patient's exercise tolerance by a combination of vasodilator and sedative drugs is sometimes, but by no means invariably successful. The following has proved useful :—

Erythroltetranitrate	-	gr. 1/20,
Theobromin. pur.	-	grs. iiss,
Papaverin. hydrochlor.	-	gr. j,
Phenobarbitone	-	gr. 1/6.
T.d.s., p.c.		

The doses of the individual ingredients are small and should be increased according to the patient's reaction and requirements. If, with much larger doses, no effect is seen in about a month, there is no object in continuing.

Another combination, sometimes useful in angina of effort, but particularly in nocturnal angina of rest, is :—

Chloral hydrat.	•	-	grs. v
Theobromin. sodiosal.		-	grs. viiss
Phenobarbiton. sod.		-	gr. $\frac{1}{4}$
Spir. menth. pip.	-	-	m x
Aqu.	ad	-	$\frac{1}{2}$ ounce.
$\frac{1}{2}$ ounce at bedtime (or t.d.s., p.c.)			

Here again, the individual doses are small and should be increased as required.

Some patients respond well to Peritrate.

ANGINA OF REST.

Anginal pain on going to bed may be due to cold sheets. True nocturnal angina 'decubitus' is common in aortic incompetence. If, in a patient with angina of effort, pain occurs after smaller and smaller amounts of exertion and eventually at rest, this is in most cases due to progressive coronary disease and often heralds, as a premonitory symptom, the onset of myocardial infarction. It is also the basis of the so-called "coronary insufficiency." The use of this term in a clinical sense should be discouraged, since it is, and should remain, a physiological term denoting a disproportion between blood requirement and supply. Clinically, in most of these cases the condition is due to coronary occlusion without infarction, or to hæmorrhage, mostly subendocardial.

Some other conditions, giving rise to more prolonged anginal pain not related to effort, without evidence of infarction, merit a brief discussion.

Paroxysmal tachycardia may give rise to severe anginal pain, and cardiographic signs of myocardial anoxia may be found for many hours or even days after such an attack, the "post-tachycardic syndrome." Occasionally this is also seen with the sudden onset of atrial fibrillation. A less common cause is *phæochromocytoma*, but its recognition is important because of the prospects of a cure by surgery. In these cases the pain is typically associated with a paroxysmal rise of blood pressure accompanied by pallor, sweating, and hyperglycæmia; arrhythmias of various kinds are common. These features are due to a paroxysmal increase in the amount of circulating adrenaline and noradrenaline. It is far more difficult to diagnose the condition in patients in whom typical attacks are absent and the hypertension is sustained. The possibility suggests itself in patients in whom a family history of vascular disease is absent, particularly in younger patients, in whom coarctation and renal disease can be excluded. The most reliable diagnostic test at present is the quantitative determination of pressor substances (adrenaline and noradrenaline) in the urine. An even rarer cause of anginal pain not related to effort is *spontaneous hypoglycæmia*. This condition was suspected in a patient in whom a detailed history revealed that no attack ever occurred less than two hours after the last

preceding meal. The diagnosis was confirmed by a blood sugar tolerance curve : about 1 hour and 40 minutes after the ingestion of glucose the patient became very distressed while, at that time, the blood sugar dropped steeply from 150 to 78 mg. per 100 ml. within less than half an hour. A high protein low carbohydrate diet with frequent small meals prevented the attacks (Schott, 1949).

MYOCARDIAL INFARCTION.

This is now considered in the first instance in all patients with more prolonged anginal pain not related to effort. The typical symptoms and signs are too well known to merit discussion. More recently, in cases where the diagnosis is uncertain, determination of the transaminase in the blood has been employed. This is an enzyme, normally present in many tissues and particularly in the heart, which is set free in larger quantities by a myocardial infarct, increased amounts being found from 24 to about 96 hours after the attack. A further test, also applied more recently in doubtful cases, is the determination in the blood of C reactive protein, an abnormal globulin which reacts with the somatic "C" polysaccharide of pneumococci to form a precipitate. It is found later after an attack than the transaminase, and remains raised for far longer subsequently. This test is not specific, but gives positive results in transmural infarcts, though not during the premonitory stage.

A few points about treatment : Once the diagnosis of myocardial infarction is established, trinitrin should not be given. The writer's impression has been for years that, in this condition, the drug not only is useless, but tends to aggravate the condition. An explanation of this seemingly paradox observation seems to be contained in observations by Wégria et al. (1951). These authors found in ten healthy subjects that 0.6 mg. trinitrin, given sublingually, increased the cardiac output per minute, the systolic output and the heart rate, while the blood pressure did not change. Cardiac work per beat was therefore increased. In view of these findings the authors concluded that trinitrin relieves anginal pain by increasing coronary flow relatively more than the work of the heart. Such increase in coronary flow is no longer possible in the event of a structural obstruction. In their own words, the observations "appear to suggest a physiological basis for caution in using nitroglycerin when the cause of the anginal pain is not definitely established to be simple temporary myocardial ischæmia and may be due to coronary occlusion."

The scope of anticoagulants is still controversial. Strict control of the prothrombin time is indispensable, and with this proviso there is no objection to giving it in all cases, though this is not a practicable proposition to be universally applied in domiciliary practice. It should certainly be given in all more severe cases ; if the attack is not the first one ; if the condition is complicated by diabetes ; and if there are arrhythmias. These are usually ectopic in origin, either atrial or ventricular. Except for very occasional extrasystoles, such arrhythmias should be immediately suppressed. In the atrial varieties, quinidine sulph. is the drug of choice (0.2 g. four-hourly ; if necessary, at shorter intervals, or in doses of 0.4, rarely 0.6 g.). In ventricular ectopic arrhythmias, procaine amide is an alternative (initial dose

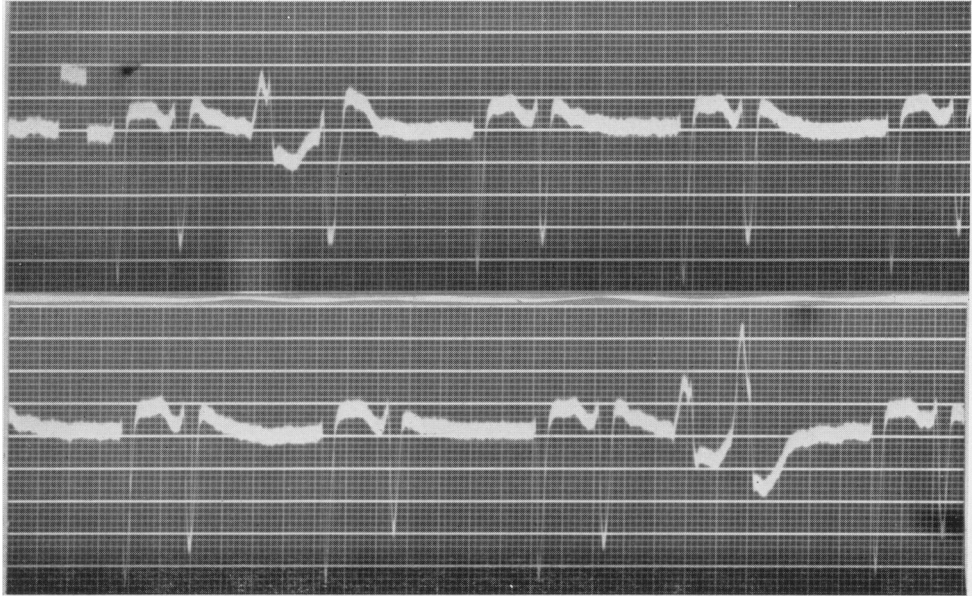


Fig. 1.—From a woman with advanced congestive heart failure who had been treated with large doses of digitalis. The clinical impression was atrial fibrillation with a high ventricular rate. The tracing shows atrial fibrillation with multiform extrasystoles, at times several occurring in succession. Recorded a few days before death. Lead V-2; the two strips are continuous.



Fig. 3.—From a woman with congestive heart failure who had been taking digitalis for a considerable time. Atrial fibrillation with a low ventricular rate and bigeminy due to extrasystoles. Clinically, this arrhythmia might be mistaken for complete A-V block with triple rhythm.

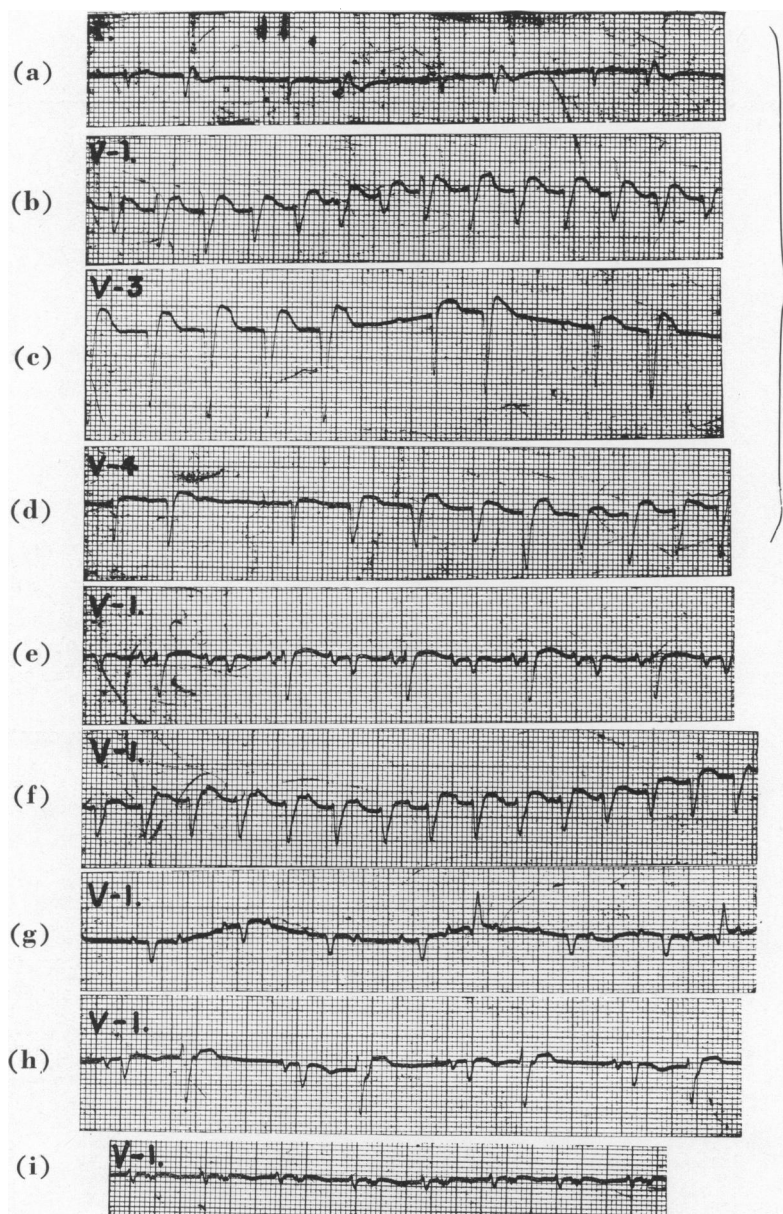


Fig. 2.—Various types of arrhythmia due to, or aggravated by digitalis intoxication, recorded over a period of two months in a woman of 64 with congestive heart failure. a - d are portions of the same record, taken on 19. 12. 1956, when the patient had been on Digoxin for some time, medication being stopped that day. a: Atrial tachycardia of about 150, first degree A-V block (P-R: 0.28 sec.), bigeminy due to ventricular extrasystoles. b: Paroxysmal ectopic ventricular tachycardia, rate about 166. c: End of paroxysmal ectopic ventricular tachycardia, rate about 130; then bigeminy due to ventricular extrasystoles. d: Bigeminy due to ventricular extrasystoles; then ectopic ventricular tachycardia, rate about 166. e: 18. 1. 1957. On Digoxin since previous day. Bigeminy due to ventricular extrasystoles occurring late in diastole; sinus rate about 94. f: 22. 1. 1957. Digoxin stopped that day. Ectopic ventricular tachycardia of about 166, independent atrial tachycardia of about 150. g: 24. 1. 1957. Without Digoxin for the last two days. Atrial tachycardia of about 166 with A-V block varying between 3 : 2 with aberrant ventricular conduction of the second beat, and 2 : 1. h: 29. 1. 1957. Still off Digoxin. Bigeminy due to ventricular extrasystoles, sinus rate about 88. i: 15. 2. 1957. Sinus tachycardia of 110-115. Patient died the following day.

1.75 g, followed by 0.75 g if the tachycardia persists after four hours). It is advisable subsequently to tail off these drugs gradually within about three weeks, but in some cases a maintenance dose is necessary for a longer period. Not all such arrhythmias are ectopic ones: In posterior infarcts, disturbances of atrio-ventricular conduction are not uncommon. These should not be treated as they invariably disappear; besides, they may actually be beneficial by lowering the ventricular rate.

Periarthritis of the shoulder and the shoulder-hand syndrome are now recognised as complications occurring in some cases of myocardial infarction, mostly after, but sometimes before the attack. Periarthritis is characterised in the acute stage by pain in the shoulder which may be very severe indeed, particularly at night, and limitation of abduction and internal rotation. Recognition of this condition as a separate entity is important because otherwise it may be misinterpreted as signifying a further infarct. In the acute stage it may require liberal use of analgesics, particularly to ensure sleep, and rest of the shoulder is important. Manipulation is contra-indicated at this stage. If necessary, the affected area should be infiltrated with novocaine. When the acute stage has subsided, injections of hydrocortisone into the joint are sometimes effective: 50 mg. in a 2 ml. suspension plus 1000 units of hyaluronidase plus 2 ml. procaine. If the shoulder becomes stiff ("frozen") and the condition has become entirely inactive, manipulation under an anaesthetic is the treatment of choice, followed by physiotherapy.

Regarding the connection between periarthritis of the shoulder and coronary disease, there are two main views: disuse of the shoulder, and reflex changes in the sympathetic. The latter seems more likely. One main connecting link is pain (Schott, 1947). Judging from a personal study on twenty cases, referred primarily for the shoulder lesion, the high incidence (fourteen) of cardiovascular disease in that small group suggests also a relation based on vascular disease affecting particularly the supraspinatus (Ellman and Schott, 1948).

Mistakes in the diagnosis of myocardial infarction may consist, either in not diagnosing one that has occurred, or in mistaking another condition for it.

Failure to diagnose a painless infarct tends to occur in cases where the condition presents as a sudden deterioration of the circulation, or the sudden occurrence, in a seemingly healthy subject, of heart failure, e.g. pulmonary oedema. Another group consists of patients with a cerebrovascular accident occurring simultaneously, or almost simultaneously with a myocardial infarct which it overshadows. This may be due to cerebral embolism, but sometimes the common basis is vascular disease. Post-operative myocardial infarction is probably commoner than believed, and tends to be missed because the patient is still under the influence of analgesics or anaesthetics. It should be thought of in cases of unexplained post-operative pyrexia and/or circulatory failure. Pre-operative cardiograms would be desirable on a larger scale than recorded at present.

Regarding conditions mistakenly diagnosed as myocardial infarction, it is instructive to remember that when Herrick described coronary thrombosis in 1912 and again in 1919, it attracted very little attention. The same Herrick found in

1938 "some 30 altogether" conditions mistakenly diagnosed as coronary thrombosis..

Pulmonary embolism may mimic myocardial infarction to an extent that even the most experienced physician may be misled. In such cases the cardiogram may establish, or at least strongly suggest, the correct diagnosis by showing deep S waves in lead 1, deep Q and inverted T waves in lead 3 and inverted T waves in right ventricular chest leads; incomplete pictures of this type may also be diagnostic (see the recent review of this subject by Cutforth and Oram, 1958). However, in a large proportion the cardiogram either remains normal or shows inconclusive changes. In *acute benign pericarditis* the pain may be indistinguishable from that of myocardial infarction both in character and distribution. However, the condition is often preceded by an acute upper respiratory infection, and the pain is greatly aggravated by deep breathing and change of position. Though first described over one hundred years ago by Hodges (1855) it is often missed, yet its recognition is important because of its excellent prognosis. In most cases the diagnosis can easily be made from the cardiogram. In *diaphragmatic hernia*, too, pain may be indistinguishable from angina due to coronary disease; this is true particularly for small hernias where such pain may occur in the absence of any digestive symptoms. It also resembles angina by the importance of emotional tension as a precipitating factor, and relief by belching. Anæmia, often present in diaphragmatic hernia, may aggravate the pain. It is essential to think of this possibility in cases with upper abdominal symptoms of doubtful origin, especially if they occur chiefly or only at night, or are associated with slight dysphagia or anginoid symptoms (Hurst, 1934). Once the diagnosis is established and the not infrequent co-existing coronary disease is excluded, reassurance that the chest pain is not due to heart disease is of paramount importance. Antispasmodics are usually more effective than trinitrin. Experimental findings suggest that the pain is due to a vago-vagal reflex (Gilbert et al. 1940).

Chronic cholecystitis and particularly *gall stones* are known to give rise to pain which, because of its retrosternal radiation or even sole retrosternal location, may mistakenly be diagnosed as myocardial infarction. Without going into the still controversial nature of the relation between gall bladder disease and angina pectoris, it may be said that, generally, such patients stand up well to, and benefit greatly by, removal of the diseased gall bladder.

Cervical spondylosis may simulate myocardial infarction if it produces root pain of sudden onset in the distribution of the left seventh cervical segment, as the pain may radiate into the left pectoral region and down the left upper arm and may be associated with pain in the neck. If there is disc protrusion, this involves the interspace between the sixth and seventh cervical vertebræ, but the root may also be compressed by the disc one segment below where, owing to its oblique course, it passes through the intervertebral foramen (Brain, 1948; 1956). Points in differential diagnosis are: in spondylosis, there may be torticollis and spasm of neck muscles; passive movement of the neck is painful and intensifies the irradiating pain (Brain et al., 1952); the pain in the hand tends to affect the middle finger or

radiates down the radial border of the forearm to thumb, index and middle finger (Dimsdale, 1954). The left triceps jerk may be diminished (C 6-7). X-rays of the cervical spine are of paramount importance by revealing reduction of one or more disc spaces, arthritic changes in the neurocentral and articular joints, osteophytes, and disturbance of the normal cervical lordosis. If necessary, they are supplemented by a myelogram.

Lesions of the thoracic cage. Sudden pain caused by fracture of a rib due to violent coughing, and traumatic strain of the pectoralis minor muscle may be recalled. Slight displacement of the second dorsal vertebra, sometimes also of the third, is quite common. This may give rise to agonising pain, closely simulating myocardial infarction. This condition may be related to, and sometimes be actually the main underlying mechanism in some cases of, the costo-chondral syndrome, also called Tietze's syndrome who first described it in 1921. In a series of sixty-two patients with this condition, studied by Benson and Zavala (1954), the third left cartilage was most frequently involved, and tenderness of the corresponding costo-vertebral junctions was often found. The vertebral displacement responds well to appropriate physiotherapy, which consists in overcoming the protective muscle spasm and restoring proper alignment by means of gentle manipulative massage.

There seems also to be some connection between anginal pain and *herpes zoster* which occurs not infrequently in the area of anginal pain (Spillane and White, 1939; Cohen, 1944). In its initial stages, herpes zoster may in such patients give rise to special diagnostic difficulties.

DIGITALIS THERAPY.

Reverting to angina of effort, it is a common experience that patients lose their pain with the advent of congestive heart failure. This is usually attributed to the fact that heart failure so reduces the amount of activity that exertion bringing on the pain is no longer possible. This may be so, but is unlikely to be the whole story. For, if digitalis is given to a patient with congestive failure, who had pain on effort before and no pain after the onset of failure, anginal pain may recur after digitalisation and improvement of failure even without any increase of activity. This has the practical importance that, in these cases, the optimum dose of digitalis is that which results in a maximum improvement of failure, with a minimum, if any, increase in angina of effort. This leads to a consideration of some aspects of *digitalis* treatment.

“Un remède expérimenté vaut mieux qu'un nouveau inuenté.” This wise dictum of Paré of 1575 is to-day as valid as, if not more valid than, it has ever been. For it is essential in clinical practice to acquire experience with a very few reliable digitalis preparations and to bear in mind the following approximate equivalents : 0.25 mg. Digoxin (Lanoxin) = $1\frac{1}{2}$ grains of Powdered Leaf B.P. = 15 minims of the B.P. Tincture. Failure to recognise these equivalents is likely to lead to under-digitalisation with powdered leaf. It is a mistake to consider the heart rate as a guide to dosage in cases with normal rhythm; this is a mistaken application of conditions prevailing in patients with atrial fibrillation, where stabilisation of the ventricular rate round about 75 is the aim. In both groups, i.e., those with normal

rhythm and those with atrial fibrillation, a rise in heart rate during digitalis treatment is often misinterpreted as a sign of under-digitalisation, the true cause, namely, tachycardia or arrhythmia due to digitalis overdosage being missed. Examples are provided by patients with atrial fibrillation with multiform ectopic ventricular beats (Fig. 1), or with ectopic ventricular tachycardia (Fig. 2), in whom the high ventricular rate induced the physician to continue medication or even increase the dose of digitalis until the true state of affairs became obvious from the cardiogram. Another arrhythmia, more recently recognised as often due to digitalis overdosage, is ectopic atrial tachycardia with atrio-ventricular block (Fig. 2) (Lown and Levine, 1955; Fletcher and Brennan, 1957). This arrhythmia may, however, also occur without digitalis and be a dreaded complication of myocardial infarction, where it causes an increased strain on the diseased heart, aggravates the prognosis and sometimes does not respond to any treatment. In some cases of atrial arrhythmia the decision when to use digitalis, and what doses to give, may be extremely difficult.

Occasionally, a slow regular pulse, associated with a triple rhythm, is mistakenly diagnosed as sinus rhythm with complete A-V block and gallop rhythm, whereas the condition is actually due to atrial fibrillation, bigeminal rhythm and complete (or nearly complete) A-V block; the 'gallop rhythm' was simulated by an extra-systole occurring early in diastole after each conducted beat (Fig. 3). This arrhythmia is often another manifestation of digitalis intoxication.

Ventricular extrasystoles, and bigeminal rhythm due to one ventricular extra-systole occurring after every conducted beat (Fig. 2), are, of course, a common sign of digitalis intoxication in patients with normal rhythm as well as with atrial fibrillation. It should be stressed, however, that extrasystoles present without digitalis medication not only are no contra-indication to the exhibition of the drug, but an additional indication since they often disappear early during digitalis treatment. Should they recur during the exhibition of digitalis, their re-appearance calls for the same caution in the administration of the drug as when they appear for the first time while it is given.

In conclusion, one variety of heart failure may be mentioned, for a special reason, in which digitalis is useless: vitamin B₁ deficiency. In this country, this condition is usually found in alcoholics though occasionally encountered as a result of a grossly inadequate diet. In one personal observation in a patient in whom the condition was due to alcoholism, vitamin B₁, given by injection and by mouth, considerably improved his condition within three weeks, but the cardiogram, compared with that taken initially, showed marked deterioration, with inverted T waves in lead 1, absent T waves in lead 2, and further lengthening of the previously already prolonged duration of electrical systole. Three weeks later, the patient felt fit and his cardiogram was then normal. Subsequently, this patient started again to drink heavily and discontinued taking vitamins, with the result that he went downhill both physically and mentally, but his cardiogram remained normal on repeated re-examinations (Schott, 1944). These observations are in accordance with experimental findings obtained in rats fed on vitamin B₁ deficient diet, namely,

temporary inversion of T waves occurring after injections of vitamin B₁ in some animals, which was not consistently reproducible on repeated inductions of vitamin B₁ deficiency (Weiss et al., 1938). These interesting discrepancies between cardiographic and clinical findings should remind us—and such a reminder is timely in these days of increasing reliance, by some doctors, on an ever increasing number of technical tests—that we are, and should remain, clinicians first and foremost, to whom the progress of the patient as a whole human being is the goal that alone matters.

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Miliary and Meningeal Tuberculosis:

A Review of 354 Cases

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THE 354 cases dealt with in this study were treated in the Whiteabbey Hospital from late in 1947, when streptomycin first became available, to the end of 1956. 114 of the cases died. There were 76 cases of miliary disease alone, 160 cases of meningeal disease in which miliary spread was not detected, and 118 cases of miliary and meningeal disease combined. The age group with the highest incidence was 0-4 years, and in this group there were 120 cases. The lowest incidence occurred in the 10-14 age group in which there were 33 cases. In the adult group there were 95 cases aged from 20 to 66 years, with 5 patients over 60. Sixty per cent. of these adult patients were in the 20-30 age group.

TABLE I.

Cases by age and type of disease, and deaths
by age, type of disease and duration of illness.

AGE GROUP IN YEARS	MILIARY					MENINGEAL					MILIARY AND MENINGEAL				
	Cases		Deaths occurring			Cases		Deaths occurring			Cases		Deaths occurring		
			Under 1 month	Over 1 month	Total			Under 1 month	Over 1 month	Total			Under 1 month	Over 1 month	Total
0-4 ...	21		4	2	6 ...	65		20	9	29 ...	34		8	6	14
5-9 ...	9		—	—	— ...	30		8	6	14 ...	16		—	2	2
10-14 ...	7		1	—	1 ...	16		4	2	6 ...	10		—	2	2
15-19 ...	14		2	—	2 ...	15		2	1	3 ...	22		2	5	7
20+ ...	25		4	1	5 ...	34		11	6	17 ...	36		—	6	6
TOTAL ...	76		11	3	14	160		45	24	69	118		10	21	31

When streptomycin first became available this hospital was one of the centres to which a supply of the drug was given for clinical trial. The amount that could be allotted was limited, and only a small number of patients could be treated at this time. The very advanced cases could not be treated. When streptomycin became freely available, and later when PAS and isoniazid were introduced, almost all the cases admitted received some chemotherapy, except those obviously moribund.

CLINICAL FEATURES.

The age incidence and deaths are shown in Table I. The highest death rate occurred in the youngest age group. The number of advanced cases was high in all the three disease groups and at all ages. Sixty per cent. of deaths took place in

under one month, many of them within a few days of admission. Early diagnosis was difficult, particularly in the very young. Many of the children were said to have had recent fevers such as measles or whooping cough, though it was not always clear if these fevers had in fact occurred. The variability in duration and degree of the prodromal symptoms was a striking feature. Some patients seemed to have been vaguely ill for several weeks or months. Some of them appeared to have had a primary infection merging into miliary or meningeal disease. Other patients gave only a short history of malaise or an indefinite febrile illness before diagnosis. Many had been at work till a few days before admission to hospital. One boy attended a mobile mass X-ray unit, and was found to have well marked miliary tuberculosis.

History of contact with an infectious case of tuberculosis was given by many cases, particularly the children, though frequently the infectious case was not discovered till after the patient's admission to hospital. Absence of history of contact by no means excluded contact—in one case after an interval of two years it was discovered that a baby with meningitis was the illegitimate child of a mother who was a patient in the same hospital. There were several instances of more than one case of miliary or meningeal tuberculosis occurring at the same time, or within a short interval, in members of the one family. During one year, three children of a father with pulmonary disease developed miliary or meningeal disease from which two of them died. It was not only young children who showed this marked susceptibility to infection—there were some cases of young adults being equally vulnerable. A brother and a sister, both over 20, developed meningitis within a few months of each other, both presumably having been infected from the same source.

Intrathoracic lesions, demonstrated by radiology, and suggestive of recent primary infection were found in 109 cases, mostly in the 0-10 age groups, but at least one was over 20. In several cases, presenting initially as meningitis, the radiological signs of primary infection developed some months later. Absence of such signs did not exclude an intrathoracic primary, since in some cases coming to post-mortem evidence of primary infection was so small as to preclude detection by radiology. Evidence of extrathoracic primary infection was found or suspected in a few cases. One child of a tuberculous parent suffered a burn on a finger. It shortly afterwards was proved to have a tuberculous gland in the axilla, and after a brief interval developed miliary disease. From this it fortunately recovered. It has been shown recently by Miller (1958) that primary infection by some route other than by inhalation is not uncommon. History of erythema nodosum was rare—less than ten cases could be presumed to have occurred. Evidence of abdominal tuberculosis was also very uncommon. Previous clinical tuberculosis was more often found in the adolescent and adult groups than in the children. There were only 36 such cases—bone, genito-urinary or glandular. The adult type of pulmonary disease was also uncommon—only 52 cases. There were a few cases of miliary or meningeal disease following surgical operations—removal of a tuberculous kidney, incision of a septic finger (probably tuberculous dactylitis) diagnostic curettage of the uterus, thoracoplasty—but these may have been coincidental.

There were slightly more females than males in the miliary group, the excess being in the 0-4 and 15-19 group. This tendency has also been noted by Debre (1952) and Bentley et al. (1954).

DIAGNOSIS.

In the *miliary* cases diagnosis was usually confirmed by the radiological appearance and by the detection of choroidal tubercles. These tubercles were found in 25 cases of miliary disease alone, in 59 cases of combined miliary and meningeal disease and in 8 cases of meningeal disease. Occasionally they were not found till some weeks after the diagnosis had been made. The Mantoux reaction was almost invariably positive, though it was sometimes necessary to repeat it with progressively lower dilutions of tuberculin. Bacteriological confirmation of miliary disease was usually obtained by the finding of *Myco. tuberculosis* in the fasting gastric residue. Positive cultures were found in 49 of the 76 miliary cases. During the early years of this investigation a few of the cases gave a positive urine culture (not renal cases), but during the later years the isolation of tubercle bacilli from the urine has become very unusual. The reason for this is not clear—it may be that the cases during the first few years were admitted at a more advanced stage of the disease, but this was not always clinically evident. Rarely there was some other lesion, glandular, genital or osseous, from which the organism could be recovered. A few attempts were made to isolate the organism from blood or bone marrow, but without success. Too many investigations tend to delay the initiation of specific treatment, and are perhaps undesirable, particularly in a very young child. A lumbar puncture was a routine procedure in the pre-treatment survey. It was found to be absolutely essential to obtain the specimens for bacteriological examination before any specific therapy was given. Frequently only a single positive culture was obtained—usually from the gastric residue—to give bacteriological confirmation, and this in spite of repeated examinations after treatment was started.

Confirmation of *meningeal* disease was made by examination of the cerebro-spinal fluid. There were also two cases of tuberculoma presenting as brain tumour, where tubercles on the meninges were seen during operation; in both of these cases tubercle bacilli was subsequently isolated from cerebro-spinal fluid. The combination of raised CSF protein and cells, with lowered sugar was the usual finding. The degree of deviation of these components from the normal reflected to some extent the stage to which the disease had advanced. High protein (e.g. 100-200 mg.) and very low sugar values were more often associated with late diagnoses. Low chloride content also appeared to be more common in advanced cases. However, an exact correlation of clinical condition and CSF changes was never possible, as the latter varied greatly in the speed of their development and in their intensity. Rarely a case presented in which the sugar was normal but a repeat puncture after an interval of one or two days showed a fall. In fact, a falling sugar level was considered to a diagnostic feature of significance, and its presence or absence was often found valuable in differential diagnosis. Cell counts varied widely from about 60-300, lymphocytes usually predominating. Occasionally polymorphonuclears were the more numerous for the first few days—this was sometimes the case in

very young children. In rare cases a very high cell count was found giving a turbid fluid with polymorphonuclears predominating. These cases were sometimes initially thought to be due to infection with pyogenic organisms, unless some other diagnostic feature such as tubercle bacilli in the smear or associated miliary disease indicated the correct diagnosis. The high cell count as a rule subsided after a few days to give the more usual pattern. An interesting group of 11 cases gave an unusual picture. In some of these the cell count remained low (10-20) with protein content rising to the usual level. In a few cases both protein and cell counts remained low throughout the illness (protein under 50, cells 30-40). The sugar content was decreased and tubercle bacilli were in every case recovered by culture. The patients were, in the main, children of under 3 years, but a few were adults. Coexistent miliary disease was found in 7, clinical signs of advanced meningitis were present in all, and none of them survived. It would appear that the absence of reaction in the CSF indicated a profound lack of resistance in the patient, whereas a sharp reaction did not conflict with a favourable prognosis.

Tubercle bacilli were found in the fasting gastric residue of 40 out of 160 cases who had meningitis alone, and not necessarily accompanied by radiological evidence of disease in the thorax. Choroidal tubercles were found in only 8 cases of meningitis without overt miliary spread.

There was one patient, a girl of 17, who had a double infection — with pneumococcus and tubercle bacilli. Both organisms were isolated from the purulent CSF on admission. She had previously been trephined in another hospital, and the pneumococcal infection may have been secondary. Giusti and Barilli (1952) describe 60 such cases, most of them associated with intraventricular drainage.

There were 118 cases of combined miliary and meningeal disease, 63 males and 55 females. Incidence and deaths were highest in the 0-4 age group: 64 cases had both conditions on admission, and 54 cases presented initially as miliary disease and developed meningitis after treatment had been commenced. The interval after which meningitis developed varied from a few days or weeks in the majority to several months in a few cases. These patients in whom meningitis supervened afforded an interesting study in insidious onset. Almost invariably, slight changes in the CSF occurred before any clinical signs or symptoms were apparent. The earliest sign was the isolation of tubercle bacilli from a fluid which in all other respects was normal. (Since the isolation was by culture its value was only retrospective). In a few days, or even one to two weeks later, very slight increase in cells and protein occurred, still without any definite clinical signs of meningitis. The fully developed clinical picture might be further delayed by a few days. A clinician, experienced in performing lumbar puncture in these cases, could sometimes detect a slight increase in fluid pressure as the earliest clinical sign.

These cases, in which the development of meningitis could be observed as a gradual process during treatment of miliary tuberculosis, were most common when streptomycin alone was used in treatment. After PAS was added to the treatment regime, such cases were encountered, but much less frequently. A few of those which did develop presented an unusual syndrome. Slight increase in cells and

protein were noted in the CSF, and tubercle bacilli were isolated by culture. The slightly abnormal fluid, without definite clinical signs, persisted for two or three weeks, and then returned to normal. There may have been some almost imperceptible deterioration in clinical condition, but these 'abortive' cases of meningitis resolved without intrathecal therapy.

After isoniazid became available, its administration together with streptomycin and PAS proved effective in preventing the development of meningitis in miliary cases. No case of miliary disease developed meningitis while actually on treatment with the three substances. Meningitis supervened in one case which had had 180 days' treatment for miliary disease. This patient, a woman of 24, had been off treatment for four months when meningitis developed, and her condition gave rise to some suspicion of an intracranial tuberculoma. Two other cases had had short pre-meningitis courses of isoniazid, but the drug had been discontinued for some reason before meningeal disease developed.

TABLE II.

Cases by age and type of disease and recovery of *Myco. tuberculosis*.

AGE GROUP IN YEARS			MILIARY			MENINGEAL			MILIARY AND MENINGEAL		
	Cases		M.T. isolated by culture			M.T. isolated by culture			M.T. isolated by culture		
			F.G.R.	CSF	Other	F.G.R.	CSF	Other	F.G.R.	CSF	Other
0-4	21	...	12	-	- ...	18	58	- ...	34	22	30
5-9	9	...	5	-	- ...	6	28	- ...	16	9	14
10-14	7	...	6	-	- ...	5	15	- ...	10	8	10
15-19	14	...	10	-	- ...	4	12	- ...	22	20	21
20+	25	...	16	-	- ...	7	29	- ...	36	17	29
TOTAL	76	...	49	-	3	40	142	2	118	76	104

N.B.—F.G.R.=Fasting Gastric Residue.

Other=Glandular, osseous, genito-urinary or post-mortem material.

LABORATORY INVESTIGATION.

The isolation of *Myco. tuberculosis* is indicated in Table II. The organism was recovered from fasting gastric residue by culture on Loewenstein-Jensen medium. The specimen of residue was obtained by aspiration without lavage of the stomach. A Ryle's tube was used, which had been sterilized by autoclaving, to avoid the possibility of the tube being contaminated from previous use. In the miliary cases the greatest number found positive (88 per cent.) was in the 10-14 age group. In the meningeal cases the greatest number (33 per cent.) was again in the 10-14 age group. In the 118 miliary and meningeal cases 76 (64 per cent.) had positive gastric residue, the greatest number being in the 10-14 and 15-19 groups (80 and 95 per cent. respectively).

Cerebrospinal fluid was examined in all cases. In a few moribund patients the fluid was taken after death. Tubercle bacilli were isolated in 144 out of 160 meningeal cases, in 110 out of 118 combined miliary and meningeal cases, and in

none of the miliary cases. In addition to direct smear examination, cultures were made on Loewenstein-Jensen medium and on Dorset medium without glycerine. The fluid was collected from the patient into a small centrifuge tube (5 ml.). This saved wastage of the sample, and helped to prevent loss of the fibrin clot. Particular care was taken to include the clot in the culture, as it was often found that colonies would grow in and around the clot when no other growth could be obtained. Guinea-pig inoculation was used frequently during the early years, but it was seldom found to be superior to the culture method, except in the rare cases due to the bovine type. It was found that more economical utilisation of guinea-pigs could be made by storing a portion of the fluid in the refrigerator for a few weeks

TABLE III.
Cases by age and treatment.

AGE GROUP IN YEARS	MILIARY					MENINGEAL					MILIARY AND MENINGEAL				
	1	2	3	4	Total	1	2	3	4	Total	1	2	3	4	Total
0-4 ...	5	6	8	2	21 ...	10	28	25	2	65 ...	6	12	15	1	34
	(2)	(1)	(1)	(2)	(6) ...	(6)	(11)	(10)	(2)	(29) ...	(3)	(5)	(5)	(1)	(14)
5-9 ...	—	5	4	—	9 ...	3	15	11	1	30 ...	1	8	7	—	16
	(—)	(—)	(—)	(—)	(—) ...	(—)	(9)	(4)	(1)	(14) ...	(—)	(2)	(—)	(—)	(2)
10-14 ...	2	2	3	—	7 ...	2	3	11	—	16 ...	4	3	3	—	10
	(—)	(—)	(1)	(—)	(1) ...	(2)	(2)	(2)	(—)	(6) ...	(2)	(—)	(—)	(—)	(2)
15-19 ...	2	6	5	1	14 ...	1	8	6	—	15 ...	7	12	3	—	22
	(—)	(1)	(—)	(1)	(2) ...	(1)	(1)	(1)	(—)	(3) ...	(4)	(3)	(—)	(—)	(7)
20+ ...	4	3	17	1	25 ...	4	13	12	5	34 ...	12	7	17	—	36
	(1)	(—)	(3)	(1)	(5) ...	(3)	(4)	(5)	(5)	(17) ...	(4)	(1)	(1)	(—)	(6)
TOTAL ...	13	22	37	4	76	20	67	65	8	160	30	42	45	1	118
	(3)	(2)	(5)	(4)	(14)	(12)	(27)	(22)	(8)	(69)	(13)	(11)	(6)	(1)	(31)

N.B.—(1) = Streptomycin.
(2) = Streptomycin and PAS.
(3) = Streptomycin, PAS and isoniazid.
(4) = No chemotherapy.

Figures in brackets indicate deaths.

to await the result of a culture. Failure to obtain bacteriological confirmation was almost invariably due to specific treatment having been given before the specimens were taken. When streptomycin was the only therapeutic agent, positive cultures were frequently obtained from CSF for 14-16 days after the commencement of treatment. The persistence of organisms in the fluid did not necessarily coincide with the more severe forms of the disease, as many cases which ultimately were fatal only gave one or two positive cultures. Since the addition of isoniazid, it has become unusual to recover organisms from the CSF after the first week. Strains of tubercle bacilli isolated were all typed. Only four cases of infection due to the bovine type were found in this series—two children had abdominal lesions, one

child had a cervical gland lesion, and one adult had long-standing disease of the epididymis.

Tests of sensitivity to streptomycin and later to PAS and isoniazid, were done on all pre-treatment strains, and also on any cultures that were recovered after a period of treatment. These latter were occasionally obtained from relapsed or dying cases. Two fatal cases of meningitis resulted from infection with strains highly resistant to streptomycin. One, a baby, was a contact of her mother, who had advanced pulmonary tuberculosis and had become resistant to streptomycin. The other, a young child, was a contact of a neighbour, also an advanced case harbouring resistant organisms. Later, there were two cases where some resistance to PAS was suspected, but by then isoniazid was also available, and the patients recovered. Fortunately, infection with resistant organisms never became a serious problem, because the supply of streptomycin was at first very restricted and its use was confined mainly to hospitals. Before any serious dissemination of streptomycin resistant strains could occur, the other chemotherapeutic agents were introduced, and the value of combined therapy was appreciated. Even when streptomycin alone was available the development of resistance during treatment in miliary and meningeal cases was very rare. Only two cases produced resistant strains in CSF shortly before death, and both these patients had pulmonary tuberculosis.

TREATMENT.

Treatment, as indicated in Table III, is only dealt with in broad outline, because the cases extend over many years and the patterns of therapy have changed greatly during the period of this survey. At first, the routine was streptomycin given intramuscularly—and intrathecally when meningitis was present. The adult intramuscular dose was usually one gram. Larger doses were very seldom given. Dihydrostreptomycin was used for a time, but was discontinued because of unfavourable results. During 1949 PAS was added to the treatment routine (daily adult dose 15 g.), and isoniazid came into use towards the end of 1952 (daily dose 8 mg. per kilo body weight). Some cases who were admitted about this time did not have isoniazid at the beginning of their illness, but were given it later in the course of the disease. The general rule was six months treatment with streptomycin, PAS and isoniazid, and then streptomycin was gradually withdrawn and the PAS and isoniazid continued for a time as indicated by the clinical condition. The response to treatment after the introduction of PAS and isoniazid, and particularly with isoniazid, improved greatly, both in time and recovery rate. The improvement was most marked in the cases where meningitis was present. Fifty per cent. of all meningitis cases died with streptomycin treatment, 35 per cent. died with streptomycin and PAS, and 25 per cent. died with streptomycin, PAS and isoniazid. With isoniazid the duration of illness became progressively shorter and the incidence of 'chronic meningitis' much less frequent. The CSF also returned more quickly to normal. Severe complications were unfortunately not entirely eliminated—late diagnosis was still a problem and irreversible brain damage could not be prevented by any form of chemotherapy, though life might be prolonged.

Intrathecal streptomycin was given to the majority of meningitis patients. Courses were repeated and prolonged when streptomycin was the only drug available. What is often a difficult form of therapy became part of the routine for the medical staff, who acquired much skill in performing lumbar puncture with little trauma or adverse effects, and usually without a local anæsthetic. Cisternal and intraventricular punctures (the latter via the fontanelle in young children) seemed to present no difficulty and often proved valuable. Trephining was only done in a few cases. Since the introduction of isoniazid, a group of 37 meningeal cases were given streptomycin, PAS and isoniazid without intrathecal therapy, and all of them recovered. This group gave an early and satisfactory response to intramuscular and oral therapy. Where the response to this regime was not favourable, it was usually considered advisable to give some streptomycin by the intrathecal route, though, with isoniazid, this form of therapy has been used less intensively and for shorter periods. Frequently, a course of about 30 injections was found sufficient to bring about improvement. The dose was from 25 mg. for an infant to 100 mg. for an adult, given at first daily and then two or three times weekly according to the patient's response.

The large number of advanced cases included in this survey and the high proportion of deaths occurring within one month of admission have already been mentioned. In one group, that of miliary and meningeal disease combined, the death rate (30 per cent.) is lower than in the meningeal group (43 per cent.). The explanation of the rather higher recovery rate in this series may be due to earlier diagnosis. Many of the 118 cases in this group were sent into hospital when the miliary disease dominated the clinical picture, and the meningitis was not so evident. Fifty-four of the cases actually developed meningitis after treatment for miliary disease had been started, and were therefore in the category of very early cases. Apart from the few 'abortive' cases, the meningitis that did develop usually ran a course indistinguishable from the ordinary case of meningitis admitted as such. Of these 54 post-admission cases, none died under one month, but nine deaths (17 per cent.) occurred later in the course of the disease. The highest death rate was encountered when streptomycin alone was the only treatment available.

COMPLICATIONS.

The incidence of the different complications and their frequency under different forms of therapy are given in Table IV. Symptoms referable to the auditory or vestibular systems were complained of by many patients, most particularly when dihydrostreptomycin was used in treatment. These symptoms in many cases cleared up, or were compensated for, after a time. A small number of patients were permanently affected to some extent. Tinnitus and vertigo were complained of by 14 patients, 13 of whom had had meningitis. All had been rather slow to improve and had required long courses of treatment. Eight of them were also deaf. Deafness occurred in 24 patients, 10 of whom were slightly affected and 14 more severely. All of these had meningeal disease. Four of them were also blind and mentally deficient. Twenty-two cases complained of ataxia, all of them meningeal

TABLE IV.
Cases by treatment and complications.

COMPLI- CATIONS	TOTAL CASES		MILIARY (76 Cases)					MENINGEAL (160 cases)					MILIARY AND MENINGEAL (118 cases)					
	354	1	2	3	4	Total	1	2	3	4	Total	1	2	3	4	Total		
Deafness	... 24	...	-	-	-	-	...	-	7	4	-	11	...	1	9	3	-	13
	(-)	...	(-)	(-)	(-)	(-)	...	(-)	(-)	(-)	(-)	...	(-)	(-)	(-)	(-)	(-)	
Ataxia	... 22	...	-	-	-	-	...	-	8	3	-	11	...	3	5	3	-	11
	(1)	...	(-)	(-)	(-)	(-)	...	(-)	(-)	(-)	(-)	...	(1)	(-)	(-)	(-)	(1)	
Blindness	... 16	...	-	-	-	-	...	1	7	2	-	10	...	-	1	5	-	6
	(3)	...	(-)	(-)	(-)	(-)	...	(-)	(2)	(1)	(-)	(3)	...	(-)	(-)	(-)	(-)	
Spinal Block	... 39	...	-	-	-	-	...	9	6	13	-	28	...	5	3	3	-	11
	(22)	...	(-)	(-)	(-)	(-)	...	(7)	(3)	(7)	(-)	(17)	...	(3)	(2)	(-)	(-)	
Mental	... 19	...	-	-	-	-	...	1	6	4	-	11	...	2	2	4	-	8
Retardation	(2)	...	(-)	(-)	(-)	(-)	...	(-)	(1)	(-)	(-)	(1)	...	(1)	(-)	(-)	(-)	
Obesity	... 10	...	-	-	-	2	2	...	2	-	2	-	4	...	2	-	2	-
	(1)	...	(-)	(-)	(-)	(-)	...	(-)	(-)	(1)	(-)	(1)	...	(-)	(-)	(-)	(-)	
Relapse	... 28	...	-	-	-	-	...	2	8	2	-	12	...	7	9	-	-	16
	(8)	...	(-)	(-)	(-)	(-)	...	(2)	(4)	(-)	(-)	(6)	...	(1)	(1)	(-)	(-)	
Pleural	... 20	...	-	2	3	1	6	...	2	-	2	-	4	...	2	4	4	-
Effusion	(3)	...	(-)	(-)	(-)	(1)	(1)	...	(1)	(-)	(-)	(1)	...	(-)	(1)	(-)	(-)	
Spontaneous	... 7	...	-	1	1	-	2	...	-	-	-	-	...	-	3	2	-	5
Pneumothorax	(3)	...	(-)	(-)	(1)	(-)	(1)	...	(-)	(-)	(-)	(-)	...	(-)	(1)	(1)	(-)	
Pregnancy	... 9	...	1	1	2	-	4	...	-	1	-	1	...	1	2	1	-	4
	(1)	...	(1)	-	-	-	(1)	...	(-)	(-)	(-)	(-)	...	(-)	(-)	(-)	(-)	

- (1) Streptomycin.
(2) Streptomycin and PAS.
(3) Streptomycin, PAS and isoniazid.
(4) No chemotherapy.

A patient may appear in more than one column of the table.

Figures in brackets indicate deaths.

cases. With the exception of one case all the auditory and vestibular complications were in patients suffering from meningitis, and all had had some intrathecal therapy. The addition of isoniazid did not rule out the possibility of these complications, though where they did occur, the disease was more intractable than usual. Blindness developed in 16 cases, all of whom had meningitis. Four cases were totally blind, and 12 had some vision in one or both eyes. One patient had a tuberculous panophthalmitis for which an enucleation of the eye was performed, and he is now well. Seven of the blind cases were mentally deficient and 3 of them died. Spinal block occurred in 39 cases, 22 of whom died. This complication lasted only a short time in some of the cases, while in a few it persisted for months or till death. Transient cranial nerve palsies occurred frequently. The more extensive paralyses were mainly in patients who died.

Mental retardation occurred in 19 cases, 8 of whom were said to be 'slightly retarded.' Of the 11 who were severely retarded, 4 were blind and 7 were deaf. Two

of these severely affected patients died, one of them due to a relapse of meningitis after 5 years. It is an unfortunate circumstance that an apparent complete cure of meningitis can occur, in spite of the most severe mental retardation. A minor degree of mental change is more difficult to assess particularly in young children. Very few of the children in the follow-up were admitted to be backward at school, when allowance was made for the long break in their education. Many later successfully finished a training school or university course.

Obesity developed in 10 cases. Several of these had multiple lesions—glandular, osseous or renal—one had a confirmed tuberculoma of the cerebellum, and two others had a suspected tuberculoma. No deaths occurred in this group.

Relapse of meningitis complicated 28 cases, 8 of whom died. Ten patients relapsed when streptomycin was the sole treatment, some of them more than once. It was at that time very difficult to know when treatment could be safely discontinued. Seventeen cases relapsed on streptomycin and PAS, and two cases relapsed after a course of streptomycin, PAS and isoniazid lasting six months or longer. One was a case in which the protein level of the CSF remained raised for some months after other signs and symptoms had subsided. The patient, an intelligent little boy, recovered, but is almost completely deaf. The other patient suffered a recurrence of meningitis and died four years after her original attack. Obesity and amenorrhœa had developed after the first attack, and she also had an osseous lesion. No case of relapse of miliary disease occurred. One patient, a young man of 21, was initially treated for miliary disease with a good response and was later found to have a lesion with cavitation in one lung. This was successfully treated by lobectomy.

Pleural effusion, shortly prior to or coincident with miliary or meningeal disease, was found in 20 cases, 3 of whom died. Spontaneous pneumothorax was a complication of 7 cases, all of whom had miliary disease, 5 of them also with meningitis. Five of these patients died, one death being directly due to this complication. Prolonged pyrexia in meningeal cases was often associated with an intrathoracic lesion which was very slow to respond. Acute thrombocytopenic purpura occurred in one child with miliary disease. He had treatment with streptomycin, PAS and isoniazid, the latter for 7 days. He recovered spontaneously from the purpura, and later developed meningitis—perhaps because of withdrawal of isoniazid. He eventually recovered. Two patients with miliary disease, a boy of 17 and a woman of 60, were found at post-mortem to have tuberculous endocarditis with involvement of the mitral valve. Pregnancy or the puerperium were coincident with 9 cases. Four of these had miliary disease, one had meningitis and four had miliary and meningeal disease combined. The one death in this group was attributed to a pulmonary embolus.

Several cases admitted as meningitis were found not to be tuberculous. Three cases, from whom tubercle bacilli were never isolated, were of unusual interest. A girl of 3 had evidence of meningeal irritation with blood and high protein content in the CSF. A medulloblastoma of the cerebellum was eventually diagnosed. A girl of 3½ was clinically very suggestive of meningitis. There was a probability of contact infection, the Mantoux reaction was positive, there were increased protein and

cells (initially polymorphonuclears) and lowered sugar in the CSF. Anti-tuberculous treatment was given and the condition improved. Two years later, signs of a pituitary lesion became evident. Post-mortem examination revealed a craniopharyngioma of the pituitary with carcinomatosis of the meninges. A girl of 7 presented with glands in the neck, which had been present for 4 years. Mantoux reaction was positive. Shortly after she was first seen, radiology revealed lung infiltration suspicious of miliary tuberculosis. A course of anti-tuberculous therapy failed to produce an improvement. A gland from the neck was excised, and was found to be the seat of secondary carcinoma, the primary being an adenocarcinoma of the thyroid. The 'miliary' nodules in the lungs were metastases. This patient died a few months later. She had never previously received any radiation, and there was no family history of thyroid disease. Duffy and Fitzgerald (1950), out of 430 cases of thyroid carcinoma, had 28 patients under 18 years. Ten of these presented with lymph node enlargement, and two were originally diagnosed miliary tuberculosis. Ten of the cases had received radiation for enlarged thymus between the fourth and sixteenth month of life.

The survivors in this survey have all been followed up for at least two years, and many of them for much longer periods. Deaths after discharge from hospital have been rare, and usually from some cause other than tuberculosis. One boy, who recovered from miliary and meningeal disease after a long course of streptomycin treatment, was killed in a motor accident shortly after his discharge. The improved results since isoniazid was included in the treatment régime have been more striking in the meningeal cases than in those with miliary disease alone. Miliary and meningeal tuberculosis have become much less common during the last few years. In 1950, 62 cases were admitted to this unit, in 1957 the number had fallen to 17. The death rate from all forms of tuberculosis in Northern Ireland during 1950 was 54 per 100,000, and 1957 it was 12.6. A tuberculin survey of 6,000 school entrants in 1950 gave 25 per cent. positive reactors. A survey of 1957 gave 3.9 per cent. reactors in children who had not had B.C.G. (Calwell, 1957).

In early cases with the therapeutic agents now available, recovery might be expected in almost 100 per cent. The achievement of early diagnosis is still a problem, and it is not made any easier by the fact that the disease is becoming rarer and that those who will be called upon to make the diagnosis may be less familiar with the condition. The striking decrease in incidence during the past few years must be due to diminished opportunity for infection, and it may be hoped that control of infection will achieve virtual elimination of this form of tuberculosis.

SUMMARY.

Three hundred and fifty-four cases of miliary and meningeal tuberculosis occurring since 1947 are reviewed and 114 of these died. The number of advanced cases was large, and 60 per cent. of the deaths occurred less than one month after admission to hospital. Survivors have been followed up for at least two years. Type of onset and duration of prodromal period were found to vary greatly. History of contact with open pulmonary tuberculosis was usual in the younger age groups. Diagnostic

features and methods of bacteriological confirmation are described. Examination of the fasting gastric residue was found to be of great value, particularly in cases of miliary disease. All strains of tubercle bacilli recovered were examined for sensitivity to the anti-tuberculous substances used, and the type of organism (human or bovine) was determined.

Treatment has been briefly described and falls approximately into three phases—streptomycin alone, streptomycin with P.A.S., and later isoniazid in addition to the other two substances. Improvement in recovery rate, reduction in length of illness and a lower incidence of complications are evident following the introduction of isoniazid. The addition of isoniazid to the treatment made it possible to dispense with the use of intrathecal streptomycin in many cases. A group of 37 cases treated with the three substances without intrathecal therapy, made a full recovery.

The most serious complication of meningitis was severe mental retardation, usually with blindness and deafness. Eleven patients out of 178 cases of meningitis developed this complication and some of them still survive.

Early diagnosis offers the best hope of complete recovery. A marked reduction in incidence of the disease has occurred in the last few years.

I am indebted to Dr. P. J. Steen for permission to use the hospital records and to review the patients under his care, to many of my colleagues who have greatly assisted me in the follow-up, to Dr. F. F. Kane of the Northern Ireland Fever Hospital for help and advice, and to Dr. E. Cheeseman and Mr. J. D. Merrett of the Department of Social and Preventive Medicine, Queen's University, Belfast, for help in compiling the tables. I am also much indebted to Mr. J. H. McWatters, Chief Technician and the staff of the laboratory for very efficient technical assistance.

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Tuberculin Sensitivity in Co. Fermanagh, N. Ireland, 1952-55

By W. T. WARMINGTON, M.D.

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THE remarkable scarcity of new cases of tuberculosis throughout Britain during the past four or five years, has in Northern Ireland been most pronounced in country districts. County Fermanagh is one of these districts in which a very low tuberculin reactor rate has already been recorded (Warmington, 1952). In the period of falling incidence a corresponding reduction in the numbers tuberculin positive would be expected, and of this the present survey is a record.

The groups studied are the same as in the 1949-51 survey, namely :

- | | | | | | |
|---|---|---|---|---|-----|
| 1. Attenders at Enniskillen Chest Clinic | - | - | - | - | 965 |
| 2. Boys from Fermanagh homes attending a public school in Enniskillen | | | | | 58 |
| 3. Employees in an Enniskillen factory (some tested in 1956) | - | | | - | 328 |

TUBERCULIN TESTS USED.

The accuracy of the Heaf multiple puncture test using pure Old Tuberculin (O.T.) as measured against the Mantoux test using O.T. 1/100 as the standard test has been demonstrated in many studies. Irvine (1955) using O.T. on 243 persons found 86 per cent. accuracy for the Heaf test. Townsend (1954) with 178 persons aged 18-21 years reported 88.2 per cent. accuracy. Calwell (1954) on 1,345 children aged 0-16 years in Belfast, immediately Mantoux tested the 985 non-reactors to the Heaf test, and only 5 (0.5 per cent.) showed a positive Mantoux test. This gives 99.5 per cent. accuracy for the Heaf test at this age. Bowen (1955) using P.P.D. and Gifford (1955) also report similar degrees of accuracy. Irvine's figure (86 per cent.), the lowest reported, was chosen to avoid exaggeration in correcting our own Heaf results to conform to the Mantoux test using O.T. 1/100—the accepted standard for this as for most tuberculin surveys.

For internal comparison with my own earlier chest clinic results using the Mantoux test with O.T. 1/10,000, this test has of course again been employed in these patients.

METHOD OF ANALYSIS.

The size of samples recommended by Hill (1948) is 100 or more and not less than 50. This was achieved except for individual groups in the public school. Differences were considered significant statistically when found to be twice the standard error (σ).

RESULTS.

The Chest Clinic figures for both surveys are seen in Table I.

TABLE I.

AGE	1949-51						1952-55					
	TOTAL		POSITIVE				TOTAL		POSITIVE			
	No.		No.		%		No.		No.		%	
0-5	...	209	...	26	...	12.4	...	188	...	23	...	12.2
6-14	...	—	...	—	...	—	...	313	...	57	...	18
10-14	...	307	...	66	...	21.5	...	—	...	—	...	—
15-35	...	502	...	278	...	53.4	...	389	...	110	...	28.2
35+	...	183	...	115	...	62.8	...	75	...	35	...	46.7

In Table I no material reduction in the number of tuberculin reactors is seen under the age of 15. The high percentage of contacts in this group probably explains the failure to show a reduction in tuberculin positives. In 1949-51, 66.5 per cent. of the 0-5 year group and 55 per cent. of the 5-14 year group were contacts (unpublished Enniskillen Chest Clinic figures) and a similar proportion probably still holds. The fall in reactor rate in the oldest group (35 years and over) is significant ($2\sigma=13.5$). The 15-35 year group of adolescents and young adults shows a large (25.2) and statistically significant ($2\sigma=6.4$) reduction.

THE PUBLIC SCHOOLBOYS.

The following table shows the 1953-4 results of Mantoux tests using O.T. 1/100 dilution :

TABLE II.

Enniskillen Town:			TOTAL		POSITIVE		%
	53-54	...	10	...	8	...	80
	49-51	...	40	...	20	...	50
Country Towns:							
	53-54	...	20	...	1	...	5
	49-51	...	73	...	21	...	29
Country Districts:							
	53-54	...	58	...	7	...	12
	49-51	...	56	...	8	...	14
Total:							
	53-54	...	88	...	16	...	18
	49-51	...	169	...	49	...	29

Comparison of the totals for the two surveys shows a reduction in 1953-4 which is just statistically significant ($2\sigma=10.77$).

THE FACTORY SURVEY.

Substantially the same rural-urban proportion (70 per cent. rural) and average age (males 26 and females 20 - 22.5 years) holds as in 1949-51. Males number 169 (131 Heaf tested in 1956), and females 238 (197 Heaf tested in 1956). The Heaf tested numbers positive were corrected to 86 per cent. (Irvine, 1955) of their original value before inclusion. The results of the 1949-51 and the present surveys are shown in Table III.

The number of tuberculin positive females was already very low at the date of the first survey and remains well below the male figure. Hence a dramatic drop would scarcely be expected in females and that found is just short of statistical significance, equalling 8.6 where 2σ is 9.4. For males in contrast, the drop in positive reactors is significant ($2\sigma=10.6$) and so large (22) as to produce for the factory workers as a whole, a large (19.1) and statistically significant reduction in tuberculin reactors ($2\sigma=8.0$).

DISCUSSION.

An association between a reduction in an infectious disease like tuberculosis and a decreasing tuberculin reactor rate has an important implication : more and more people now free of tubercle are only so because they have not yet been infected. Partial reduction of infection offers only a limited type of protection. Yet the type of disease now being encountered is exactly the same as in the worst days of the

TABLE III.

DATE OF SURVEY	TOTAL TESTED			No. POSITIVE			% POSITIVE		TOTAL M. and F. No. POSITIVE		TOTAL M. and F. % POSITIVE		
	M.	F.		M.	F.		M.	F.		POSITIVE		POSITIVE	
1949-51	...	248	183	...	157	66	...	62.5	36	...	223	...	51.7
1952-55	...	131	197	...	53	54	...	40.5	27.4	...	107	...	32.6
(1956 Heaf)													

nineteenth century. B.C.G. vaccination offers protection and is available for the tuberculin-negative majority. "Substantial proof," in the words of the N.I. Tuberculosis Authority's report (1956), of the value of B.C.G. vaccination in preventing tuberculosis is stated in the *B.M.J.* editorial (*B.M.J.*, 25th February, 1956) as being "beyond doubt." The proof referred to is the results of the Medical Research Council Tuberculosis Vaccination Trials (Hart, D'Arcy P., et al., 1956). Here 1.94 per 1,000 in the tuberculin negative unvaccinated group are shown to have developed tuberculosis, compared with under one-fifth of that number or only .37 per 1,000 amongst those who were given B.C.G. vaccination. Its use in specially exposed groups is practised by the writer. Such groups include contacts of the tuberculous case, emigrants, entrants to urban or industrial employment, and nurses. Educational propaganda might be specially directed to these. None of the many young persons encountered by the writer who emigrate from Fermanagh realized their need of B.C.G. vaccination. Hence it is believed that insufficient use is being made of available means of publicity such as wireless and the press.

SUMMARY.

A statistically significant reduction in the number of tuberculin reactors in Co. Fermanagh between 1949-51 and 1952-55 was found in Clinic Attenders aged 15 years and over, amongst public school boys and in factory workers. The implication of this finding is discussed in relation to B.C.G. vaccination.

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REVIEWS

SURGERY IN INFANCY AND CHILDHOOD. By Matthew White, M.A., M.B., Ch.B., F.R.F.P.S.(Glas.), F.R.C.S.(Edin.), and Wallace M. Dennison, M.D., F.R.F.P.S.(Glas.), F.R.C.S.(Edin.), F.I.C.S. (Pp. xii + 444; figs. 266. 45s.) Edinburgh and London: E. & S. Livingstone, 1958.

HERE is a clearly-written and compact account of the surgical problems of infancy and childhood. Although the book is intended primarily for senior (medical) students, it is likely to have a much wider appeal. All who deal with infants and children will appreciate the ease with which reliable information can be obtained on a wide variety of topics. In addition to valuable chapters dealing with abdominal and thoracic disease, there are comprehensive sections on orthopædic disorders, fractures, and plastic surgery. It is heartening to see needless circumcision condemned and the text here provides useful moral support for those who have to deal with parents anxious to have a child circumcised.

The necessity for conciseness in style has left little space for consideration of alternatives in treatment. For example, not all surgeons will agree that when strawberry birthmarks require treatment that radium is preferable to excision.

The illustrations, several of which are in colour, add considerably to the value of the book and the index is sufficiently detailed to allow easy reference.

The authors and publishers deserve praise for producing an attractive book at a reasonable price.

B. T. S.

THE PHYSICAL TREATMENT OF VARICOSE ULCERS. By R. Rowden Foote, F.I.C.S., M.R.C.S., L.R.C.P., D.R.C.O.G. (Pp. xii + 126; figs. 88. 15s.) Edinburgh and London: E. & S. Livingstone, 1958.

IN this small volume massage and exercises in the treatment of varicose ulcers is discussed. The various lesions are described, and surgery is considered.

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Simultaneous Admission of Two Sisters suffering from an Affective Disorder

By EDWARD S. LAMONT, M.B., D.P.M.
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Two sisters, aged 63 and 68 respectively, were admitted to hospital as voluntary patients on the same day. Mrs. A., the younger of the two, became depressed first, about six months prior to the older, Mrs. B.

Their family history is similar in that they were the only children of their father's second marriage. They were very closely attached to each other in early life as their father and mother died when they were both very young.

Mrs. A. was unable to give much detail regarding her early life but she said that she was quite happy and got on well with her school companions and her older sister and does not remember any particular neurotic traits. She was an average scholar and on leaving school at 14 she was employed as an assistant in a large drapery shop. On retirement in her mid-fifties she was in charge of a department. She was happily married from the age of 55 but her husband died four years later. She said that she had always been a cheerful, jolly individual. She was fond of taking an active leading part in the social activities connected with her Church, and until her present illness had always enjoyed good health.

In June last year she was admitted to a general hospital for treatment for hypertension. She said that she felt very much better after a course of Serpasil. In October, however, she developed pulmonary congestion and since then felt more depressed and physically weaker. On physical examination the patient showed thickening of peripheral and retinal vessels and had a blood pressure of 250/120.

On admission her presenting symptoms were depression, generalised weakness and inability to sleep at night (wakening frequently in the early morning and lying awake). She was friendly and co-operative and able to give a coherent history but she spoke slowly and her movements were rather retarded. The patient said she was very depressed and felt at times that life wasn't worth living but that she had not the courage to commit suicide. She was extremely tearful and expressed feelings of guilt regarding her earlier associations with her husband prior to his previous wife's death. She felt that her neighbours who were always looking through the windows were doing this because they knew about her previous premarital associations with her husband. The patient showed marked hypochondriasis and was constantly demanding purgatives for her bowels which she said were blocked. She showed no intellectual impairment and attributed her depression to her physical condition. She responded satisfactorily to six electro-convulsive treatments, vitamins, occupational and ward therapy and separation from her older sister. On discharge from hospital she was much brighter and was eating and sleeping well.

Mrs. B., the older and quieter of the two, had been attending Mrs. A. night and day from the onset of her illness last year and at times she was very demanding and was constantly nagging if things were not up to her expectations.

Like her sister she was unable to give details of her childhood days but regarded them as happy. She attended school until she was fourteen and thought that she must have been an average scholar as her headmaster asked her to remain as a monitress until she was 17. After leaving school she worked as a book-keeper in the same shop as her sister until her marriage at 36. She said that she was happily married for four years when her husband died suddenly after an abdominal operation. She was a bright, jolly sort of person until her sister's illness. On admission her presenting symptoms were depression and inability to cope with the housework. She had been feeling like this for about six months but had become much worse in the four weeks prior to admission. On physical examination she showed thickening of peripheral and retinal vessels and had a blood pressure of 190/100.

She was co-operative and friendly and appeared bright superficially but became very tearful and was obviously depressed. She could converse quite freely and showed no paucity of movement. When questioned about the neighbours looking in she replied, "My sister used to think people were looking in at us—I suppose they were." She said that she had not been sleeping well because she was constantly being called by her sister. Her intellectual functions showed no impairment and she attributed her depression to overwork and anxiety about her sister.

She also responded satisfactorily to six electro-convulsive treatments, vitamins, occupational and ward therapy and separation from her younger sister. After her fourth treatment she became very confused and disorientated, but this cleared quickly.

She was feeling very well on discharge from hospital and was correctly orientated.

Social inquiry revealed that relatives of the previous Mrs. A. were living in a house overlooking the one occupied by the two sisters. On occasions some of the neighbours had been genuinely worried about the patients' welfare and had looked in to see if they were all right. It was confirmed that Mrs. A's. premarital friendship with her husband was a well known topic of conversation in the neighbourhood.

DISCUSSION.

These two women are of interest because on admission, at first they resembled the condition of folie a deux. They had become closely attached to each other in childhood after the deaths of their parents and had worked and lived together until Mrs. B's marriage at 36 when they parted for a few years. After Mr. B's death they reunited and lived together for another 14 years until Mrs. A's marriage at 55 and after a further period of separation of four years they got together again and have been living with each other for the past five years. Mrs. A. regarded herself as a leader and seemed to act in this capacity in her relationships with her older sister. Mrs. B. was the quieter and more passive of the two and she admitted on questioning that her ideas about the neighbours were due to her sister talking all the time about their looking in. When it became known from the social inquiry

that these ideas were not really delusions then they were considered in the light of the affective disorder as a misinterpretation of the genuine interest on the part of the neighbours. The belief that the previous Mrs. A's relatives were looking down at them was also an illusion connected with the feelings of guilt about her previous relationship with Mr. A. Their social isolation was probably a definite factor in the establishment of these wrong ideas. Wolff (1957) stresses social isolation of a small group as an important factor in the production of an induced psychosis within the group but in these two cases there was no induction of delusions but a definite misinterpretation of what was happening.

As they were both definitely depressed on admission they were given E.C.T. and were kept as much apart as possible. Mrs. A., however, continued to be the more dominant of the two and wished to give advice about her sister's treatment and referred frequently to "our illness." Although there were signs of arteriosclerosis in both these cases they showed no impairment of memory or other intellectual functions. During treatment, however, Mrs. B. became confused and disorientated but this was considered due to E.C.T. as it cleared up completely four days after the last treatment.

Constitutional predisposition for an affective disorder seems to be an important factor in these two cases. They did not, however, develop their illness until they reached their 60's and Roth and Kay (1955) suggest that physical illness is an important ætiological stress factor for affective disorders in this age group. In the case of Mrs. A. the hypertension and arteriosclerosis and congestion ensuing later have probably been the main causes of her affective disorder. Mrs. B., on the other hand, had the added burden of looking after her nagging, overbearing sister while suffering from hypertension and arteriosclerosis herself and this acted as an extra precipitating factor.

SUMMARY.

1. Two cases of depression are reported in which misinterpretation of the neighbours' actions was at first considered delusional until the social investigation was completed.
2. The interesting points in these cases are :—
 - (a) Dominant role of the younger sister which would have supported the diagnosis of a communicated illness if there had been actual induction of delusions.
 - (b) The association of hypertension and arteriosclerosis as precipitating factors.

I wish to thank Dr. C. B. Robinson, Resident Medical Superintendent, and Dr. D. M. Gardner, Consultant in charge of these two cases, for their permission to submit this report, and I am grateful to Professor J. Gibson, Department of Mental Health, Queen's University Belfast, for his suggestions and constructive criticism, and to Mrs. I. E. Teuton, Psychiatric Social Worker, for her social investigation.

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Serological Investigation of University Students following the 1957 influenza epidemic in Northern Ireland

By H. G. S. MURRAY, M.B.(BELF.), and J. J. McALISTER, A.I.M.L.T.

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DURING the 1957 influenza epidemic in Northern Ireland we were able to confirm the clinical diagnosis of influenza in the majority of patients from whom specimens were received. There remained, however, a number of patients with a clinical diagnosis of influenza from whom we could neither recover virus nor demonstrate a rise of antibody in the convalescent specimen of paired sera. We decided, therefore, to try to discover what proportion of individuals, who had had attacks regarded as influenza, had serological evidence of infection with the Far East influenza virus/1957. The fact that the Far East/1957 virus strains showed no cross-reactions in the hæmagglutination inhibition (H.I.) test with other strains of Influenza A virus (Jensen, 1957; Meyer, Hilleman, Miesse, Crawford and Bankhead, 1957) made this a relatively simple problem.

A group of university students consisting of sixty-two fourth-year medical students and twenty-one residents of a women students' hostel were investigated. Blood samples were obtained from each of the students. The medical students were asked to provide a written account of their illnesses during the previous month and the histories of the residents of the women's hostel were recorded.

MATERIALS AND METHODS.

Sera were stored at -20°C , and were tested both by complement fixation (C.F.) test with soluble C.F. antigen which is common to all influenza A strains and by the H.I. test which gives a strain specific result with the Far East virus. The viruses used in the tests were A/Singapore/57 and a strain of Far East influenza virus/1957, isolated in Belfast. Sera which were negative in H.I. tests were also tested by C.F. with influenza B, adenovirus, Sendai and mumps V and S antigens. In the complement fixation test, a four volume technique was used with $2\frac{1}{2}$ MCD₅₀ of complement and eighteen hours' fixation at 4°C . The hæmolytic system contained 4 per cent. sheep erythrocytes sensitized with 4 MHD hæmolysin. For the H.I. test all sera were treated with *Vibrio cholerae* filtrate and tested by the method described by Isaacs, Gledhill and Andrewes (1952).

RESULTS.

The fifty per cent. end points of the H.I. antibody titres of the sera tested were as follows :

H.I. titre	-	< 6	6	12	24	36	48	72	96	144	192	384
No. of sera	-	37	1	7	7	4	8	3	8	3	2	3

*Supported by grants from the Northern Ireland Hospitals Authority.

It may be seen that 46 (55.4 per cent.) of the 83 students tested had titres of 6 or more, which we considered as positive serological evidence of infection with the Far East influenza virus/1957, and 37 (44.6 per cent.) were negative.

The proportion of the positive and negative group who had symptoms regarded as clinical influenza is shown below :

H.I. Test Result	Proportion with Symptoms		
Positive	-	-	45/46 (98%)
Negative	-	-	28/37 (76%)

It will be seen that all but one of the students with H.I. antibody to the Far East virus had symptoms of infection. On the other hand, 76 per cent. of the students with no serological evidence of infection with Far East influenza virus/1957, had a clinical influenza-like illness.

A comparison of the symptoms of the serologically positive and negative group is presented in the table.

TABLE
Showing frequency of symptoms in serologically
positive and negative groups.

SYMPTOM	FREQUENCY OF SYMPTOMS (%)			
	In 45		In 37	
	Serologically Positive Students		Serologically Negative Students	
Sore throat	-	-	53	41
Cough	-	-	69	22
Coryza	-	-	51	41
Headache	-	-	42	27
Weakness	-	-	47	16
Myalgia	-	-	31	8
Malaise	-	-	20	19
Expectoration	-	-	18	5
Anorexia	-	-	22	0
Ocular symptoms	-	-	9	8
Shivering	-	-	11	5
Sneezing	-	-	2	11
Sweating	-	-	9	3
Pain in back	-	-	2	0
Abdominal pain	-	-	2	0
Pain in chest	-	-	2	0
Dizziness	-	-	2	0
Insomnia	-	-	2	0

In general the symptoms of the two groups were similar to those described in other outbreaks of influenza (Stuart-Harris, 1953). There were, however, significantly fewer individuals with cough ($P < 0.001$), weakness ($0.01 < P > 0.001$),

anorexia ($0.01 < P > 0.001$), and myalgia ($0.05 < P > 0.02$), in the serologically negative group than among those with titres of H.I. antibody of 6 or more.

All sera from the students with H.I. antibody titres of less than 6 and a proportion of the positive sera were tested by C.F. test with influenza B, adenovirus, Sendai and mumps V and S antigens. With the exception of two possible infections with an adenovirus (C.F. titre 1 : 64) there was no serological evidence of recent infection with any of these agents.

In comparing the results of C.F. antibody titres with influenza A soluble antigen it was found that 91.3 per cent. of sera showing an H.I. antibody titre of 6 or more had C.F. titres of 16 or more. Of the H.I. negative sera 78.4 per cent. had titres of less than 16.

DISCUSSION.

In the present study of 73 students with a clinical infection diagnosed as influenza, 45 (62 per cent.) had H.I. antibody titres of 6 or more, and only one of these was devoid of symptoms. On the other hand, of 37 students who showed no demonstrable H.I. antibody, 28 (76 per cent.) had an influenza-like illness. The majority of individuals with no demonstrable H.I. antibody also failed to show C.F. antibody at levels which would suggest a recent infection with an A strain of influenza virus. There was no serological evidence of infection with influenza B, adenovirus, Sendai virus or mumps virus in these cases.

One possible explanation of our results is that the H.I. test was positive in only about 60 per cent. of infections with the Far East influenza virus. Comparable results have been obtained by Clarke, Heath, Sutton and Stuart-Harris (1958) in Sheffield, who demonstrated H.I. antibody to the A/Singapore/57 strain of Far East virus in 70 per cent. of convalescent sera from 80 cases of influenza. If this is so, then it appears that the H.I. test is more often negative in milder infections in that cough, weakness, anorexia and myalgia were more common in the group showing demonstrable H.I. antibody.

An alternative explanation of our findings is that the H.I. negative infections were due to an infectious agent other than influenza virus causing influenza-like infections at the same time as the outbreak of A influenza. If there is such an agent we will expect to find "influenza" epidemics with no serological evidence of infection with influenza virus.

We wish to thank Professor G. W. A. Dick for his help and advice.

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REVIEWS

HOMOSEXUALITY TRANSVESTISM AND CHANGE OF SEX. By Eugene de Savitsch, M.D. (Pp. viii + 120. 12s. 6d.) London: Heinemann, 1958.

THERE seems to be some ambiguity concerning those for whom this little book was written. The author, a surgeon, in his introduction states that he undertook the task in order to satisfy numerous inquiries about the so-called "change of sex" operation, supplying at the same time in general terms sufficient background information about homosexuality and transvestism, for better understanding of the problems involved.

The publisher's note on the inside of the dust cover indicates that professional men, clergymen, lawyers, schoolmasters, and others will profit by reading it. The book cannot be regarded as a scientific treatise, nor indeed is it claimed to be one. In the reviewer's opinion the psychiatrist can do little but accept the author's diagnoses because of lack of sufficient information for critical appraisal. For instance, the case of Mr. B. (page 54), who sought God's forgiveness through castration for masturbation and extra-marital heterosexual relationships, suggests a strong depressive element in his illness. In spite of his suicidal tendencies and the course of his illness following castration, this is not discussed. The surgeon will find little to help him if he finds himself with his back to the wall because of some patient's suicidal threats should he refuse to operate. The theologian will rapidly demolish humanitarian arguments put forward in favour of the operation, while schoolmasters will learn that Napoleon's body had many feminine characteristics, and that he had inconspicuous genitalia, but they could hardly use this information to shatter their pupils' illusions regarding such a heroic figure. The problem of what in law constitutes male and female is not any nearer its solution as a result of this booklet.

The Wolfenden Report (chapter V) is dealt with very briefly, and given almost complete approval.

The author has collected interesting historical material. It is mostly from this point of view that the booklet may be of interest to some. For others it may emphasise the need for a closer co-operation, not only between specialists concerned with the mind, body, and soul of man, but with those who administer the laws governing his behaviour in the community.

J. G. G.

MODERN PRACTICE OF OBSTETRICS. By D. W. Stern, M.A., M.B., F.R.C.S., F.R.C.O.G., and C. W. F. Burnett, M.D., F.R.C.S., F.R.C.O.G. Second Edition. (Pp. x + 258; figs. 141. 45s.) London: Baillière, Tindall & Cox, 1958.

It is now six years since the first edition of this book appeared. The good points of the first edition—layout, classification, and illustrations—are retained. The chapter on antepartum hæmorrhage has been re-written, but many may consider it the weak link in an otherwise sound chain.

There are many places where dogmatic statements are made with which agreement may not be by any means complete. The chapter on uterine bleeding during early pregnancy is very full and very well written, with the emphasis perhaps placed a little heavily on the rare chorion-epithelioma.

The illustrations are clear and eminently functional, and what inconsistencies there are are amenable to correction in subsequent editions, for example, the rather brief and confusing chapter on obstetric operations.

This is a sound textbook in most ways, and provides a very refreshing change from the perhaps more solid and more "standard" textbooks. The undergraduate will find most of his questions answered and the postgraduate will be stimulated to compare, contrast, and search further.

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PRINCIPLES OF SURGICAL MANAGEMENT. By H. A. F. Dudley, F.R.C.S.E. (Pp. vii + 203; figs. 68. 27s. 6d.) Edinburgh and London: E. & S. Livingstone Ltd., 1958.

THIS book is written primarily for the newly qualified house surgeon, but it would be very useful to anyone who has to care for surgical patients. It is well written and very easily read, and covers all aspects of pre- and post-operative management except that of fluid and electrolyte balance. It seems a pity that such a comprehensive book should have been marred by this omission.

No book on surgery, however good, could possibly please everyone in all its details, and this book is no exception. There is lack of detail in pre-operative preparation of the patient for adrenal surgery, the removal of skin sutures from a grid iron incision on 10-12th day seems excessively cautious, the examination of all post-operative patients at least once daily for tenderness in the calves and for limitation of dorsi-flexion at the ankle would be very difficult to carry out in most hospitals and also of doubtful value, not removing the rectal tube after hæmorrhoidectomy until the second day would give the patient twenty-four hours more discomfort than is necessary, the use of 4 per cent. lignocaine for every male catheterisation is unnecessary and dangerous, testing renal function solely by the specific gravity of urine is inadequate for some cases, and the sole use of the metric system for dosage of all drugs is confusing.

However, apart from these few criticisms of detail, the book is excellent and well worth reading.

H. C. D.

FOUNDATIONS OF NEUROPSYCHIATRY. By Stanley Cobb. (Pp. ix + 305; figs. 16. 40s.) London: Baillière, Tindall & Cox, 1958.

FOR six editions of this book to appear in twelve years indicates that practitioners and medical students have found it valuable. Recent advances in our understanding of the physiology of the central nervous system have been included in this edition. Dr. Cobb writes with authority, not only as a neurophysiologist, but as a psychiatrist who is familiar with the psychiatric problems common in any big general hospital.

Throughout the book the author does not lose sight of his intention to emphasise principles rather than to present long lists of facts. By so doing he hopes that his readers may readily understand the simpler workings of the nervous system. At the beginning the reader's attention is drawn to the fact that the nervous system should be regarded as active and dynamic, and not passive and static. Central modulation of sensory perception and negative feedback affecting motor output suggests to the author a closer approximation to what actually happens in the C.N.S., than does the simpler stimulus-response concept of psychology. The limbic system—MacLean's "Visceral Brain"—is dealt with in chapter two, and experimental evidence in favour of regarding it as that part of the brain concerned with the externalisation of emotional behaviour is summarised.

For simplicity of description and ease of understanding the cerebrospinal nervous system is divided into segmental and suprasegmental mechanisms. This follows closely the teaching of Adolf Meyer, who has applied it to the question of neurological integration; each successive level of integration including all the antecedent ones. This is a fundamental fact to Maierians for the understanding of the total organism. The problem of pain, including referred pain, is discussed. Motor integration and locomotion are dealt with in the same dynamic way.

There is an interesting chapter on consciousness and "mind-body" problem. The author emphasises his dynamic theme when he points out that consciousness is a function of the organism in action. He summarises briefly the latest work on the importance of the reticular activating system in this respect. Mind is the integration itself of the living brain in action; the relationship of one functioning part of the brain to another. With such a concept "centres" and "levels" become too restricting. The anatomical and physiological proof that feed-back mechanisms and reverberating circuits do exist within the brain stresses the need

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to think in terms of the integration of parts of the nervous system, not in terms of higher and lower centres.

The chapters on neuropathology follow the same pattern of dealing with principles rather than lists of pathological conditions. The student may find these chapters useful for revision purposes. The author is very conservative in his views on the part played by psychological factors in the precipitation of epileptic fits. He does not go beyond observed facts when he draws his conclusions. It is rather disappointing, however, that he does not deal more fully with temporal lobe epilepsy. Some reference to the important contributions of British workers to the understanding of this subject would have helped to develop his thesis of mind-body unity.

Only a small part of the book, just over one-fifth, deals specifically with psychology and psychopathology. However, he introduces the reader to the work of Lorenz and Tinbergen on the comparative study of animal behaviour, and draws attention to the views of those who oppose their idea that innate behaviour patterns are laid down in the neurological pattern of the brain to be released by appropriate stimuli. The classification of emotion is simple and is attempted on a physiological basis.

The final chapter dealing with psychopathology expresses some views that would be sharply debated here. It is not helpful to the student that he should regard affective disorder and schizophrenia as a clinical continuum. Here the author would appear to have departed with disadvantage from his principle of simplification and schematisation.

This book supplements but does not replace a textbook of psychiatry. It is intended to start the student with a three-dimensional orientation towards neurology and psychiatry. It does this admirably, and so it should be read with profit by the student, whether he be undergraduate or postgraduate. Had more been included concerning modern psychophysiological investigations in humans, a further valuable step would have been taken in bridging the gap that exists in minds of many who regard psyche and soma as separate entities. J. G. G.

THE DETERMINATION OF THE ABO AND RH (D) BLOOD GROUPS FOR TRANSFUSION. Medical Research Council Memorandum, No. 36. (Pp. vi + 46; figs. 1; tables 7. 3s. 6d.) London: Her Majesty's Stationery Office, 1958.

THIS is a new edition of the admirable War Memorandum No. 9 (1943). The rapid advance in this branch of hæmatology has necessitated the rewriting of most of the text, with the enlargement of some sections and the addition of new ones.

Minor criticisms are that Chown's well-tried capillary tube method for rapid and economical Rh testing is not mentioned, whereas the rather more laborious "sandwich" slide techniques of Stratton is explained in detail. In the bibliography one author's name is misspelt.

Highly recommended.

C. C. K.

CUNNINGHAM'S MANUAL OF PRACTICAL ANATOMY. Volume II. Revised and edited by the late J. C. Brash, M.C., M.A., M.D., D.Sc., LL.D., F.R.C.S.Ed., F.R.S.E. Twelfth Edition. (Pp. xii + 492; figs. 237. 28s.) London: Oxford University Press, 1958.

VOLUME II, on the dissection of the thorax and abdomen, is the last of the three volumes of this edition of the manual to be published. The design for the edition, as outlined in Volume I, has been carried to a successful conclusion. Professor G. J. Romanes, who was responsible for the final revision of the volume, has endeavoured to simplify still further the transition from the older terminology to the new Paris Nomenclature (1955) by means of typographical changes in the index. The publishers are to be congratulated on the production of this fine volume, and on completion of publication of the whole edition within a year. This volume, and the manual as a whole, can be strongly recommended to all students and teachers.

W. R. M. M.

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THE DETERMINATION OF THE ABO AND RH (D) BLOOD GROUPS FOR TRANSFUSION. Medical Research Council Memorandum, No. 36. (Pp. vi + 46; figs. 1; tables 7. 3s. 6d.) London: Her Majesty's Stationery Office, 1958.

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Minor criticisms are that Chown's well-tried capillary tube method for rapid and economical Rh testing is not mentioned, whereas the rather more laborious "sandwich" slide techniques of Stratton is explained in detail. In the bibliography one author's name is misspelt.

Highly recommended.

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CUNNINGHAM'S MANUAL OF PRACTICAL ANATOMY. Volume II. Revised and edited by the late J. C. Brash, M.C., M.A., M.D., D.Sc., LL.D., F.R.C.S.Ed., F.R.S.E. Twelfth Edition. (Pp. xii + 492; figs. 237. 28s.) London: Oxford University Press, 1958.

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The arrangement of chapters in this second part follows the traditionally descriptive pattern of disease which served neurology so well at the beginning of the century but which, in the light of recent knowledge, might well be modified to take greater account of the localization of lesions in the nervous system and the causation of disease. For example, the chapter entitled "Muscular Atrophies" includes several diverse conditions such as muscular dystrophy, motor neurone disease and acroparasthesia, while polioneuritis and poliomyelitis are described elsewhere. However, the author's awareness of the need of some change is shown by the recasting of the chapter entitled in previous editions "Subacute Combined Degeneration of the Cord" under the heading of "Manifestations of Vitamin B12 Deficiency," but it is odd that the manifestation of vitamin B1 deficiency have not been gathered together in the same way; Wernicke's encephalopathy is barely mentioned, and in the account of alcoholic neuritis no reference is made to thiamin.

The borderland between general medicine and neurology receives more attention than in previous editions. There is a new chapter on the neurological complications of liver disease, but more space might have been devoted to other metabolic diseases, such as diabetes, which present with neurological symptoms. The management of the comatose patient is a common therapeutic problem, but advice on this point is hard to find, for it is scattered throughout the book, and at times archaic (camphor is the sole recommendation for a suitable stimulant, and no mention is made of the lateral decubitus position). The dangers of neostigmin overdose in the treatment of myasthenia gravis are ignored. The value of positive pressure respiration in respiratory failure receives no attention; admittedly in a book intended for practitioners and students elaborate details are not required, but some mention of them is essential to maintain the balance.

Despite these criticisms, the reviewer is convinced that this book still remains the best of its kind and that it has many virtues to commend it to the non-specialized reader, in particular the thoughtful style, the clarity of description, and the advice on the management of disabled persons, so representative as they are of the author. We are glad to see too that this edition, unlike the earlier editions, contains a section of psychologically determined illnesses, such as anxiety neurosis, hysteria, and the "traumatic" neurosis.

J. H. E.

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In any future edition, however, one would hope for further revision. The chapter on the hæmorrhages of pregnancy diverges in places rather markedly from thought and teaching in other centres. Placenta prævia has in most centres lost its place high on the list amongst the causes of maternal mortality, and the wisdom of teaching Braxton Hicks' half-breech compression and vaginal tamponade as methods of treatment might be questioned.

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THIS is a just and fitting tribute from a most distinguished consultant surgeon to the Middlesex Hospital and from the Professor of Anatomy in that medical school to Bell, who served the hospital for more than twenty years and who, above all others, brought that medical school into being.

Apart from the coupling of his name eponymously with certain anatomical structures and clinical states, many will know little of this giant among the surgical giants of London and Edinburgh one hundred and twenty-five to one hundred and fifty years ago. The authors are concerned to show what manner of man he was and the measure of his achievement. The development of his work on the nervous system is clearly described. His life was on a crowded stage, and there is a tendency to catalogue names and events, but his struggle for recognition and much of his public work does emerge clearly. It is doubtful if the man himself is ever clearly seen.

In a book of 288 pages, eighty-eight pages are used as appendices. It is doubtful if many of these appendices are worth including. There is indeed a tendency to supply so much detail throughout the book that it makes heavy demands on the reader. However, everyone interested in the period and in the development of our knowledge of the nervous system must study this work.

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THIS is an excellent little book by the author of "The Hygiene of Marriage." It deals with every aspect of the "change of life" or "climacteric" in a simple straightforward way and gives practical suggestions as to how those symptoms which are distressing can be dealt with.

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THE BRAIN AND HUMAN BEHAVIOUR. Association for Research in Nervous and Mental Disease. Publication 36. (Pp. xi + 564; figs. 200. 120s.) London: Baillière, Tindall & Cox, 1958.

THIS volume is a record of the proceedings of the 1956 meeting of the Association for Research in Nervous and Mental Disease. In the preface it is stated that the programme committee decided "to consider separate areas of the brain from the standpoint of what these areas might contribute to behaviour." Pharmacology and biochemistry were included on a small scale, whilst all other aspects of this almost limitless field were deliberately excluded. Had this statement of policy not been recorded, then the student and those whose interest is not primarily psychiatric could have mistaken that part dealt with as representative of every aspect of psycho-physiological research. This is certainly not the case.

Provided the reader's psychiatric visual fields remain intact, then this volume is one that will be read with great interest and profit. A galaxy of contributors of the first order of magnitude summarise their work to date. For those who want to pursue any subject further the stage is admirably set, even on occasion in historical perspective.

It is not the reviewer's purpose to examine critically every contribution but to deal with a representative sample.

Greenblatt and Solomon's contributions to the study of lobotomy are well known. They summarise their twenty years' work on a procedure that is now well past its zenith. Leucotomy would appear to be at the mercy of a 'changing treatment culture.' Attention is drawn to the advantages and disadvantages of the procedure on relationships within the patient's family circle. They discuss the functional loss suffered both by non-psychotic and psychotic patients, but point to considerable net gains in those who suffered pre-operatively from prolonged and disabling tensions. They admit that leucotomy may be only one of several procedures that will kindle the spark of recovery in the chronic schizophrenic. No fresh criteria emerges for the selection of patients for operation.

Denny-Brown and Chambers report a detailed investigation of the parietal lobe syndrome in animals and in man. In man parietal lobe symptoms can be divided into two main groups, namely, the true agnosias (ascertained by speech, writing or drawing) and the amorpho-synthesis group affecting a lower level of perception and involving behaviour. They found that the conventional approach to the problem of localisation of lesions producing specific patterns of symptoms, although useful clinically in recognising parietal disease, is of limited value when applied to the determination of function. The very general common factors that emerge from clinical analysis, for instance, the concepts of body image and spatial perception, are ultimately derived from the method of testing and have no known counterpart in more simple behaviour reactions. Their classification enabled them to get over a philosophical impasse and bring the problem within reach of experimental neurophysiological techniques. Apart from its intrinsic value, their article should serve as a model for those who try to apply the findings in the experimental animal to the problems of psychiatry, whether it be in the field of drug induced effects or otherwise.

Penfield reviews his work on functional localisation in the temporal lobe and deep sylvian region, and comes to the conclusion that the major contribution of the temporal lobes to brain function has to do with memory recording and with perception. His "memory strips," though a useful analogy, may be misleading, for it stresses multiple static patterns rather than functional rearrangement of relatively few components. He discusses interpretive illusions and their relationship to the non-dominant hemisphere. The same subject is discussed by Milner from the psychological viewpoint. She found that in patients with unilateral epileptogenic lesions of the non-dominant temporal lobe there was an impairment in the comprehension of pictures which tended to become accentuated after operation. Dominant temporal lobectomy, on the other hand, gave rise to difficulties with verbal recall, whilst bilateral damage to the hippocampal zone produced profound and generalised loss of recent memory without any other intellectual changes. Penfield believes then that the perceptual

cortex contains a mechanism that is normally employed in the interpretation of current experience which must include a comparison of past with present.

F. A. Gibbs discussed abnormal electrical activity in the temporal regions and its relationship to abnormalities of behaviour. He deals mainly with spike discharges and points out that focal or generalised abnormalities are largely age determined, and that foci tend to shift with increasing age. He deals with the clinical differences usually found between mid-temporal and anterior temporal foci and discusses the differences between ictal and non-ictal psychiatric disorder in these patients, concluding that the evidence suggests that they are not only independent, but fundamentally different. Dr. Gibbs regrets that some of his cases did not have the close psychiatric scrutiny on this point that he would have liked. The reader will share his regret, for a very important question remains unanswered.

Hoch discusses psychomimetic agents and tranquillisers. A considerable volume of literature has appeared since this article was written, but there has been little progress in our understanding either the site or mode of action of these compounds. Woolley's authoritative article on serotonin and its anti-metabolites summarises a very important field of enquiry, but it is a valuable contribution also because of the discussion it stimulated. Kety's remarks are well worth reading. He drew attention to the fact that the anti-metabolites of serotonin have very varied behavioural effects, thus suggesting that serotonin is only part of the answer.

Harold G. Wolff and his co-workers report on an ambitious study of the highest integrative functions in man during stress. They utilised psychological test batteries to assess learning, memory, the ability to categorise and to generalise, adaptability, affective expression and resistance to disorganisation. Amongst the patients tested were those who had been subjected to brain surgery. The authors found that the site of the damaged region in the cerebral hemispheres was obviously important as regards the effect on functions such as sensation, speech, writing, etc., but that the form and degree of impairment, as measured by their test batteries, was independent of the site of tissue loss within the neopallium, but was closely related to the mass of tissue removed or damaged. If one accepts that the tests actually measured what was expected of them, then this contribution could be regarded as further evidence in support of the idea that mind is the integration itself, the relationship of one functioning part to another.

This book can be thoroughly recommended to neurologists, neurosurgeons, and psychiatrists. It will serve as a stimulus to the latter to develop techniques of examination that will provide information of a kind that can be categorised and correlated with that obtained by workers in allied fields. Those working for a D.P.M. would do well to refer to it. J. G. G.

LUMBAR DISC LESIONS. By J. R. Armstrong, M.D., M.Ch., F.R.C.S. Second Edition. (Pp. xii + 244; figs. 60. 45s.) Edinburgh and London: E. & S. Livingstone, 1958.

THE first edition of this book was published in 1952 and the beliefs of the author are now brought up to date in this new edition. The main changes are to be found in the chapters relating to the pathogenesis of lumbar disc prolapse. This condition has been investigated experimentally by many workers and the acquired knowledge is woven into this book in an expert manner. The great value of the work is the almost provocative way that dogmatic statements are made about questions, which are still not answered in most doctors' minds and are still very much under consideration. Such dogmatism is most stimulating, and the reader is not left in any doubt about the author's views. The particular passages, which will cause some controversy, are those in which the operative treatment is discussed. Points of technique could be argued, as also could those about the assessment of so-called "bad results."

It must be made clear that this is a most valuable and comprehensive volume, which must be read by everyone who is asked to cope with "sore backs" and sciatica. Indeed, it would be money well-spent by our employers to buy a copy for each general practitioner and each consultant who has to deal with these cases—and give them a few days' leave to study it.

Mr. Armstrong is to be congratulated on this excellent work.

R. I. W.

cortex contains a mechanism that is normally employed in the interpretation of current experience which must include a comparison of past with present.

F. A. Gibbs discussed abnormal electrical activity in the temporal regions and its relationship to abnormalities of behaviour. He deals mainly with spike discharges and points out that focal or generalised abnormalities are largely age determined, and that foci tend to shift with increasing age. He deals with the clinical differences usually found between mid-temporal and anterior temporal foci and discusses the differences between ictal and non-ictal psychiatric disorder in these patients, concluding that the evidence suggests that they are not only independent, but fundamentally different. Dr. Gibbs regrets that some of his cases did not have the close psychiatric scrutiny on this point that he would have liked. The reader will share his regret, for a very important question remains unanswered.

Hoch discusses psychomimetic agents and tranquillisers. A considerable volume of literature has appeared since this article was written, but there has been little progress in our understanding either the site or mode of action of these compounds. Woolley's authoritative article on serotonin and its anti-metabolites summarises a very important field of enquiry, but it is a valuable contribution also because of the discussion it stimulated. Kety's remarks are well worth reading. He drew attention to the fact that the anti-metabolites of serotonin have very varied behavioural effects, thus suggesting that serotonin is only part of the answer.

Harold G. Wolff and his co-workers report on an ambitious study of the highest integrative functions in man during stress. They utilised psychological test batteries to assess learning, memory, the ability to categorise and to generalise, adaptability, affective expression and resistance to disorganisation. Amongst the patients tested were those who had been subjected to brain surgery. The authors found that the site of the damaged region in the cerebral hemispheres was obviously important as regards the effect on functions such as sensation, speech, writing, etc., but that the form and degree of impairment, as measured by their test batteries, was independent of the site of tissue loss within the neopallium, but was closely related to the mass of tissue removed or damaged. If one accepts that the tests actually measured what was expected of them, then this contribution could be regarded as further evidence in support of the idea that mind is the integration itself, the relationship of one functioning part to another.

This book can be thoroughly recommended to neurologists, neurosurgeons, and psychiatrists. It will serve as a stimulus to the latter to develop techniques of examination that will provide information of a kind that can be categorised and correlated with that obtained by workers in allied fields. Those working for a D.P.M. would do well to refer to it. J. G. G.

LUMBAR DISC LESIONS. By J. R. Armstrong, M.D., M.Ch., F.R.C.S. Second Edition. (Pp. xii + 244; figs. 60. 45s.) Edinburgh and London: E. & S. Livingstone, 1958.

THE first edition of this book was published in 1952 and the beliefs of the author are now brought up to date in this new edition. The main changes are to be found in the chapters relating to the pathogenesis of lumbar disc prolapse. This condition has been investigated experimentally by many workers and the acquired knowledge is woven into this book in an expert manner. The great value of the work is the almost provocative way that dogmatic statements are made about questions, which are still not answered in most doctors' minds and are still very much under consideration. Such dogmatism is most stimulating, and the reader is not left in any doubt about the author's views. The particular passages, which will cause some controversy, are those in which the operative treatment is discussed. Points of technique could be argued, as also could those about the assessment of so-called "bad results."

It must be made clear that this is a most valuable and comprehensive volume, which must be read by everyone who is asked to cope with "sore backs" and sciatica. Indeed, it would be money well-spent by our employers to buy a copy for each general practitioner and each consultant who has to deal with these cases—and give them a few days' leave to study it.

Mr. Armstrong is to be congratulated on this excellent work.

R. I. W.

CLINICAL BIOCHEMICAL METHODS. By A. L. Tárnoky, B.Sc.Tech., Ph.D.
(Pp. x + 239; figs. 11. 50s.) London: Hilger & Watts Ltd., 1958.

In this new textbook the author describes the biochemical analyses in routine use in the laboratory of the Royal Berkshire Hospital, Reading. It is essentially a practical book. Few alternative methods are given and those procedures which require expensive and highly specialized apparatus have been omitted.

The book is well planned; it is printed on good quality paper and the type is bold and distinct. The contents are listed alphabetically and so descriptions of methods can quickly be found. Accurate stepwise directions are given for each procedure. Subject index and author index are complete and there are eighty-four references.

Certain fairly common biochemical tests have been omitted and not all can have been excluded on the grounds of expense or need for specialized apparatus: namely, electrophoresis of cerebro-spinal fluid protein, determination of blood pyruvic acid, estimation of serum glutamic oxalacetic transaminase and the cephalin-cholesterol flocculation test. Estimation of ketosteroids and amino-acid chromatography are beyond the scope of this book. A method for the quantitative fractionation of serum proteins by electrophoresis is explained, but their respective normal ranges are not disclosed. The modern technique of estimating sweat electrolytes is set down in detail, although a word of caution might well have been added to the instructions dealing with the placing of the patient in a plastic bag, covering with blankets, and allowing him to sweat for one to two hours—a dangerous procedure in a young child. The benzidine test is the only one given for detecting the presence of occult blood in faeces; this is unfortunate, because for the past year this substance has no longer been manufactured on account of its carcinogenic properties. Determination of the basal metabolic rate is well described, although few workers can spare the time to subject the patient to the recommended procedure of three recordings on two successive mornings.

These criticisms apart, this book will be of value to a laboratory where uncomplicated routine biochemical procedures are carried out. There is a valuable chapter on analytical control.

C. C. K.

THE ART OF CLINICAL REFRACTION. By Theodore H. Whittington. (Pp. ix + 286 + vii; figs. 78. 30s.) London: Oxford University Press, 1958.

To the physician with an interest in ophthalmology the fascination of the subject is the manner in which so many different fields of knowledge are brought to bear on the eye, and are found to throw each its own light on the efficiency of the individual's sight or lack thereof. From the combination of anatomy and optics is drawn the science of refraction and it is the virtue of this volume that, as its title implies, there is added to the lucid account of the scientific facts an informed and balanced review of the art whereby these facts are used for the benefit of the individual patient.

Dr. Whittington has based his book on lectures given to post-graduates and medical students and has drawn on the experiences of many years to illustrate with case histories the varying aspects of his subject. He touches on many points on which information is not readily found in medical textbooks, notably the chapters on modern optical lenses and other aids to vision. Chapters are devoted to binocular vision and to squint, and the beginner will find correct lines laid down for him in the section devoted to consulting-room practice.

The more experienced practitioner of ophthalmology will also find that instead of dipping in here and there he will be drawn on from one chapter to another until the whole has been covered. This is due to pleasant and businesslike format of the book and the manner in which the author has interspersed his material with clinical and other observations which show how much he has made his own the art of clinical refraction which he sets out so attractively for his readers.

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YOUR pet cat stretches fully and daily, why don't you? This is the thesis of this little book, which can be read easily in two hours. Lack of proper muscular activity, bad posture resulting from sedentary occupations and the general "flexed" attitude of society are, so says the author, the cause of a high proportion of those painful conditions of limbs and back which patients, with the profession's agreement, call "rheumatism."

The scope of the book is the field of minor orthopædics in general practice, with emphasis on painful conditions of the back and the feet. The author believes that many of these can quite easily be attended to by the doctor and need never be referred to hospital for corsets, physiotherapy and other measures which are of doubtful value.

Instruction on the proper use of the muscles of the back and feet and special exercises for them is contained in the book, and really this section forms the highlight of it.

This is a book for the general practitioner and, in the opinion of the reviewer, is much more likely to help him than more learned and bigger tomes on rheumatic disorders.

R. J. W. W

COFFEE AND CAFFEINE. By R. Ulrick. Translated from the German by Janet Ellingham. (Pp. 52. 7s. 6d.) Bristol: John Wright & Sons Ltd.

I HAVE often searched for examples of a really bad piece of medical writing. My search is now ended, and I can recommend all medical students and all who may ever have occasion to write an M.D. thesis to peruse the fifty-two pages of this monograph.

Even allowing that it is a translation from the original German, the style is appalling and the writing lacks clarity and is verbose. A thick haze of jargon lies between the reader and data which is often incorrect or outdated, generalizations which should never have been derived and some magnificent non-sequiturs.

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After reading this monograph I turned once again to that small but instructive masterpiece by Clifford Allbutt entitled "Notes on the Composition of Scientific Papers," and if this review introduces this book to any who have not read it before, then my time has not been wasted.

O. L. W.

THE MEDICAL PRACTITIONERS' HANDBOOK. (Pp. 285. 12s. 6d.; members of the B.M.A. 10s., final-year students and new graduates 5s.) London: B.M.A. Publications.

THIS short book serves a useful purpose in providing the answer to many of the personal administrative problems confronting us as we attempt to carry on the practice of our profession. Though designed primarily for the new graduate, it will be of value to those of more maturity, if they will refer to the mass of factual information between its covers. Postgraduate education, entry into practice, contracts and agreements, medical protection and insurance are all discussed. Many aspects of concern to practitioners labouring in the National Health Service, such as details of duties, remuneration, pension rights, etc., which are of importance to us all, but which often seem shrouded in mystery, are explained clearly and concisely. There is nowhere any reference to the National Health Service in Northern Ireland where the relevant Acts contain minor differences from those of Great Britain. A few paragraphs explaining the essential differences would be of value to those in practice in this part of the United Kingdom, and could with value be included in the next edition. The handbook is well printed and adequately indexed.

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THE well-known textbooks of anatomy generally used by undergraduates are really works of reference and are not suitable for reading through from the beginning to the end. Moreover, the body is dissected region by region, whereas most textbooks present their information system by system. Professor Woodburne has made an admirable attempt to provide a regional textbook of anatomy which can be read by the student in conjunction with his dissecting-room studies. It is beautifully written, accurate, and gives all the information the medical student needs about the gross anatomy of the human body, apart from the brain, in six hundred pages. Furthermore, every opportunity is taken to co-ordinate structure with function, and to emphasize facts and relationships of clinical importance. The reference lists at the end of each chapter are particularly welcome. The majority of the illustrations are simple and admirable, but some are too small and detailed.

Of course some would have anatomy for the medical student pruned down to the stage where it was no longer worthy to be called a university discipline, but those who regard anatomy as the foundation on which all medical science ultimately rests will welcome this book as the first serious attempt to provide the medical student with the sort of textbook that is available to him in other subjects of his course.

J. J. P.

CLEFT PALATE AND SPEECH. By Muriel E. Morley, M.Sc., F.C.S.T. Fourth Edition. (Pp. + 271; figs. 86. 27s. 6d.) Edinburgh and London: E. & S. Livingstone Ltd., 1958.

THIS book was first published in 1945, and the fact that a fourth edition has now appeared is clear indication of the high regard in which it is held as an authoritative work on a specialised subject. This new edition has been very considerably enlarged and the early chapters on the development, anatomy, and function of the palate now include information on the incidence, ætiology, and inheritance of lip and palate deformities. Recent findings concerning the mechanism of naso-pharyngeal closure have been described and the importance of free mobility of the lateral pharyngeal walls in aiding sphincteric closure is stressed.

The section outlining the development of cleft palate surgery has been brought up to date and is well illustrated with photographs and diagrams.

As in previous editions, the second part of the book is concerned with the various speech defects and gives detailed information on their treatment. Miss Morley emphasises the vital importance of close co-operation between surgeon, orthodontist, and speech therapist throughout treatment if the best possible results are to be obtained.

The book is full of valuable information and should be read by anyone who undertakes the treatment of the cleft-palate patient.

The publishers are to be commended on the very great improvement in the print and general format of this edition.

N. C. H.

LAW AND ETHICS FOR DOCTORS. By Stephen J. Hadfield, M.A., M.B., B.Ch.(Cantab.), M.R.C.S. (Pp. xvi + 399. 42s.) London: Eyre and Spottiswoode, 1958.

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TEXTBOOK OF VIROLOGY FOR STUDENTS AND PRACTITIONERS OF MEDICINE. By A. J. Rhodes, M.D., F.R.C.P.(Edin.), F.R.S.C., and C. E. Van Rooyen, M.D., D.Sc.(Edin.), M.R.C.P.(Lond.), F.R.C.P. Third Edition. (Pp. xl + 692; figs. 81. 80s.) London: Baillière, Tindall & Cox, 1958.

THE third edition of this textbook, first published in 1939, has been considerably revised and brought up to date. Virology is advancing so rapidly that no comprehensive work covering the whole field can be fully up to date at the time of its completion, but the authors have managed to be so nearly so that the reviewer feels that they must have revised and amplified their text up to the last minute. One of the authors' purposes is to present an account of the essential features of the virus and rickettsial diseases of man in a form suitable for undergraduate students. No medical student in this country could be expected to master the immense amount of detailed information on the characteristics of the various viruses and of the many laboratory techniques involved in diagnosis. For the postgraduate student it is excellent, but the undergraduate will have to read it selectively. It is, however, the best book of its type which the reviewer has read.

Following a section on the fundamental characteristics of virus infections of man and animals, the viruses of human disease are grouped according to the bodily system affected. There are sections on virus diseases of the skin and of the respiratory system, eye disease, exanthemata, etc., and such sections should be of very great value to specialists who wish to keep abreast of virology in their own fields. The layout of this textbook has much to recommend it to all readers.

In a textbook written for doctors and concerned with human disease it seems to the reviewer unnecessary and perhaps even tantalising to list at the beginning of the book the virus and rickettsial diseases of the various species of animals such as Long Island duck disease and virus enteritis of mink which are neither indexed nor mentioned again in the text.

The reviewer considers that in the first section particularly, but indeed also elsewhere in the book, many illustrations and diagrams have been selected because of availability rather than suitability. Thus nearly two full pages are given over to photographs and a diagram of the Spinco centrifuge. The diagrams of sections of chick embryos are embryological diagrams with excessive detail. The plates of monkey testis cultures, fig. 16, (a) and (b), are very poor, and it seems a pity in 1958 to have reproductions of drawings (fig. 1) of elementary bodies from a book published in 1937. In figs. 12 and 13 the electron microscope photographs have no inset scale such as is present in other plates of the same type. The photograph of the R.C.A. electron microscope again has no scale to indicate its size. The reviewer showed this plate to a student and asked how large he thought the machine was. The student said he thought it would go on top of the bench. The diagrams reproduced from a W.H.O. monograph showing annual attack rates of poliomyelitis extend only to 1953. The diagrams of tissue culture techniques are good, but are not referred to in the text.

The only other general criticism which the reviewer has is a slight lack of balance. For instance, there is no plate to illustrate the technique of the hæmagglutination inhibition test, which would be helpful, and the complement fixation test gets little attention, yet there are two half-pages of diagrams of ultraviolet irradiators which have been used in attempts to inactivate serum hepatitis virus in plasma. Cat scratch fever, a disease of doubtful virus etiology, occupies about the same space as a typical pneumonia.

In spite of these general criticisms there is very little of the text which is not well written and clearly set out. The only serious disagreement the reviewer would have with the authors is the implication (p. 110) that specimens for virus investigation can be shipped in screw-cap bottles on dry ice, for CO₂ may have a deleterious effect on some viruses.

This book is well bound and well printed, and its price seems low considering the number of illustrations it contains. It would serve as a valuable introduction to the postgraduate beginner in virology, a very useful reference book to the non-specialist, and should be readily available to general pathologists and physicians. It is highly recommended. G.D.

REHABILITATION AFTER ILLNESS AND ACCIDENT. By Thomas M. Ling, M.D., M.R.C.P., and C. J. S. O'Malley, C.B.E., M.B. (Pp. vii + 119. 12s. 6d.) London: Baillière, Tindall & Cox, 1958.

THIS is a most interesting up-to-date little book on the subject of rehabilitation after illness and accident, and there are chapters dealing with the emotional factors in rehabilitation—return to work, rehabilitation in the various specialities, chest conditions, neuro-surgery, orthopædics, and general medicine and surgery. In other words, all aspects of the speciality are very adequately covered in this edition.

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THE interference microscope is a valuable research tool in that it enables measurements to be made of the amount of intra-cytoplasmic components. These objects are far beyond measurement by conventional methods; and objects considerably smaller than those whose mass can be determined by the X-ray absorption method can be studied by it even in the living cell.

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