NOVEMBER, 1955

# THE ULSTER MEDICAL JOURNAL


PUBLISHED BY
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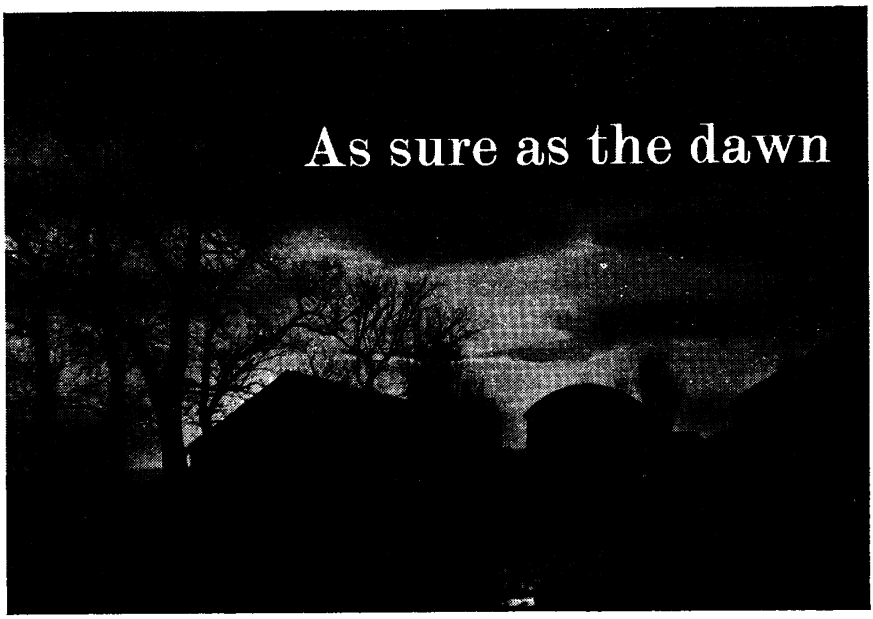


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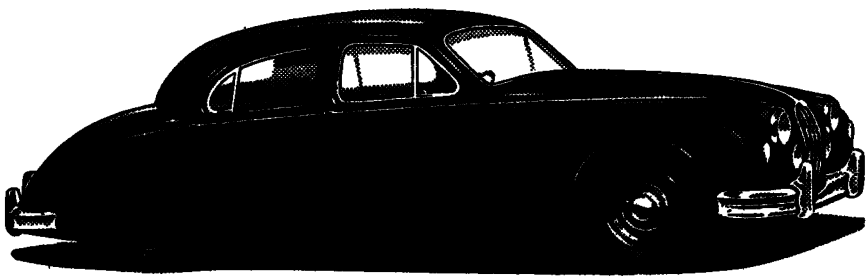

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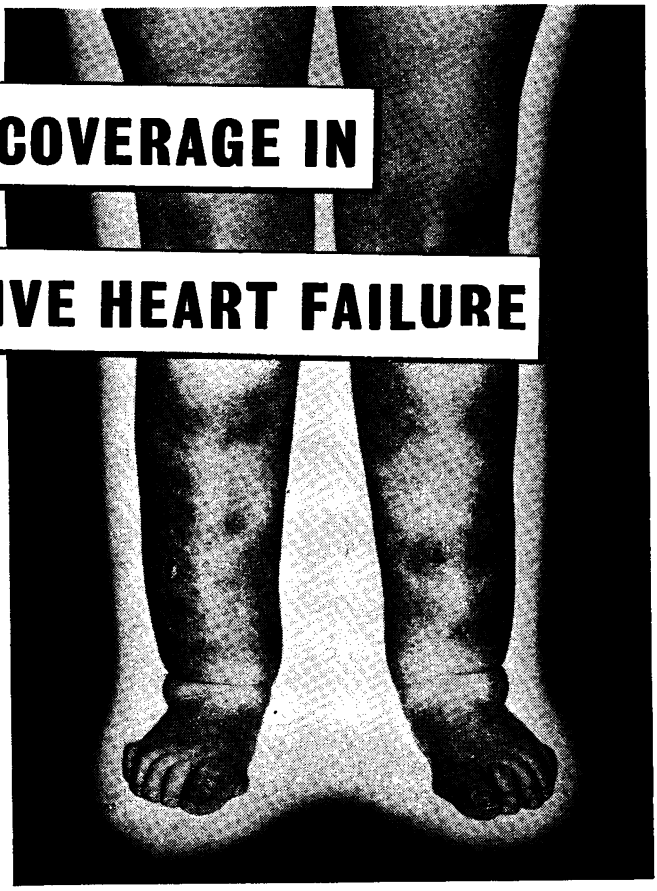

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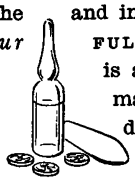

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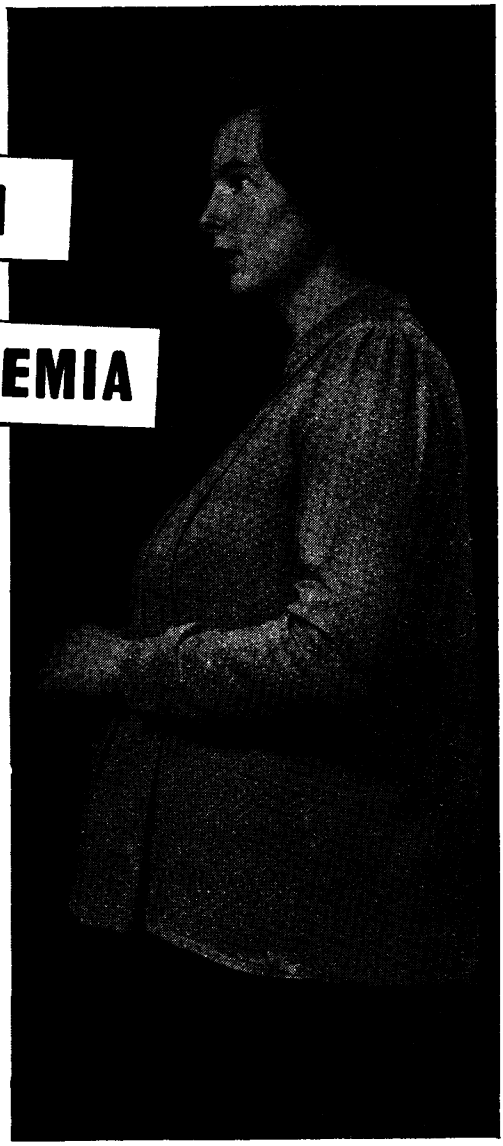

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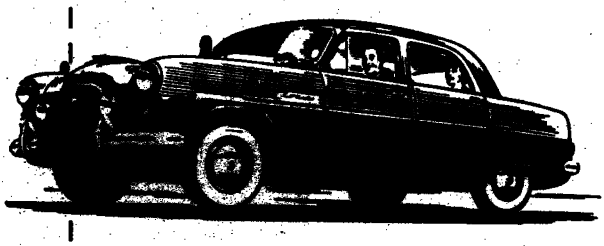

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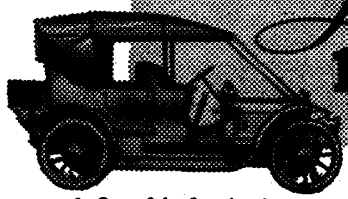

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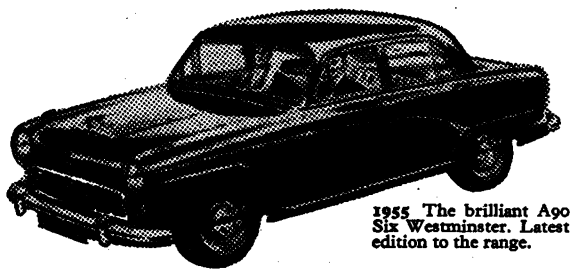

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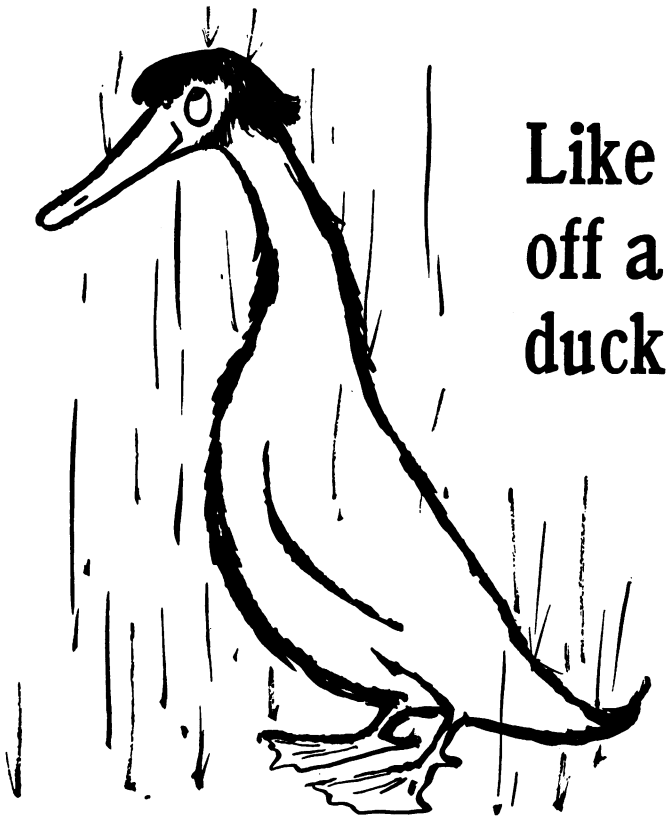

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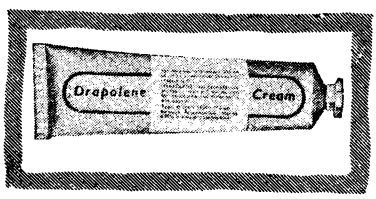


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## No. 1 : May, 1955



## No. 2 : November, 1955

# The Ulster Medical Journal

VOL. XXIV



PUBLISHED BY
THE ULSTER MEDICAL JOURNAL
1955

# CONTENTS






**Fellows and Members of the Ulster Medical Society receive the Journal free.**
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3. References should be given as in the publications of the British Medical Association and in most other modern British journals. If contributors are uncertain of the correct abbreviation for the title of any journal, as given in the World List of Scientific Periodicals, they should give the full title.

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THE
ULSTER MEDICAL JOURNAL

PUBLISHED ON BEHALF OF THE ULSTER MEDICAL SOCIETY

Vol. XXIV 1st NOVEMBER, 1955 No. 2

# The Tragedy of Man-Made Disease

*By* F. M. B. ALLEN, M.D., F.R C.P.,(LOND.)

*Presidential Address to the Ulster Medical Society, 20th October, 1955*

## I. SOME TRIUMPHS.

I YIELD to no one in my admiration of and praise for our predecessors and our colleagues who have achieved so much success in the science and art of medicine. It is true to say that more progress has been made in the last fifty years (especially in the last thirty-five) than in the previous five hundred years. Death rates, both general and particular, have crashed dramatically; infectious diseases which used to carry a heavy mortality are now under control; diseases hitherto regarded as mysterious and "idiopathic" are now diagnosed with alacrity and accuracy; treatment which was often non-existent or empirical is now becoming scientific and rational.

The overall death rate of the general population has shown a steady decline—in Northern Ireland from 15 per 1,000 to 10.8 in less than thirty years. During the period 1730 to 1789 between 50 per cent. and 70 per cent. of children died before reaching the age of 5 years, and one hundred years ago the number of deaths under 1 year was consistently above 150 per 1,000. Infant mortality has declined from 79 in 1926 to 38 in 1953 in Northern Ireland, and in England and Wales from 117 in 1906 to 68 in 1926 and 27 in 1953.

In 1850 it is estimated that 65,000 people died of tuberculosis out of a population of 20,000,000 in England and Wales; in 1953 this was reduced to 9,000 out of a population of 45,000,000. The death rate from tuberculosis in Northern Ireland during the past four years has fallen steadily from 48 per 100,000 to 30, 23, 18, and almost certainly to a still lower figure for the current year.

The same story holds for diphtheria, where notifications have fallen from 18,596 to 182 and deaths from 722 to 9 in England and Wales between the years 1945 and 1954. Scarlet fever used to be a mortal disease, often killing three or four children in a family and causing serious illnesses in all age groups. Now it is a relatively benign inconvenience in children, only rarely being associated with complications.

These are some of the triumphs of which we may legitimately be proud; but they carry new responsibilities. The power of medicine has increased and is likely to increase further. We can relieve pain, keep a patient unconscious for prolonged periods, perform intricate operations not even contemplated before, prevent conception, terminate pregnancy, prevent and treat successfully an increasing number of infections, modify the reactions of the mind with drugs and influence the personality of an individual with a scalpel.

A medical philosopher recently said that "medicine is tending to become a science and much less an art; but more important is its increasing power over so much of human health, welfare, and even existence. It has become so large a field of intellectual exercise with so many details in and development of every subject that any one individual knows relatively less and less about medicine as a whole."

In former times many diseases did not lend themselves to successful treatment even when we knew the cause. Early and precise diagnosis was not of any great consequence in the face of our therapeutic futility. Tuberculous meningitis was all but invariably fatal in less than three weeks from its diagnosis. Now, if modern therapy is to have the best chance of success early recognition of the disease is imperative.

Every departure from the normal health rhythm is the subject of anxiety to the patient or his relatives—and is a challenge to the physician. Therapy is becoming more and more scientific, specific and rational. Therapeutic efficiency demands a precise diagnosis; it is no longer sufficient to know that an infection is due to staphylococci, we must know the sensitivity of the particular staphylococcus to the range of drugs that are at our disposal. A wide knowledge of the effects of therapeutic measures is essential so that the treatment may be not only successful in overcoming the disease; but also that it may not give rise to ill-effects.

## II. Some Fortuitous Discoveries.

It is strange how so much of medical discovery has been due to a fortuitous association of two or more individuals with complementary knowledge or cognate ideas, of the meeting of the man and the opportunity. How much, too, is due to inspiration occurring in the enthusiastic searcher for truth. Pasteur noted that, in the field of observation, chance favours only the mind that is prepared.

Banting qualified as a doctor in 1916, and in 1919 was resident surgeon in the Children's Hospital in Toronto. He combined general practice with a part-time assistantship in physiology in 1921. One day he had an inspiration that all the frustration of the past in extracting the anti-diabetic hormone from the pancreas was due to the presence of trypsin. "Carbohydrate physiology in the thirty years following Minkowski's fundamental discovery had left a trail strewn with the wreckage of attempts, many by workers of ripe experience, to extract the supposed hormone from the pancreas." Pursuing this idea Banting succeeded where others have failed.

It was fortuitous that a man of Fleming's temperament, enquiring mind and intelligence should have been the victim when the mould *Penicillium notatum* contaminated one of his plates of staphylococci. Many others would have cast the

plate away and the discovery of penicillin might have been delayed indefinitely or never made at all. Fleming studied the "spoiled" plate and appreciated the novelty of its effects. It was left to Florey and Cheyne to isolate the substance in a form suitable for administration to humans.

The discovery of folic acid as a valuable principle in the treatment of certain forms of anæmia was due to the association of two minds who jointly recognised the significance of the drug and its possible use in treatment. The possibility of therapeutic usefulness was the suggestion of a general practitioner and the evolution of the drug for certain forms of anæmia was the work of a clinical scientist.

Similarly with pyridoxine (vitamin $B_6$). Its absence in milk accounts for the occurrence of convulsions in babies and when this is replaced in the feeds the convulsions can be controlled. It was the combination of the observation of the general practitioner in whose patients convulsions had occurred, with the fortuitous meeting with the physiologist who was aware of the effects of pyridoxine-deficiency in causing them, which solved a baffling (but short-lived) mystery.

Hirschsprung, in 1888, assumed that the form of constipation later associated with his name was caused by congenital megacolon. In fact, the megacolon is now recognised to be due to congenital constipation. Neurohistological observations in 1920 by Dalla Valle, by Robertson and Kernohan (1938) and others recorded the absence of ganglion cells in the distal alimentary canal in this condition. But clinicians were slow to realise the significance of their absence. It was only when Swenson in Boston fully appreciated that the failure of relaxation of the terminal portion of the gut caused the constipation, which accounted for the megacolon that a rational surgical procedure for the cure of Hirschsprung's disease was evolved.

Collaboration has been necessary in solving some problems of considerable complexity. It is not essential that this should take place in the same laboratory, or even in the same city. Todd and Coburn, working in cities three thousand miles apart, between them presented anti-streptolysin 0 and anti-streptolysin S to man's knowledge, so that a better evaluation of rheumatic infection is now available.

In the search for a new dye sulphanilamide (prontosil) was produced by the chemists. But, more valuable to mankind, was the discovery that this drug was a specific agent against streptococci. It was first used to combat puerperal infection. From this beginning a series of "sulpha" drugs has flowed with specific action in overcoming specific infections of which the end is not yet in sight.

These experiences should encourage doctors to realise that close observation of their patients permits fundamental contributions to be made without the paraphernalia of a hospital research centre. Conspicuous phenomena daily pass us unseen, but we must use our eyes, our ears and our hands if we are to recognise them in their course before our consciousness. Admittedly, the store of human knowledge might have been increased if men of an enquiring mind and endowed with the spirit of research had not been frustrated.

## III. Some Tragedies.

Osler names less than twelve drugs which he regarded as being therapeutically useful; but added the warning that almost all (if not all) of them had side-effects.

Mercury was a great stand-by of the older physicians because, while it was the sheet-anchor in the treatment of syphilis, it also acted as a purgative and as a diuretic. But it had, in addition, serious effects upon the mouth and teeth. Digitalis introduced into medicine by Withering as a diuretic can cause anuria and cardiac death. Citrate can result in "intoxication" when administered in large doses or for prolonged periods. Serious conditions have arisen from massive transfusions of citrated blood and hypocalcæmic tetany and cardiac depression have occurred. Even oxygen can cause disease, as we know from our experineces in premature infants where its administration is believed to account for retro-lental fibroplasia—the greatest single cause of blindness in young children. It is also known to disturb the electrolyte balance and non-protein nitrogen by its presence.

Osler's dictum that we should be sure our treatment does not harm the patient is very pertinent in these days of therapeutic enthusiasm. It is estimated that there are somewhere between 100,000 and 150,000 remedies available and the number is increasing at the rate of 10 per cent. every year. Thus it comes about that a doctor who has reached 50 years of age will probably know little of the indications for the proper use (or avoidance) of the vast majority of these therapeutic arms and will be well advised to avail himself more of post-graduate instruction and not to fall too readily to the charms of the specious advertiser.

1. Every drug is potentially dangerous. Even aspirin may cause great inconvenience or even death; citrate may cause tetany; water injected into a megacolon may cause "intoxication" with convulsions.

2. Every diagnostic procedure carries a risk, and when one contemplates the hazards of venupuncture as regards infection and the serious consequences which may result from catheterisation of the bladder, visceral punctures, angiograms, lumbar punctures, the injection of opaque solutions, suspensions and emulsions into organs, body cavities and canals one sympathises with and often admires the conservatism of the more experienced physician or surgeon who justifiably hesitates to embark upon heroic exploits. He uses his judgment to arrive at an accurate diagnosis by the safest procedure which does not jeopardise either the comfort or survival of the patient. He regards with disquiet the ill-founded complacency with which the impetuous and inexperienced will undertake procedures which carry an unseen and unrecognised risk.

3. Drugs of high potency demand care in their use and disposal. Digitalis is a remedy widely used and of extreme value; but it can be death-dealing if administered without discrimination. To the toddler it is a death sentence if left about the house within his reach.

Curari, dicoumarol, heparin and the analeptics (coramine and nikethamide) must be treated with discretion. An error in dosage of curari will be fatal, dicoumarol must be under effective control in its use, the indiscriminate use of analeptics has been known to "flog a failing heart to death."

4. The modern practice of parenteral therapy is not without risk. There is the ever-present menace of the introduction of infection by faulty aseptic technique in

the operation; by the lack of sterility of every item of the infusion apparatus; and by the lowering of the natural resistance of the tissues at the site of injection. Those of us who have witnessed the prolonged administration of fluids are only too well aware of the risks of local infection, thrombophlebitis and even of septicæmia.

There is further the profound disturbance to body metabolism which takes place with the introduction of solutions containing sodium and potassium—admittedly of known quantity and in the presence of precise biochemical information. Profound changes in body chemistry can be readily created and cause complicated chemical pathology of which we, as yet, know relatively little.

Apart from the partially understood or unknown effects of drugs there is the risk of the injection of the wrong preparation. The coroners' courts are often the scene where the story of an error due to ignorance or carelessness is exposed. A patient was given mersalyl intrathecally instead of lipiodol, developed paraplegia, eventual urinary infection, and died; an infant was given flaxedil instead of coramine; paraldehyde was given in ounces instead of drachms—and so the story could be multiplied.

5. Industrial diseases are largely "man-made," in coal mining, in textile mills in chemical factories and in the other complicated processes of our modern civilisation. The excreta of chimneys, along with climatic conditions, gives rise to "smog," which can be death-dealing, especially to the elderly. Fifty tons of coal consumed in a furnace annually can account for the deposit of two tons of soot, especially if combustion is in unskilled hands.

Hospitals derive a high proportion of their patients from accidents—on the roads, in factories, and at home. In ten years 200,000 persons in Britain have died as the result of accidents, and approximately 10,000,000 have been injured. Every day 45 people die, 16 from travel, 5 from workshops, 17 from home accidents, and 7 in "everyday pursuits." Children are pathetic victims of street accidents, of falls in the home, and of accidental poisoning. The dangerous age for children is when they display the human spirit of adventure and begin to toddle, to explore drawers and cupboards and to taste the contents of bottles, boxes, and tubes.

6. Allergic Reactions. It has been stated that some five hundred drugs used in modern therapeutics are potentially allergic. It is common knowledge that inhalants such as horse hair, feathers and dust and ingestants such as milk, eggs, shell-fish, etc., can induce asthma, urticaria, eczema, vaso-motor rhinitis. Most doctors are aware of the unpleasant reactions which occur with horse serum products and of the effects of a relatively innocent drug such as aspirin in some persons. The scope of allergens has been considerably increased by the introduction of antibiotics, as they are produced from moulds—the richest source of allergens. Penicillin, the safest of the antibiotics, is known to produce at least two hundred severe reactions yearly.

I have seen patients in acute distress as the result of the administration of an antibiotic. This has been so pronounced that parents have been warned not to agree to the use of the offending drug without it being known that the distressing

condition may recur or that even a fatal issue may ensue. I am in sympathy with the doctor who insists on these patients in his practice wearing a label under their clothing that they are not to be given this particular antibiotic.

Medical literature in recent years contains the record of experiences by practitioners of severe allergic reactions to antibiotics—sometimes sudden death. It is tragic to read of a mother of five children, 42 years of age, dying after an injection of penicillin given during labour. This mother had had penicillin for a miscarriage four years previously. It should by now be realised that patients (especially the allergic type) may become sensitized to it and discretion used in prescribing it.

7. Antibiotics. The introduction of insulin and the evolution of sulpha drugs must have satisfied the soul of the searcher for dramatic events. But to these there has been added the discovery of penicillin by Fleming, and now the development of the series of antibiotics since then has been accepted as almost commonplace. Perhaps every one of us owes the recovery of a relative or friend from a dangerous illness to one or other of the antibiotics. Many operations could not be undertaken without them—lobectomy, cardiac and colon operations, tonsillectomy and dental extractions are often safe only under their shielding influence; many chronic, invaliding conditions such as bronchiectasis are made tolerable for the patient by their use; overwhelming infections likely to prove fatal can be controlled; puerperal sepsis is almost non-existent as a cause of maternal morbidity and death; infections in the newborn which were hitherto a major cause of death are now treated with hope of success; the hæmolytic streptococcus which causes rheumatic fever responds to penicillin and there is evidence that its use over a prolonged period may go far to reduce the number and severity of recurrences; pneumonia which used to be associated with a high death-rate, especially at the extremes of life, is now regarded with complacency in the presence of penicillin; this illness, calling for all the skill of the nursing staff and the all but futile treatment of the physician, is now shorn of most of its drama.

Unfortunatey, these remedies are not without their hazards and are outstanding examples of the Oslerian warning that practically all drugs have unpleasant side-effects. The antibiotics are associated with complications of glossitis and stomatitis; nausea, vomiting, and diarrhœa; anal pruritus; vestibular and auditory disturbances; aplastic anæmia; allergic reactions of many kinds, including fatal anaphylactoid reactions, serum sickness and skin rashes.

Most of the reactions to antibiotics are uncommon when related to their widespread use and, fortunately, the majority of unpleasant consequences are no more than temporarily inconvenient; but sufficient of these side-effects are productive of serious damage and fatal outcomes to justify the earnest pleas of many people that caution is necessary and indiscriminate use is to be avoided.

There is a fallacious generalisation that if a little of something does good, then a lot will do proportionately more good. It is too often assumed that antibiotics which are effective in grave illness will be useful in minor illnesses. It should be more generally appreciated that many of these ailments are not caused by infective

agents—and if any of them are so caused, the sensitivity of the organism to the proposed antibiotic should be assured. The general experience is that the use of antibiotics in minor illnesses is disappointing and the most probable outcome is that the patient becomes sensitised and is converted into a potential victim of allergic reactions. It has been said that antibiotics "are not for minor illnesses and penicillin umbrellas should be erected for impending storms and not for minor showers."

More serious, however, is the danger that the patient may become a reservoir of resistant organisms, especially of staphylococci. It has been shown that the more frequently staphylococci in a community are exposed to a particular antibiotic the more likely they are to become resistant to it. We are all familiar with the current reports (and some of us have had personal clinical experience) of severe—or even fatal—staphylococcal enteritis arising during the energetic (and probably fully justified) use of a group of antibiotics to deal with the primary and unrelated infection.

Staphylococci and Gram-negative organisms are unpredictable, and before they are attacked by antibiotics they should be subject to laboratory study for resistance. It is different with tuberculosis, where it is known that streptomycin along with isoniazid is safe, that enteric organisms and *hæmophilus* respond to chloramphenicol and that the hæmolytic *streptococcus* yields to penicillin.

It is surely folly on our part to indulge in the indiscriminate use of these valuable remedies. It has been stated that in the instances in which a fatal outcome has resulted from the use of an antibiotic the treatment was misdirected or was unnecessary in one half. In a survey of a hospital medical unit it was determined that of all the patients receiving treatment one in four was having some antibiotic! In another survey in a surgical unit it was found that in 95 per cent. of patients treatment with antibiotics was not indicated and was unnecessary (Garrod). In prophylaxis Garrod estimated that the abuse of antibiotics was 40 per cent. as prophylactics and 14 per cent. for treatment.

The family doctor is too often the victim of the modern custom of the patient who demands as a right a "shot of penicillin" at the slightest sign of malaise; and too often the doctor, to avoid losing a patient or to ensure a worry-free night, agrees. An unexplained temperature is often treated with an "injection" where, if patience had been exercised, the next day might reveal in all clearness the correct diagnosis and a different line of treatment be indicated. Instead, the correct diagnosis remains shrouded in mystery. It is the experience of many of us that the patient with an "unexplained" temperature in the evening, if left alone until morning, will be found to have a normal temperature or the diagnosis will be more readily ascertained in the absence of complicating therapy.

It has been stated that the annual production of antibiotics in the United States is more than 900 tons—enough for 100 million courses of 10 grams—and Wayne (1954) concludes "not more than 5 per cent. is administered on proper clinical indications." It may surprise you to know that there are at present forty-seven preparations of penicillin from which to choose.

I would suggest, therefore, that regard should be paid to the widespread warnings against the indiscriminate use of these valuable therapeutic agents, especially in minor ailments which will respond equally well to more conservative measures. It is tragic to learn of a patient with peptic ulcer being given chloramphenicol only to die of aplastic anæmia; and it is surely the prostitution of antibiotic therapy to see a child with cervical adenitis due to *Pediculi capitis* being given daily injections of penicillin. More discrimination would avoid the tragic examples of a case of pernicious anæmia which converted to aplastic anæmia as a result of chloramphenicol for intercurrent infection; or of laying the alimentary tract open to an overwhelming onslaught by resistant staphylococci; of sudden death due to penicillin and all the unpleasant, inconvenient side-effects of administration.

8. Sulphonamides were introduced in 1935 and their advent was hailed as one of the therapeutic miracles of the century. The potency of sulphanilamide against the *streptococcus* and its success in combating puerperal sepsis assured it of a position in therapeutics. The handicaps of the early products were overcome to some extent by refinements in manufacture, and development in the production of new compounds reduced most of the unpleasant effects associated with the administration of the original preparations. Blocking of the renal tubules with crystals, skin rashes and even profound mental changes were accepted as a price to pay for ease of administration and the dramatic effect on infections which hitherto yielded only imperfectly to older therapeutic routines. Pneumococcal infections were, for the first time, successfully overcome by specific therapy; gonorrhœa was treated with speed and success instead of by prolonged and often ineffectual measures; the *streptococcus* causing puerperal sepsis or tonsillitis was assaulted with efficiency.

Before, however, they could be properly established in therapeutic favour, penicillin was successfully prepared for administration to the human subject in somewhat similar infections. The novelty and drama of its presentation, its outstanding success in the treatment of war wounds almost swept the sulphonamides out of the therapeutic orbit in spite of the inconvenience of administration by injection. Fortunately, the chemists persisted in evolving new sulpha compounds with less harmful side-effects and with a more specific purpose.

The occurrence of sulphhæmoglobinæmia was a common result of sulphanilamide administration, but does not occur with modern compounds; nor is agranulocytosis so frequent. Crystalluria may be an unpleasant complication of some of the preparations but can usually be avoided by an adequate fluid intake. Polyarteritis nodosa is a risk common to more than one potent drug and rashes are frequent with many preparations in common use.

It is my opinion that if sulphonamides had been introduced to medicine in 1940 instead of in 1935 their wide field of usefulness and their ease of administration would have considerably restricted the development of antibiotics and would at the same time have resulted in their more popular use. It seems to me that the future will bring forth chemical compounds based on the sulpha radicle with an increasingly valuable specificity against known infections and largely devoid of dangerous and unpleasant side-effects.

9. Hazards of Blood Transfusion. Blood transfusions play a large part in modern therapeutic activity. Many major operations are accompanied, and quite justifiably, by concurrent infusion of blood. The loss of blood by injury or childbirth, or during an operation, can be rapidly made good by this life-saving measure. In severe anæmias it may be the only means of giving the patient an opportunity to respond to other slowly acting remedies. A blood transfusion is a dramatic event which evokes discussion in the press and provides a conversational topic for the drawing-room—especially when a relative is in the hero's rôle of being the donor. Nowadays it is a commonplace exercise with an annual distribution of well over half a million bottles of blood.

Do all those who administer blood transfusions lightheartedly realise the risks? The donor may transmit homologous serum jaundice or even an unsuspected tropical disease, the virus of measles or of influenza. Blood which is stored may become contaminated in spite of all recognised measures adopted for the preservation of sterility; it may also contain an excess of free hæmoglobin. Incompatibility may be unrecognised or a false assumption of suitability of blood for a specific patient may be made. Further, there is the danger of introducing an Rh-positive blood into an Rh-negative patient already sensitised by a previous Rh-positive transfusion or Rh-positive pregnancy. Other risks include overloading of the circulation, air embolism, thrombophlebitis, excess of citrate in the blood and the lack of judgment in giving transfusions to patients with cardiac or renal inefficiency or in anæmia when the increased fluid is too great for the blood-starved cardiac muscle.

The mortality attached to the operation (in spite of all the precautions of storage, sterility and testing) has been assessed as about equal to that due to uncomplicated appendicectomy—admittedly not very high, but creating a definite hazard—and the advice which might be given to surgeons and other members of hospital staffs is—"A blood transfusion, like marriage, should not be undertaken lightly, but with care and competence" (James, 1954).

10. A.C.T.H., Cortisone. The introduction of cortico-steroids in the treatment of rheumatic disorders was hailed with worldwide interest and accompanied by an urgent, clamorous demand for their universal distribution. It was not long after their introduction, however, until enthusiasm for their use became dampened by the more circumspect and cautious physicians and surgeons.

Deaths after the administration of A.C.T.H. for asthma were recorded and other untoward effects resulted. In a series of 185 patients there were three gastro-intestinal perforations (with two deaths), three "psychotic episodes" and one case of steroid diabetes. There is now available a cumulative list of side-effects from the administration of cortico-trophin which includes hyperadrenalism, endocrine depression of the thyroid and gonads, potassium deficiency, psychoses, peptic ulcer, occult œdema, Cushing-like syndrome, secondary infections, increased susceptibility to infection, purpuric and thrombo-embolic phenomena as well as examples of hypersensitivity.

11. Hypotensives. Hypertension, whether "essential" or associated with constitutional factors, cardiac or renal disease, endocrine gland disorders or obesity, is a diagnosis which must disturb the equanimity of the patient and create a feeling of alarm. The discovery of drugs which were capable of reducing the pressure in the blood vessels was therefore of outstanding importance. The young parent, 35 years of age, with a systolic pressure of 280 mm. of mercury, is no longer the subject of dietary control, sedatives and placebos whilst the disease progresses to its ultimate end without hesitation. Hexamethonium, by its action in blocking impulses at the ganglion level, is capable of reducing the pressure and maintaining it at a level appropriate with the survival of the victim. Other drugs are available, some are natural in origin, others are complex chemical compounds. Now no less than thirty-eight preparations in more than a dozen colours and shades are available. (Palmer, 1955.) Palmer states that fifteen million Americans are being treated for hypertension, and the comment is made that dietary regulation would be adequate in a high proportion of cases.

If these drugs had as their sole effect the reduction of systolic and diastolic blood pressures there would not be the criticism that they are expensive or unnecessary. Tragedies, however, have happened with their use. Disturbing symptoms arise and even death may occur, e.g. ,a patient developed ileus as a result of treatment with hexamethonium and died. It should be realised that "in these drugs we have a powerful weapon which is life-saving in suitable cases; but their administration does require close and careful supervision."

12. Narcotics, Hypnotics, Sedatives.

> "O sleep. O gentle sleep!
> Nature's soft nurse, how have I frighted thee,
> That thou no more will weigh mine eyelids down
> and steep my senses in forgetfulness?"

To many, if not most, of us sleep comes naturally at the end of the day's activities. The mother in labour desires respite and is given a hypnotic or sedative; the industrialist, harassed by his problems, brings his worries home to his bedroom and justifiably is provided with a sedative; the neurotic, with his disturbed psyche, full of anxieties, demands the blessed means of securing the repose which evades him. Morphia and similar drugs were first replaced by the hypnotics which had the disadvantage of a prolonged effect persisting far into the following day. Sedatives of the barbitone series have the advantage of quick action and relatively rapid excretion, thereby avoiding dullness of perception after a night's sleep. Finer and better compounds, each with its own particular advantage, appear at frequent intervals.

The barbiturates are much used in modern medicine, reflecting possibly the state of mental anxiety of the individual citizen of this turbulent world. At least 10 per cent. of prescriptions on the form E.C. 10 were for barbiturates, and this may be an understatement (Dunlop, 1953). Surely it is difficult to justify such a high proportion of sedatives in our therapeutic activity!

It should be appreciated that these drugs are true drugs of addiction; that they provoke systemic toxic effects such as rashes; fatalities occur as a result of sensitivity; porphyria occurs in acute form in susceptible persons. More serious, perhaps, is the fact that, by making the drug so easily accessible, we are facilitating the would-be suicide and opening a door to accidental poisoning, as these figures show :—

| | | |
|---|---|---|
| Total suicides - - - - - | 5,147 ... | 4,469 |
| Suicides due to barbiturates - - - | 12 ... | 248 |
| Percentage - - - - - | 0.23 ... | 5.5 |
| "Accidents" - - - - - | 12 ... | 117 |

Discretion must be exercised before the patient embarks upon a career of phenobarbitone addiction and emphasis must be placed upon the doubtful practice of "sedating" (horrible word !) during waking hours people whose symptoms are the result of anxiety and frustration and those suffering from what it is fashionable now to call psychosomatic disorders.

13. Chlorpromazine, phenylbutazone are potent drugs with severe side-effects which demand from us circumspection and control in their exhibition. Rashes, toxic hepatitis, blood changes occur with alarming frequency. The administration of gold has been all but abandoned because of its side-effects. Iron has inconvenient consequences if not used with discretion; fersolate can cause ulceration of the gastric mucosa and lead to pyloric stenosis; it can cause death in an infant or young child. Novalgin may cause agranulocytosis. The dangers associated with amidopyrine are generally appreciated; but unfortunately the presence of this drug (or some other equally dangerous one) in a well-known proprietary is not always recognised. Epanutin (phenytoin sodium) is widely used in epilepsy; but it is known to produce hypertrophy of the gums and less frequently megaloblastic anæmia, purpura, ulcerative stomatitis, and death. Even vitamins are suspect. I am unable to contradict the statement that the excessive consumption of the liver of a polar bear will give rise to headache, nausea, giddiness, drowsiness, and cramp, due to the high vitamin A content. An unduly large dosage of vitamin D may be responsible for the recently recorded cases of hypercalcæmia in this country.

Even the babies' napkins are not without danger. Modern detergents can account for contact dermatitis; a baby was seriously ill with napthalene poisoning due to storage of napkins in moth balls; marking ink caused fatal methæmoglobinæmia and boric acid used as a powder has had serious consequences. A baby of three months died from boron poisoning due to the application of "boracic acid powder."

Synthetic preparations of vitamin K are not beyond suspicion, and it has been recently asserted that kernicterus may be due to the enthusiastic use of this preparation in endeavouring to avoid the risks of hæmorrhage in the newborn in a difficult or prolonged delivery.

I do not wish to subscribe to the creed of nihilism, but rather to appeal for discrimination in selecting a drug for therapeutic action. I suggest that we should cultivate a healthy scepticism and not attribute too many of our therapeutic

successes to the potency of the drugs we use and far too little to the tendency of many diseases to remit spontaneously. It might be better if, more often, we pondered on when not to treat and when to treat.

Discretion in diagnostic procedures and the avoidance of heroic therapeutic measures is desirable—"The patient died on the sixth day. He had had no operation, nor arteriogram performed. In other words death was spontaneous," said the cynic.

Disease—a departure from health—is regarded by the victim as a catastrophe: by some it is looked upon as a divine visitation for the performance of an evil act; by others as a purely fortuitous, haphazard incident in the life of an individual. But to us, as doctors, it is a challenge—a mental exercise to determine the correct diagnosis, an opportunity to evaluate the probable outcome of the illness and, more importantly, an occasion for the application of the appropriate treatment.

Leonardo da Vinci said, five hundred years ago: "You know that medicines, when well used, restore health to the sick: they will be well used when the doctor, together with his understanding of their nature, shall understand also what man is, what life is, and what constitution and health are."

We must realise that by our advances in knowledge, particularly in therapeutics, we have created a revolution. Let us, therefore, have a sober assessment of these remedies we use and a stern criticism of the multiplicity of their actions and effects.

Let me conclude with a "Modern Litany" composed by Sir Robert Hutchison:—

> "From inability to let well alone; from too much zeal for the new and contempt for what is old; from putting knowledge before wisdom, science before art, cleverness before common sense, from treating patients as cases, from making the cure of the disease more grievous than the endurance of the same, good Lord, deliver us."

# A Tribute to our Surgical Pioneers :

## A History of Surgery and Surgeons of the Royal Victoria Hospital, Belfast, from 1792 to 1920

*By* ERIC W. McMECHAN, M.B., F.R.C.S.

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*Opening Address, Winter Session 1955-56, Royal Victoria Hospital, Belfast*

SOMETIME about one hundred and twenty years ago the first oration or opening address was delivered to students about to commence their clinical studies. Having read a great number and listened to quite a few of them, I realise my own imperfections in attempting to follow this great tradition which has been handed down from year to year. I will therefore have to crave your indulgence, and content myself with giving expression to the hope that, whilst I recognise my inability to emulate the example of my predecessors, my efforts may not be altogether fruitless.

On such occasions as this one must look back over the past year and record our losses and gains. I sadly recall that we have lost two most distinguished members of our medical staff.

John Campbell Rankin was one of the most senior members of the consulting medical staff and was associated with "the Royal" for almost half a century. He was the pioneer radiologist in Ireland and was responsible for much of the early development of X-rays in Belfast. His interests also extended to the fields of radiotherapy, bacteriology, and venereology. It can honestly be said he was a friend to all, a friendship that is a valued memory.

Death struck a severe and unexpected blow with the passing suddenly of Cecil John Alexander Woodside. He was our senior surgeon, a position he held with an unobtrusiveness which characterised much of his work. He had special interests in genito-urinary surgery and in administration, and was an active member of the Hospitals Authority. His work was always of the highest standard and his premature removal from our midst is a sad loss not only to his colleagues but also to the Hospital and the community.

One of our colleagues, Dr. Norman Graham, has reached the Consulting Staff. His work on the growth of microbes has now been replaced by an interest in the growth of flowers. May his years of faithful duty be followed by many happy years of retirement.

It is with very great pleasure that we welcome three new members to our medical staff committee :—Dr. James Elliott, Dr. T. T. Fulton, and Dr. J. L. E. Millen, all graduates of our own university and medical school. We wish them many happy years of service in "the Royal."

On behalf of my colleagues on the Visiting Medical Staff it is my pleasant duty and privilege to-day to welcome those of you who are attending the opening of

session for the first time. You have registered your names on the roll of this Hospital and medical school to receive training which will enable you to qualify as doctors. You are also, however, becoming the inheritors of a noble and honourable tradition which is centuries old, and which you are charged to keep as a sacred trust, so that when the time comes you may be in a position to hand it on to your successors untarnished and unsullied.

You have reached an important milestone in your careers, your main interest has shifted from the University to the Hospital. You will now have to deal with patients and you will see the ravages of sickness and disease probably for the first time. One of your first reactions will be of sympathy, a response which I hope you will retain. You will be subject to many other reactions—fear, when you discover that you yourself have the signs and symptoms of several serious diseases all at the same time; pride and humility when you watch the courage and fortitude of those battling with serious illness; surprise and elation at unexpected victories; depression at expected or unexpected failures; you will see the joy and gratitude of recovery, the sorrow of death, the anxiety of waiting, and the tears of relief and distress. Your emotions will be stirred, and yet you must preserve an outward calm. But do not become hardened; each patient is an individual with a heart and soul and not just another case of "such and such" disease. Remember most patients come to hospital in a state of fear and apprehension, but also with faith and trust in the Hospital and in you; you must see that their faith is not misplaced.

It is perhaps trite and commonplace to say you must work. However, I believe that work and the manner of its accomplishment will make your success or failure in the years to come. The old saying of "come easy, go easy" applies to knowledge as well as money, so let us hope that the evils of spoon-feeding are not being forgotten. Each year more and more of your time is being taken up by lectures, with less and less time left for you to devote to clinical work. You must see that the little time that is left is used by you to the best advantage. You must see and observe the individual variations of disease at the bedside and avoid becoming the rule of thumb doctor who must look to others for guidance at every step, or whose practice is governed by the last journal read or even by the last glowing circular that escaped the wastepaper basket.

It is said that there is no more difficult art to acquire than that of observation. As we have become more and more dependent on the laboratory and other special investigations in making a diagnosis, there is a tendency to lose the faculty of clinical observation which enabled our predecessors to make an accurate diagnosis in the more common diseases almost with a glance at the patient. Of course, X-rays and the laboratory play an exceedingly important rôle in the medicine of to-day, but let us beware of using them as a substitute for a full clinical observation and examination. It should follow, therefore, that there are no short cuts to diagnosis. After all the lectures, the demonstrations, the clinics, and discussion groups you will still at last have to sit down at the bedside of the patient and become familiar with the intricate workings of disease. For if you reflect what may be the amount of happiness or misery which may flow from a right or wrong interpretation of the

signs and symptoms as they are displayed to you at the bedside, you will readily appreciate the importance of extreme vigilance and perseverance in your work.

William Osler once said that it is good to look back to the olden days and gratefully to recall the men whose labours in the past have made the present possible. It is my intention to take that advice and to tell you something of the history of surgery in the Royal Victoria Hospital and *pari passu* something about the men who have made that history.

Like most good things, the Royal Victoria Hospital had a very humble beginning. It owes its origin to the foundation of a dispensary in the year 1792, when the population of Belfast was barely twenty thousand. Industrial development was, however, taking place, and about this time the first shipbuilding yard and the first iron foundry were opened, but the linen industry had been in existence for several centuries. The first public school and the first theatre had just started and showed that there was also a desire for education and the arts.

The idea of the dispensary and Hospital had originated in the minds of a group of benevolent men whose leader was Dr. James McDonnell. It was first accommodated in rooms lent free of charge by the Belfast Charitable Society. In the prospectus the dispensary was described as being necessary for the relief of sick poor of all descriptions whether strangers or natives, so that they could be supplied with medicines and medical attention. It also offered inoculation of the children of the poor against smallpox and a scheme for the recovery of persons apparently dead from suffocation or drowning. A list of regulations was drawn up, one of which stated that no important operation was to be undertaken without a prior consultation with the physicians unless in cases of emergency—an indication of the dominance of the physician over the surgeon in those days. Another regulation stated that patients, when cured, were required to present a letter of thanks.

The dispensary was opened when the subscriptions had realised £50, but in the early days great difficulty was experienced in getting sufficient funds to meet the demands. Many were the methods used to collect the money, great help was given by the clergymen in preaching charity sermons, and men like the Rev. William Bristow, in spite of public indifference, were inspired with an indomitable zeal to ensure that the institution would not only survive but prosper and grow. The members of the medical staff also worked for the financial benefit and each one acted as a collector in various parts of the city. In spite of all, the funds became exhausted at times and urgent appeals had to be made to the public repeatedly. Looking back, it seems surprising how the Hospital survived this troubled period, but though frequently its struggles for existence were severe, yet none were so great as to entirely extinguish its flame.

In 1797 the dispensary moved to a house in Factory Row—now Berry Street—which had been rented for £20 a year. Six beds were equipped and a nurse appointed, and it was renamed the Belfast Dispensary and Fever Hospital. Two years later it again moved to three houses in West Street, at the corner of Smithfield, and remained in this site for a number of years, where it became consolidated and went from strength to strength, though not without its difficulties.

In 1803, for instance, a special meeting of committee was called and, rather than allow the Hospital to close, each member subscribed five guineas.

It will be noted that, in its earliest days, the bed accommodation of the Hospital was used entirely for fever cases, and it was not until 1807, when, owing to a dearth of such cases, that the medical staff were empowered to admit suitable patients with other diseases. The recurring fever epidemics taxed the resources of the Hospital both as regards accommodation and finance. Indeed, nothing seemed to influence the public mind so much as the dread of fever and the fear of infection, and while they were willing to subscribe towards the isolation and treatment of fever patients, they were not convinced of the necessity for a general hospital. But when one considers that in one epidemic one in four of the population were infected and that in another an average of twenty people died every day for a period of six months, it may be that we would consider them justified in their view.

In 1810, the Hospital having become one of the necessary and established institutions of the town, the idea was formulated of building a new Hospital. The foundation stone was laid in 1815 in Frederick Street, and two years later the Hospital, containing one hundred beds, was opened, having cost £5,000. This resulted in the admission of a wider variety of medical and surgical cases in greater numbers. In 1818 pupils were admitted to the practice of the Hospital and were permitted to attend operations and act as dressers—an innovation which was unique among hospitals of those days, and which added to its popularity as a teaching centre.

In 1826 clinical lectures were established and, very appropriately, the first lecture was given by Dr. James McDonnell. One of the surgeons of this era, Dr. Forcade, had received his surgical training in the army. He had accompanied the Duke of Wellington through the Peninsular campaign and so distinguished himself as to receive the old General's commendation. He thus arrived in Belfast under the most favourable circumstances and quickly won the esteem of his colleagues not only for his past deeds but also for his slick and adept use of the amputation knife, with which he was apparently a master.

During the year 1824 there were 137 surgical cases admitted, which included mainly fractures, wounds, head injuries, ulcers, and cancer, but also a few cases of aneurysm, fistula, hydrocele, hernia, and hare lip. Only 29 of these patients were operated upon—the operations being 16 amputations of limb, 5 of breast, 3 for fistulæ, 2 for hydrocele, and 1 for sarcoma of the uterus.

In 1834 the Royal Colleges of Edinburgh and London recognised the attendance of students in the practice of the Hospital as equivalent to that of any other in the United Kingdom, and in the same year the lectures of Dr. Coffey were recognised by the Royal College of Surgeons of London. In 1835 a medical school was established, the first Professor of Surgery being Dr. John McDonnell; he was followed in the next year by Dr. Ferrar. Dr. Coffey was appointed in 1837 and remained professor for ten years.

Many of the surgeons of this period gained their early experience in one of the services. Mr. David Moore, who served the Hospital for thirty-five years, had been

in the Royal Navy. He and his colleagues were, in 1841, performing excision of joints, especially the knee and elbow, for tuberculous disease. Long stay cases were, however, limited in number, as five times more patients were applying for admission than could be received. At this time the cost of running the Hospital per year was £1,500 and tenpence-halfpenny was sufficient to keep a patient for a day. In 1847 an operating theatre and accident ward were added to the Hospital, bringing the accommodation to 128 beds. Prior to this, operations were performed in a small room on a floor above the surgical wards, which was far from ideal.

In 1847 the anæsthetic qualities of chloroform were discovered by Dr. Simpson of Edinburgh, and two years later it was used in several of the operations carried out at the Royal. The surgeons were cautious at the outset and stated that "while the facts in reference to this great agent were not sufficiently numerous to enable them to recommend or condemn its general use, they should take this opportunity of stating that it requires great caution and considerable experience to render its administration safe." Three years later, however, the annual report states that chloroform was administered with the most gratifying results in alleviating mental dread and physical pain in many hundred cases without accident or evil. It is of interest in passing to record that Sir James Simpson visited Belfast in 1867 and was entertained to dinner by the Ulster Medical Society.

Prior to the use of chloroform, there were no true anæsthetics, though certain drugs were used which dulled the pain and anxiety to some extent, but their use was limited by the fear of giving an overdose. Mandrake or Mandragora was a popular narcotic, as in Shakespeare's Antony and Cleopatra we read :—

> "Give me to drink Mandragora,
> That I might sleep out this great gap of time
> My Antony is away."

The most pleasant of the alternatives to drugs was to make the patient drunk and the most unpleasant to throttle him into insensibility by compression of the carotid vessels. It would appear that the anæsthetic qualities of alcohol were fully appreciated in Belfast as shown by the purchases of the Hospital in one year of 30 gallons brandy, 35 gallons whisky, 7 gallons gin, 64 dozen sherry, 60 dozen port, 1 dozen claret, 80 dozen ale, and 262 dozen porter. But before you think of them as "the good old days" let me read to you the observations of a patient of the times awaiting an operation. He states he felt like a condemned criminal preparing for execution, he counted the days and the hours, he listened for the noise of the surgeon's carriage, for the sound of his foot on the stairs, the clatter of the dreaded instruments. He heard the surgeon's firm, grave words, and then surrendered his liberty, revolting at the necessity of being held and bound, and helplessly gave himself up to the cruel knife. The strain of operating in pre-anæsthetic days was very great on both the patient and the surgeon. It was said of John Hunter that he turned as pale as death when he used the knife. The only way of reducing the strain was to complete the operation in a minimum of time, a requirement which was not always conducive to good surgery. The speed with

which some of the surgeons carried out their work is almost incredible. It was said of one surgeon that he was able to perform the operation of lithotomy—removal of a stone from the bladder—in one minute and that on one occasion he managed it in fifty-four seconds.

In 1854 there was described a case of fatal peritonitis, due to impaction of a concretion in the appendix. Another patient was admitted who complained of pain in the right temporal region. His tongue was thrust to the right side and he had ptosis of the right eye, difficulty in speech and weakness of the left arm. He was diagnosed as suffering from a tumour of the brain, which was later confirmed.

Of the surgeons to the Hospital Dr. Samuel Browne had the unique distinction on retiring of being succeeded by his son, Dr. J. Walton Browne. Samuel Browne specialised in ophthalmic work and he was the founder of the first ophthalmic hospital, and was also partly instrumental in the formation of the Ulster Medical Society by the amalgamation of the Clinical and Pathological and Belfast Medical Societies.

Dr. J. K. Wheeler was a surgeon to the Hospital in Frederick Street. He, like all the surgeons of this era, was also engaged in general practice. His son, J. R. Wheeler, is our present senior ophthalmic and ear, nose and throat surgeon.

In 1865 two new wings were added to the Hospital, increasing the bed accommodation to 186. Ether spray was used for local anæsthesia, and there is recorded that year an operation for depressed fracture of the skull, but the patient died. Experiments were carried out of the medical uses of electricity—and cases of lumbago were cured with it. A specimen was shown of an aneurysm at the junction of the left anterior cerebral and anterior communicating arteries of the circle of Willis, and it was remarked how difficult it would be to make a diagnosis in such a case.

A young surgeon of these times, Dr. William McCormac, was making great strides in the advancement of surgery. He showed cases on whom he had removed half of the tongue and one who had had a portion of the lower jaw excised for cancer. Unfortunately for Belfast, he went to London on his appointment as surgeon to St. Thomas' Hospital, and there became one of the most brilliant exponents of the art of surgery. Dr. Murney, who at that time was one of the senior surgeons, was also a man of gifted talents and with a shrewd brain. He was the first to operate for repair of non-strangulated hernia, and in 1876 he presented a patient on whom he had successfully removed an ovarian cyst. He was congratulated on what was stated to be the first such case in Northern Ireland and probably also the first successful intraperitoneal operation. He also described cases of amputation through the hip joint, skin grafts, and had thought of doing a gastrostomy for œsophageal stricture, but was dissuaded by Dr. John Moore, who had not been impressed by a similar operation carried out in London, as he had afterwards attended the post-mortem.

Professor Gordon was a colleague of Dr. Murney's and was Professor of Surgery for thirty-seven years. He was an original genius, whose great interest was in fractures, especially of the hip and wrist. He was the inventor of many splints,

and it was said of him that he transformed the treatment of fractures from a condition bordering on chaos to one based on a clear and scientific foundation. He left an unrivalled collection of fractures at the Queen's University Museum which remain to this day an enduring monument to his patient research. No less a personage than Sir William Whitla said of him, "A man of rare singleness of purpose and of unfaltering rectitude, whose great originality and practical genius marked an epoch in the progress of his art."

In 1871 the Throne Hospital was built and donated to the Royal for convalescent cases. The surgical admissions had now increased to 858 in the year, of which 400 were accidents. There was an outcry in the town against the smoke nuisance and the furious driving of cabs.

One of Professor Gordon's favourite pupils was Joseph Nelson. In 1861, before Nelson had qualified, the Italian War of Independence broke out and, being fond of adventure, he dropped his studies and joined Garibaldi, and fought with him throughout the campaign. Among his most treasured possessions was a lock of Garibaldi's hair. Garibaldi Nelson, as he became known, went to India after qualifying to take medical charge on some tea estates, and was later joined by a former school friend, John Gordon Coulter. Coulter died shortly after, and Nelson showed his esteem for his friend by raising a fund which was subsequently given to the Hospital and founded the Coulter exhibition. The first mastoid operation Nelson performed was on one of the planters on the tea estate who had developed inflammation of the mastoid cells. Nelson had never seen a mastoid operation, nor had he the proper instruments, but knowing there was pus in the cells and deeming his patient very ill, he opened the cells with a gimlet and enlarged the opening with a carpenter's chisel. The operation was a success and the patient lived. Nelson returned home and was later appointed surgeon to the Belfast Royal Hospital, as it was then known. To his credit belongs the honour of having performed the first successful operation for brain abscess in this country. The case was only recorded at one of the monthly meetings of the Ulster Medical Society and was never published. As a man, he was diffident, and nothing annoyed him more than to see men puffing and advertising themselves. Shortly afterwards cases were published in Edinburgh and in Germany, but Dr. Barr of Glasgow, in his book, gives Nelson the credit of being the first to operate successfully for brain abscess in the British Isles.

Another surgeon of this era, Dr. Henry O'Neill, was a man of many parts, being in turn successful as a surgeon, sheriff, and lawyer. He was the founder and first president of the Belfast Medical Students' Association. A record of his work shows that no sooner had he reached one goal, than he tossed it aside and looked for some new outlet for his energy. He had achieved success as surgeon, gynæcologist, and pathologist when he abandoned them and turned to public health. His true bent was in this field; he insisted on pure milk and food supplies and good housing, and was responsible for the introduction of the inspection of meat intended for human consumption. He did, however, add to the advancement of surgery, and was interested in the treatment of head injuries—he operated on many depressed

fractures of the skull and laid down a very careful prescription for the preparation of the scalp for brain operations. He was the first to wear a white coat in the old Frederick Street Hospital, a custom he introduced following a visit to Germany, and which resulted in his being known as the Baron.

About this time Joseph Lister was Professor of Systematic Surgery in Glasgow. He had made a close study of Pasteur's work and experimented with carbolic acid dressings for compound fractures, finding that with this change in technique the mortality rate was lowered and infection lessened. He sustained great opposition to his theories, and peculiarly one of his strongest opponents was Simpson, the discoverer of chloroform. Lister was always aware of the disadvantages attached to the use of disinfectants and he sometimes tried operating with strictest cleanliness. But Lister had completed the great task he had undertaken, and it was left to those who followed him to replace his school of antiseptic surgery with that of asceptic surgery.

At this most important time Thomas Sinclair was Professor of Surgery in Belfast, and he proved himself equal to the enormity of the situation, not only in the exploring of new fields in surgery and with new techniques, but also in the teaching of students and surgeons. Sinclair entered the profession when the Listerian era had already dawned, and though not a pioneer he was among the first to appreciate the fullness of its benefits to mankind. Like his predecessor, Gordon, he reigned as professor for a long period, and between them they held the chair of surgery for seventy-four years. When Sinclair took over there were two important changes—card-playing in the back seats of the lecture room ceased and not all the lectures included and concluded with a reference to fractures of the lower end of the radius. Sinclair was a fluent and voluble talker and lecturer, and his quiet voice induced at times an unnatural stillness in the lecture room and ward. He made great use of simile in his teaching, as in the following quotation from a talk on intestinal obstruction: "An abdomen the seat of an obstruction is a sort of clinical Afghanistan, very resentful of exploration and very intolerant of the intrusion of a foreign hand. Like the Afghans, the intestines oppose their sulky passivity to any efforts to induce them to act, and if by any chance they relax, it is only to run to violent extremes in a turbulent frenzy. They appear to be aware that they constitute a buffer state between medicine and surgery, on the frontier of which the physicians hold on with dogged English perseverance, while the surgeons, with ill-restrained Russian ferocity, hover around the opposite margin with a desire to invade, but with a disinclination to accept the responsibility attaching to annexation."

Of purulent peritonitis he said the early incision, lavage, and drainage of the abdomen by surgical intervention afforded the only chance of saving one in a thousand of these unpromising cases. Among surgical innovations he removed the superior maxilla for sarcoma, he did an abdominal nephrectomy and ligatured the innominate artery for aneurysm. He gave an amusing account of the treatment of intestinal obstruction by taxis. "A full anæsthetic is necessary to obliterate all muscular resistance. Next the surgeon will forcibly and repeatedly knead the

abdomen, pressing its contents vigorously up and down and side to side. The patient is turned on his abdomen and in this position held up by four strong men and shaken backwards and forwards. This done, the trunk is to be held feet uppermost and shaking again practised up and down. Finally, in this inverted position, copious enemeta are given—the whole procedure being carried out in a *bona fide* and energetic manner."

In July, 1903, the Royal Victoria Hospital was opened on the present site. The new Hospital represented a great advance in design and had cost £100,000, its inception being largely due to two great benefactors—Lord and Lady Pirrie. The transfer of patients took place on 17th September, 1903, and it was arranged that Mr. Walton Browne should perform the first operation, but on the night preceding a strangulated hernia was admitted and operated on by Robert Campbell. The popularity and the necessity for the new Hospital was shown in the figures for 1904—2,500 admissions and 25,000 extern attendances. That popularity and necessity have kept increasing, as the figures for last year show 18,000 admissions and over half a million outpatient attendances.

Although the first successful abdominal operation was performed in the Royal in 1876, little progress was made for some years, and so we find that in 1893 there were only two abdominal operations, both of whom died. But from this time onward advance was rapid; in 1903 there were thirty-nine intraperitoneal operations with a mortality of thirteen. The scope of surgery was enlarging at a tremendous pace and the operations were of a wide variety—removal of appendix, gall bladder, kidney, prostate and rectum, suture of nerves and tendons, thoracoplasty, and those dealing with obstruction of the intestine and of the bile ducts were all operations that were being frequently performed.

At this time Professor Sinclair's colleagues on the surgical staff, apart from Walton Browne, were A. B. Mitchell and T. S. Kirk, and the two assistant surgeons, Robert Campbell and Andrew Fullerton, and these were the men who were pioneering the new surgical operations and the new techniques, and who were laying the foundations of surgery in the Royal on a firm and sound basis, and it behoves us to look back on them with pride and gratitude.

Mitchell was a man intensely interested in the surgery of the abdomen and especially the stomach; his work and writings on peptic ulcer were voluminous. As a fracture was to Gordon and the prostate to Fullerton, so the peptic ulcer was to Mitchell. He followed the teachings and technique of Moyinhan closely and was outstandingly successful. Though peptic ulceration was his forte—no operation being done at the time was outside his repertoire.

Thomas Sinclair Kirk had a dominating personality and was a man with many original ideas, and if some of them did not meet with general acceptance, his enthusiasm for them was undimmed. He was treating compound fractures with the closed plaster technique before Truetta, who was considered by many to be the pioneer in this teaching. He had a great belief in sera and went so far as to collect serum from animals killed in the abattoir. This serum was given routinely to all patients under his care—even the house surgeon and the pupil did not escape. He

treated tuberculous spines with abscess formation and paraplegia by costo-transversectomy—a procedure which was then frowned upon but later became the accepted method. He was the first to remove a cancerous stomach. As a resident medical officer, he discovered an outlet for his surgical tastes in Professor Byers' little operating room, and there he introduced, for the first time, the boiling of instruments before operation—a practice which was scoffed at by Walton Browne, who still had a habit of holding the handle of the scalpel between his teeth.

Two of the men taught by Sinclair were Robert Campbell and Andrew Fullerton, and it would be difficult for any man to have had two more distinguished pupils.

Robert Campbell was a man whose work was characterised by great care, skill, and originality, and by what has been described as a restrained and discriminating boldness. He was among the first to use rubber gloves and certainly introduced them to Belfast. As early as 1898 he was operating for perforated typhoid ulcer, a condition up to then regarded as hopeless. In 1910 he distinguished between acute infective appendicitis and acute appendicular obstruction, and stressed the differences in the pathology, clinical course, and dangers—a fact which was re-discovered by some London surgeons a few years later. His operation for congenital hernia in infants was unique and, while high surgical authority elsewhere was laying down rules as to age and other limitations, he was performing them in a steady stream, regardless of such restrictions and with convincing success. His work on the operation of thyroidectomy was also characterised by the same fullness and good results. He spoke with a clearness, brevity, and discernment that said only what was necessary. At times he was the most silent of men, but he had the rare combination of a good brain, practical commonsense, and well-trained hands. His interests in surgery were widespread and his professional attainments were many. He was using catgut, which was boiled and hardened in formalin some three years before it was generally advocated. He introduced the use of caps and masks. He was a man of rugged honesty and directness of purpose, and had the faculty of brushing aside all irrelevant and non-essential material and coming with precision to a logical conclusion.

His colleague, Andrew Fullerton, was one of the most colourful surgeons of the Royal of any era—he made a name and reputation not only in Belfast and Ireland but also in England. He was intensely proud of his hospital and to it he brought fame and renown. To many of us who were his students he was an idol and hero, and it is a cause for regret that his only memorial is the record of his great work. He was an effervescent man, small in stature, but great in heart and in knowledge. His interests transcended surgery and he loved it with an unbounded enthusiasm. His writings were voluminous on all manner of surgical topics. During the 1914-18 war he produced a pneumatic tourniquet for the control of hæmorrhage in wounds of the limbs and devised a method for the direct transfusion of blood, for though the first blood transfusion was carried out in 1818 it was not until the early months of 1917 that the citrate method of transfusion was sufficiently developed for use on a large scale. He excised the joint surfaces in septic knee wounds and so avoided amputation in many cases. His main interest, however, was in genito-urinary

surgery, and in this branch he was one of the foremost consultants in the United Kingdom. He was the first to realise the presence and significance of unilateral diuresis, now unfortunately more or less forgotten. His researches into the diagnosis and treatment of enlargement of the prostate and papilloma of the renal pelvis will be well remembered by those who attended his classes and the meetings of the Ulster Medical Society. There is no doubt that the prostate was his favourite hunting-ground, but no disease or abnormality of the genito-urinary system escaped his energetic attention. In 1920 he was elected President of the Royal College of Surgeons in Ireland, and in 1922 he was elected an honorary fellow of the American College of Surgeons. These distinctions were a fitting recognition of his eminence as a surgeon and his fame as a urologist.

In more recent times there have been many other great men. I should like to mention briefly Professor C. G. Lowry—one of the greatest surgeons in the history of the Royal. He was a man whose enthusiasm, meticulous care, foresight, and dogged courage was responsible for great advances in midwifery and gynæcology and who, by the example of his thoroughness and technique, had a marked effect on the development of general surgery. Time does not permit an evaluation of the work of others, but one cannot omit mention of G. R. B. Purce, the pioneer in surgery of the chest, Howard Stevenson, who contributed a great amount to the surgery of the gall bladder, and Sir Robert J. Johnstone, for advances in the field of gynæcology; and finally the members of our Consulting Surgical Staff—S. T. Irwin, P. T. Crymble, R. J. McConnell, and H. P. Malcolm. It would not be possible to overestimate the great work they have done towards the advancement of surgery in this school. We all, and especially those of us who were taught by them, owe them a great debt of gratitude, which we can only attempt to repay by trying, however inadequately, to follow in their footsteps. They are still members of the consulting staff and the wisdom of their experience and knowledge is still available to us, and I am sure we all hope will be for many years to come.

It is a remarkable tribute to the teachers and investigators of those earlier days that, by their great earnestness, high probity, and splendid personal characteristics, they were able to maintain the standing of the profession upon so high a plane with a foundation so feeble, and to hand on to us, followers along the paths outlined by them, so great and glorious a legacy. So, in conclusion, I wish you a genuine success in the career of your choice—not judged by commercial standards, but by the ideals which have ever been held by the long line of worthy men of medicine who have preceded you.

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# Students and Teachers

*By* Robert Marshall, M.D., F.R.C.P., F.R.C P.I., D.P.H.

*Presidential Address, Northern Ireland Branch British Medical Association*

"Arthur does not seem to have been brilliant at school, and at one time it seemed likely that he would spend his life working on the farm, but after he had started as a medical student his powers developed quickly." These words are taken from the appreciation of Sir Arthur Keith, written by Dr. Maurice Campbell in a recent number of the British Heart Journal. The reason why I quote them here at the beginning of this paper is that they seem to strike a familiar note. How often has it been written of someone who achieved deserved fame in later life that he was not brilliant at school? And this leads us at once to the unsolved problem of how best to choose from the swarming applicants those who are the most likely to become good doctors. You will have noted that it was after Arthur Keith started as a medical student that his powers developed quickly. I like Dr. Maurice Campbell's instinctive choice of the word "powers," for it reminds me of the motto of the University of Bristol, which gives in three short words the true function of a university: VIM PROMOVET INSITAM. "It enhances the inherent power." In the selection of students, therefore, the first requirement appears to be to discover whether there is an inherent power already present and awaiting development. Here in Northern Ireland the problem has, at any rate until now, been less acute than in some other places. I am informed that the Medical School here can cope with the numbers of boys and girls of the school-leaving age who have been able to negotiate one or other of the academic hurdles which represent the entrance gate to the University, and also to find room for a few suitable candidates from elsewhere who have associations with Queen's and with Ulster, together with a small number of students coming from more distant parts of the Commonwealth who are recommended by the Colonial Office. Entrance to universities in general, and to the Queen's University in particular, does not become any easier as the years pass, and it will soon be required of the entrant that he will present his Senior Certificate decorated with two passes at advanced level. Much has been written, and much more will be written, about the scholastic education of the would-be medical student. Some urge the importance of a broadly-based education, preferably on the foundation stones of Latin and Greek, and that this is more important than a smattering of physics and chemistry with the somewhat limited biology which can be taught in schools. Others feel that the later school years should be devoted mainly to scientific subjects, and would even grant exemption to the time-honoured first medical examination in botany, zoology, chemistry, and physics to those who have attained a sufficiently high standard at school. In his delightful book, "Medical Students and the Medical Sciences,"

Dr. D. C. Sinclair says that: "Several attempts have been made to define the characteristics of the ideal medical student, attempts which have often ended in an atmosphere of unreality. Such a creature is a chimera, half man, half god." He goes on to quote Professor Samson Wright: "We all know the ideal student, tall, handsome, of great personal integrity, beautiful manner, cultured, highly intelligent, a tireless worker, good with his hands, skilful in exposition, a good mixer, athletic, devoting his spare time to extra-mural activities, with a good family background, and so on and so forth." Sinclair adds: "None of us has seen such a man, yet the selection committees persist in trying to admit him."

A great deal of attention has been paid to this subject in America, and one of the most interesting comments is that of Dr. A. E. Severinghaus, whose Admission Committee in New York has admitted 1,600 of 25,000 applicants: "It is relatively simple to outline the qualifications which an applicant for medical school should have, but it is difficult to devise ways and means whereby we discover the presence or absence of some of these qualities. It is even more difficult to describe for someone else how we attempt to discover them. Let me illustrate. I look for a quality which, for want of a better term, I call 'warmth.' I feel reasonably certain that I can discover it when it is present or detect its absence. But I would feel wholly unequal to trying to say how I arrive at a decision in the matter." When I read this I wondered whether Severinghaus had not been thinking of Hippocrates' old familiar words: "Where there is love of humanity there is love of the art."

In his educational number last year the Editor of the British Medical Journal was perhaps a little sententious, but he was very near the mark when he said: "It matters little what pattern of specialised pre-medical training the applicant has received, provided he has been truly educated and has the ability to think for himself, nor should it matter too much whether he possesses all the ideal personality traits, so long as he has a real sense of vocation and aims at professional achievement and not financial gain or social security." One might perhaps ask, "Who can define true education?" and whether there is not, perhaps, too selfish a note in "professional achievement." The Editor is right, however, in stating that the pattern matters little. It is probably advisable that the medical student should know some Latin, and it would be nice if he could know some Greek. A modern language is required by the authorities, but they wisely decline to specify which one. Many medical journals are now so mathematical as to be far beyond the ken of those who, like myself, are tone-deaf to mathematics. The recent wave of biochemistry which has engulfed the wards makes one realise that our acolyte must bring with him a sounder knowldege of chemistry than I had when I was a young fellow. The number of subjects which have been suggested does not lessen; the Editor of the Journal of the American Medical Association suggests that English composition, psychology, and physiology should find a place in pre-medical training as fully as physics, mathematics, and chemistry.

There are places in the temple of Æsculapius for servants with many and diverse gifts. As Sinclair has put it rather neatly, "The student can become a malariologist, a statistician, a pædiatrician or a biologist, a surgeon or a journalist."

For my own part, I believe that it is fair to demand from the pre-medical entrant a reasonable standard of general education, comparable with that demanded for admission to any other learned profession, and I think that the first year in medicine should remain much as it formerly was: physics, chemistry, and biology, but taught in a special way. I feel that if these subjects were taught as expositions of scientific methods, without the imposition of so many inessential facts, there would be ample time for the student to continue his general education. In Trinity College, Dublin, he takes a degree in Arts during his pre-clinical years, thus maintaining and improving his knowledge of English, of a modern language, and some other subject such as logic, economics, or public administration, as may be most congenial to him. At this stage he might be given some elementary instruction in the compilation and interpretation of statistics; and he might even be shown a slide-rule and told what can be done with it. On a lower plane, he might learn shorthand or preferably typewriting. There is, however, the danger that we forget that even medical students have been known to find things out for themselves, though some people seem to think that students never learn anything except in an organised course of instruction, preferably given by a specialist in that subject.

With the wider *concepts* of scientific processes there must be interwoven the collection of *percepts*. It is not enough that the student should learn from what others have *conceived* as the result of what they in turn have laboriously learnt to *perceive*. He must himself retread some at least of the steps of the journey. He must see things for himself, collecting percepts, in order that he may appreciate the significance of concepts. Sir Richard Livingstone has placed on record his own experience in these words: "I can see no use in being taught, as I was, the elements of chemistry and physics, without ever having an idea of their meaning and use, or any conception of the fascinating truth that you can transform things by analysing them into their constituent elements." If, by some juggling with a time-machine, we could have allowed young Livingstone to listen to the six lectures given to first-year medical students this year by his successor, Dr. Eric Ashby, the world might have unwittingly exchanged a distinguished scholar for an equally distinguished scientist.

Much is written nowadays about mental or academic disciplines, by which I suppose is meant bringing up the mind in the way it should go, so that when it is old it will not depart from it. It may be a discipline to the nose to dissect a dogfish in a laboratory with roof windows on a summer afternoon, but it is not truly a mental discipline if one does it merely to be able to score 50 per cent. in zoology. And, speaking of zoology, how well I remember the emphasis with which our own dear Professor deplored that "year after year he had the utmost difficulty in getting students to remember that the leech had seventeen pairs of segmental nephridia." Looking back over forty-eight years, I now realise how right they were to decline to burden their memories with so sterile a statistic. *Now* I find it hard to remember what a nephridium looked like, but I cannot forget that the leech had seventeen pairs of them. I also remember with gratitude and affection Professor Gregg

Wilson's infectious enthusiasm and his love, not only of the dead leeches on the benches, but of the acolyte "leeches" who dissected them.

During the past few years many pious thoughts have been expressed about the lightening of the present medical curriculum, which, as Sir Henry Cohen says: "Too often merits the phrase which Cromwell used of the laws of England: 'a tortuous, ungodly jungle.'" It is sometimes difficult to see what practical steps have yet been taken to lighten the curriculum in these days of ever-widening knowledge and ever-increasing specialisation. I think that the time has come when medicine should be regarded as an integrated system rather than a haphazard concatenation of diverse subjects. Some valuable suggestions have been made to this end, and to my mind one of the most valuable is that outlined by Professor O'Meara of Dublin, whose paper, published in the *Lancet* of 22nd January, I would commend to you. He considers that the first-year medical student should be taught chemistry from a more definitely medical point of view, and expresses the need for a clearly defined course "on which a standard textbook should be written. The textbook would be like no existing textbook in chemistry. . . . It would give in simple terms the more important points in chemical theory, followed by a special treatment of inorganic chemistry based upon the periodic table. Thence it would proceed to organic chemistry, . . . presenting the student with a consecutive and logical exposition of the subject. . . . The book would be further embellished by a section on elementary physical chemistry in relation to medicine. A similar pattern is suggested for physics, on which subject attention could be focused from a medical point of view." If Professor O'Meara's ideas are to be implemented, it would mean, I think, that first-year medical students would have an almost completely separate course from that set for science students, not only in physics and in chemistry, but in biology as well. A similar suggestion with regard to physics is made by Professor H. C. Burger of Utrecht, who suggests "that pure physics must be taught at school, and on this groundwork a course of medical physics at the university must be based. The teacher must be a research worker in medical physics in close relation with the medical world, and his teaching must extend throughout the whole study from beginning to end." Similarly, first-year chemistry would be part of a harmonious whole, and not separated from the bio-chemistry of pre-clinical years or the collaboration of the bio-chemical investigations carried out in the hospital at the request of the clinicians. Professor W. W. Westerfield has expressed one aspect of the matter clearly when he said that "the greatest weakness in bio-chemical training for the medical student to-day lies in the area of tying together the clinical problems with the applicable fundamentals of bio-chemistry. This is due in part to the fact that many really good clinical teachers do not know enough bio-chemistry to feel at ease in talking about it before a group of students whose exposure has been more recent." A parallel suggestion to that of Dr. O'Meara is made by Professor Zuckerman, the anatomist, and Professor Golding, the physiologist, of the University of Birmingham, who urge the re-integration of anatomy and physiology, and I understand that this policy is already in use in Birmingham with excellent results.

Integration at the clinical stage of the student's career has already begun, and, I believe, successfully begun, in our own medical school. One primary difficulty has been to determine the length and the content of the introductory clinical course. This is intended to be the bridge over which the student may be said to pass from science to medicine. If Dr. O'Meara is right, and I believe he is, he should carry his medical science with him all the way. The General Medical Council suggests that this introductory clinical course may be completed in three months, and that its aims are (1) to help students in their adjustment to new conditions of work and study; (2) to show them the relation to clinical studies of their earlier study of the human body; (3) to encourage them to carry methods of scientific thought and criticism into clinical work; and (4) to assist them to acquire without loss of time the ability to observe and to interpret the physical signs of disease. Following this introductory course, the combined clinical courses, instituted here in 1950, are a logical step in this process of integration. Pathology is taught pari passu with medicine, surgery, and obstetrics, and, as Professor Biggart emphasised, pathology is now recognised as literally the science of disease, not merely as morbid anatomy or the manifestations of past disease in bodies already dead. By this method students are taught about diseases as they are seen by the pathologist, the physician, the surgeon. Perhaps the best example is that of heart disease, where the pædiatrician, the bacteriologist, the pathologist, the cardiologist, the thoracic surgeon, and the obstetrician have each so much to say; but the principle is of increasingly wide application, and I do think it should help the student, especially if the teachers collaborate beforehand to avoid needless repetition—or contradiction. This integrating policy is to my mind the ideal one in reshaping the curriculum, and the focal point of integration must be the patient surrounded by his family. "Hoc noscomium ægrotis et arti medicæ sacrum." Not only the hospital, but the whole faculty or brotherhood of medicine must put the sick man first, and the art—or science—of medicine is only a means to that end. It is interesting and encouraging to see the growth of the concept known as Social Medicine. When I was a junior student we were taught "Sanitary Science." Later the name was changed to "Hygiene," and now metamorphosis has created "Social Medicine." This is a most welcome development, but I cannot help feeling that a department of social medicine must not be regarded as just another speciality, but as part of the *integrated* art and science of medicine. The individual care of the patient and of his family is the primary concern of the clinician, and cannot be completely relegated to the department of social medicine or its energetic and helpful allies, the almoners. I am glad, however, that the General Medical Council does not make any recommendation for the inclusion of social medicine as a pre-clinical subject, and I am also glad that the professional examination in this subject is not to be taken at the same time as the major subjects of the already overloaded Final.

Almost as a parallel to the increasing importance of social medicine is the increasing stress laid upon psychology, and I deprecate the suggestion that this, too, should be a pre-clinical subject. As Sir Geoffrey Jefferson has put it: "Although it is important that the doctor should know his patients, I am not in favour of the

student practising his immature psychiatry on them all. There are few good and helpful psychiatrists under 50 years of age, and I would not be surprised if they were best at 60 or 70. It takes us about fifty years to find out what sort of men we are ourselves. I have heard it said that in some medical schools the emphasis is on psychiatry and bio-chemistry, these being regarded as the golden keys to knowledge. Human nature and its ills are not so easily resolved into two components; if a patient's bio-chemistry is normal and he is not mad, he may still have a bad cold or an early cancer."

There has been much debate of recent years about the position of pædiatrics in the medical curriculum. In some medical schools it looms almost as large in the final examination as medicine itself. My own view of the matter is exactly expressed by Professor Alan Moncrieff: "Now that as a subject it has a sure place, I doubt if the final examination need include pædiatrics. It would be a slightly less onerous burden, and students might retain a faintly higher regard for it. . . . If pædiatrics is still to be included I favour its inclusion in a general way with the internal medicine examination, with a question or so in the paper, and the help of pædiatricians in the final examination. They should, however, examine as general physicians, and not in too specialised a capacity." This exactly describes the position in Belfast.

With this necessarily brief review of some recent developments, I think it will be agreed that the Belfast Medical School is imbued with a modern and progressive spirit. Changes are not always for the best, and many changes made in recent years still give rise to misgivings. As it says in the Preface to the Book of Common Prayer, written in 1662: "For as on the one side common experience sheweth that where change hath been made of things advisedly established, no evident necessity so requiring, sundry inconveniences have thereupon ensued; and those many times more, and greater than the evils that were intended to be remedied by such change." Is it possible that our recent enactments will wear as well in the next three hundred years as the Book of Common Prayer has for the past three hundred?

It must not be forgotten that, in recent years, English and Scottish schools are beginning to realise that the most important part of students' training is the resident pupilship, which with us is even older than the medical school or the university, having been begun in 1820.

Personally, I regret that the modern tendency is to cater for only one month's residence in a medical and in a surgical ward. These periods are too short, not only because these are the two great subjects, but because in four weeks the pupil will not be able to follow the course of any but the shortest illness of his patients. I suggest that during his pupilship the student should be given a short course of instruction in ordinary nursing procedures, and in certain first-aid techniques, notably resuscitation measures. Also, I suggest that the pupil should be invited to make the ward where he does his first pupilship his hospital base for his whole undergraduate clinical course, coming back to it as frequently as he can, daily if possible, to make it, if I may borrow a musical simile, the "continuo" or the basic

theme in the strange clinical opera. I am glad to think that many students do this spontaneously if not by invitation. The real difficulty of the student is expressed very well in the Fifty-fourth Annual Report on Medical Education in U.S.A. and Canada. "Students have been assigned to a few weeks in medicine, similar periods in surgery, pædiatrics, obstetrics, and gynæcology. Then, in rapid succession, assignments carry the student through such specialties as clinical pathology, dermatology, neurology, psychiatry, ophthalmology, otology, orthopædics, urology, and so on. Such a kaleidoscopic experience has lacked continuity of patient care throughout even a single illness, and makes it difficult to develop the sense of responsibility for the patient as a person, which is one of the major objectives in medical education."

The student of to-day has many privileges unknown in the lifetime of many of us. The great Institutes of Pathology and of Clinical Science provide a "domus medica" comparable with any in the world, and students are quick to make use of the advantage of having the medical library housed therein. Another tremendous advance has been made in the creation of the Student Health Service under the care of Dr. Wilson Johnston. This, too, is favourably comparable with anything of its kind. The men's hostel has been enlarged and students' lodgings are inspected, approved, and catalogued with many statistical data. There is a plan for a new Students' Union to replace the overcrowded one. Again the provision of good playing fields at Cherryvale and of the Rowing Club on the Lagan has come about within recent years, and the Officers' Training Corps and the University Air Squadron provide a form of recreation invaluable in the event of war and educative in peace. Last, but by no means least, the Deans of Residences of the various religious denominations are much more alive than their predecessors of forty years ago. Before we leave our students we must ask ourselves, "What are we educating them to be?" I am afraid that it is no longer possible to say that we are educating them to be good general practitioners, partly because their teachers know little or nothing of general practice, and partly because it has become a special form of practice which must be founded on general basic principles and appropriate post-graduate study. The B.M.A. Curriculum Committee has expressed the view that "The undergraduate medical course should be primarily concerned with the training in those basic principles of medicine which are the necessary foundation for all forms of medical practice." But the question implies something more than this : Are we to train them to take their place as members of an ancient, honourable, and learned profession, as citizens bearing with grace, dignity, and courage grave and important responsibilities in peace and war, or shall we, in our own time, surrender this independence of medicine so fully that we must regard the doctors of the future as little better than R.A.F. police-dogs, obeying with tail-wagging docility the curt demands of their administrative handlers? This question may be regarded as a sombre and a cynical one, but I would remind you that there are persons who would like to see doctors displaced from all boards or committees administering not only hospital but family practice, and I trust that

we will never give in to such degradation. It is our obvious duty to our fellow-citizens to see that their medicine is administered by doctors, and it is our duty to preserve for our successors what freedom is left to us.

The title of this paper was "Students and Teachers," and I have left myself but little time to discuss the latter part. If Dr. Severinghaus is right, that he seeks for the quality of warmth in the pupil, what qualities should be looked for in his teachers? I suggest that they are three in number: vitality, veracity, and variety. The first is essential. The teacher must obviously be alive, and must convey this living quality to his subject. Academic automatism merges into rigor mortis. You have heard of the dream of the professor? He dreamt he was lecturing to his class. He woke up, and he was lecturing to his class. (This is an American story, so I suppose he was an American professor.) How different is such a one from Noah Morris's celebrated description: "When a clinical lecturer has finished giving a clinical lecture to a class of students, he should be in a state of mental exhilaration and physical exhaustion." Partly for the sake of alliteration I have used the term veracity, but it must include sincerity. In medicine the teacher cannot be sure that, like the theologian, he is preaching the eternal verities, because in medicine the verities have a trick of changing, but he must try to tell the truth as he sees it. It has been debated whether there is such a character as the born teacher, and certainly some people can present their ideas more clearly, logically, and forcibly than others. I once said to Professor Biggart that teaching is like throwing mud, that some of it sticks, and that some teachers can make their mud stickier than others. He agreed, but said that he liked to rub their faces in it!

In a multitude of counsellors there is wisdom. We, in our time, were blessed by the logic of Lindsay, the Scottish thoroughness of the Milroys, the sturdiness of Symington, the scintillation of Symmers, the fearlessness of Fullerton, the dramatic quality of Whitla, to mention but a few of the great ones. We may remember but little of what they said, but we treasure the memory of what they were, for students see their teachers with a penetrating gaze. With the naïve assurance of youth we knew them, and their brightness is not tarnished by our present certainty that they were not always right in what they taught us or in their methods of teaching.

Most people agree that the medical schools of the United Kingdom must retain their own traditions and characteristics. We like to think that we have done so here, and one of our characteristics is that in the past we always welcomed teachers from other schools, absorbing them into our own substance and gaining strength from them. At present eleven of our fifteen professors who teach medical students come from other schools. It would be dreadful if all, especially clinical teachers, were stamped in the same mould, or even in too similar moulds from different mints. In a delightful article on Showmanship in Medical Teaching, Dr. Walter Freeman writes: "Like an actor, the successful teacher develops certain idiosyncrasies that set him apart from his colleagues. He may affect loud ties or a carnation in his buttonhole, or even grow a beard. An old rattle-trap of a car may be just as ostentatious as a super-duper."

There are many pitfalls which beset us when we try to teach, and some of us discover them too late to cure them. If only our wives could be invisibly present—they are so much more candid than registrars or housemen. Looking back on my own efforts, I now realise so many faults that I blush to think of them. One of the worst was to try to tell students too much! I was so worried lest I should leave some important point unmentioned—as if the creatures would never hear another lecture on that same theme, God help them!

I have no time to discuss the various aids to teaching, but I would say that clear, audible speech is the first requisite. I doubt whether a multiplicity of lantern slides is an advantage. The exposure of the student to too many auditory and visual stimuli in rapid succession is frequently the cause of mental dyspepsia. Lantern slides of written matter should contain so few words and so clearly displayed as to be readily visible from the back rows. The cinema film should be an occasional treat, rather than a daily habit. I am old-fashioned enough to believe that lectures are useful, but they should not be merely classes in dictation. I think the best method is to provide a typed synopsis for each student, preferably typed on one side of the page only, leaving the other side for his own annotations, or for doodles, or simple games such as noughts and crosses.

Much has been written about the selection of students: too little has been done about the selection of teachers. At selection committees for posts in teaching hospitals foggy questions are asked about the number of babies the candidate has, and how many papers he has published, and whether he would rather play golf or go fishing, as if procreation, publication, and putting were the principal prodromata of promotion. For teaching hospital appointments the candidate's aptitude or gift for sharing his knowledge should be a very important criterion, though not the most important one.

I have certain views on the examination—especially the final examination—of medical students, which may be briefly expressed in the following "creed":—

I BELIEVE—

That the Recommendations of the General Medical Council are acceptable, and that they are closely followed in our own Medical School;

That examination papers should follow the time-honoured pattern, and that the introduction of the American voting-paper kind is not necessary or advantageous;

That the answer to each written question should be corrected by the examiner who set it. (This is the case in Belfast.);

That marks should be awarded out of the full quota of marks allotted for each portion of the examination, i.e., if an examiner feels that a candidate has answered a question as well as a student could possibly be expected to answer it, he should not hesitate to mark that answer 100 per cent., disregarding any mark already allotted for any other question;

That the system of "close marking," i.e., giving a mark only a little above the basic requirement, is not desirable, especially in university examinations. (It is only applicable in "pass or fail" examinations, e.g., for Membership or Fellowship, and even in these it may be misleading.);

That examiners should remember that their function is not only the elimination of those unfit to pass, but that it is of almost equal importance to recognise the student who is better than his fellows;

That every oral examiner should actively remind himself that his candidate is expected to carry in his mind many thousand facts and immediately to produce any of these on demand;

That marks should be allotted having regard to the possible award of 1st or of 2nd class honours;

That out of every one hundred students there are likely to be about five who are worthy of honours—if the examiners know their job well enough to recognise them;

That an honours degree may well be of the utmost importance in a young doctor's career, and a stimulus to further effort to excel;

And, finally, I believe that Dr. Herbert Morley Fletcher was sincere when he said that the Queen's M.B. examination was the best organised "final" in the United Kingdom, and, for my own part, I do not know of a better or a fairer one.

Sir Henry Dale once said: "I am only too well aware that this tendency to reminiscence and prediction . . . is apt to become a tiresome addiction, a disease of occupation, or perhaps I ought to say, of retirement, in those who have entered life's later years."

I began this paper with a quotation from Dr. Maurice Campbell's appreciation of Sir Arthur Keith. I should like to end it with another quotation from it, but in this case the words are those of Sir John Parkinson about his old friend, Sir Arthur: ". . . As a teacher he was persuasive, rather than didactic, and his contact with us was personal, indeed, fatherly. He won you to learning anatomy, in that he never seemed to deal out information, but rather to accompany you in the search for an understanding of it."

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# The Use and Abuse of Transfusion

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The premises implicit in the title I have chosen are a critical examination of the rational indications for transfusion and of the factors which govern the proper choice of fluids and technique, as well as an appreciation of the risks. Abuse will then be self-evident whenever any of the principles are contravened or neglected, or when unwarranted risks are run.

In general, the rationale for transfusion is either to restore the volume of the circulation or to contribute some deficient or missing element. It is as well, therefore, always briefly to catechise oneself as to the purpose of a transfusion, since this clears the air for the choice of fluid and, according to the condition of the patient, may also determine the amount to be given, as well as of the rate of administration.

There is also a considerable difference in the principles which govern the emergency transfusion that has to be carried out in times of stress, accident or war, and the deliberate therapeutic prescription which is carried out for many medical conditions after all precautions have been taken and criteria satisfied.

In these days transfusion is no longer delayed until the terminal phases of an illness, when its effect can only be that of a tonic for the morale of the relatives, thereby conveniently filling the awkward gap between the respective visits of the priest and the undertaker.

## Injury: Blood and Plasma Loss.

Restoration of the volume of the circulation is urgently required whenever the volume has been suddenly and seriously depleted, as with an acute major hæmorrhage, or, less rapidly, with wound and burn shock. Both causes usually operate in the injured. In the case of acute hæmorrhage the loss of blood implies a sudden loss of water, of salts, of proteins and of cells; in wound and burn shock the loss into the damaged tissue is the same, save that there is no significant loss of cells.

In each case the prime requirement is the restoration of volume with a fluid which will remain in the circulation, thereby ensuring that the heart is adequately filled and so able to contract with a force sufficient to ensure a proper output. This simple mechanical rectification enables the best use to be made of such oxygen-carrying capacity in the form of cells as remain in the circulation after the hæmorrhage.

This is an emergency life-saving measure even though the blood-volume is not immediately restored with the most rational of all fluids, namely, blood itself. Thus, with the acute hæmorrhage of trauma or accident the blood volume may be restored, when blood is not available or must be delayed, with plasma, serum or the carbohydrate colloid known as dextran. Crystalloid solutions, such as saline, have only a fleeting effect, since they are soon lost from the circulation into the extravascular space, producing, ultimately, an œdematous patient with a reduced blood volume. The primary indication for the use of such crystalloid solutions is a state of dehydration, in which case they may be life-saving.

Admitting then that blood restoration is the first requirement in cases of serious hæmorrhage, with or without injury, it is nevertheless also recognized that if operative interference is required, the chances of survival are greatly enhanced if the hæmoglobin is not below 60 per cent. This can be accomplished ideally by transfusing, in the first instance, with blood, either fresh or stored, or by supplementing a non-oxygen carrying transfusion with a subsequent administration of packed red cells when these are available.

It is appropriate to mention here that stored blood, in fact, finds its best use in supplying the deficient oxygen-carrying power associated with acute blood loss, and that, for all practical purposes in this respect, blood which has been cleanly and properly taken, promptly and efficiently refrigerated and stored at an appropriate temperature (4°-6° C.) is as efficient as fresh blood for storage periods of 14-21 days.

On the other hand, there is a great deal of loose-thinking as to the virtues of stored blood, which is almost always—at least partially, if not completely—deficient in the more ephemeral elements which it is so often desired to transfuse in medical cases, more especially in the blood dyscrasias and the hæmorrhagic states.

There can be little doubt that the facilities of the blood bank have tended to lead to the overuse of stored blood, so that convenience has come to overweigh the therapeutic ideal.

With burns the reduction in blood volume is due to the loss of plasma into the injured tissue. Obviously, therefore, the ideal replacement of plasma loss is by plasma itself, or by so-called plasma expanders, such as dextran, but when these are not available, then, within reason, the transfusion of stored blood does not appear to give rise to the embarrassing plethora which theory would suggest should follow.

If these be the general principles governing the transfusion of the injured, as well as the choice of fluid for different types of injuries, there are, nevertheless, certain points of detail, largely learned as the result of war experience, which may make the difference between life and death in certain cases.

Transfusion is usually required in all types of serious injury, but it is not a panacea, and should never be pursued to the neglect of either proper first-aid, such as the ensuring of hæmostasis, or properly-timed surgery. There are, in fact, two hazards which operate in the case of the injured—blood loss and tissue damage. The latter may be almost as important as the former. If the tissue damage is great, the

response to transfusion may be neither complete nor sustained and, indeed, the optimum response may endure for no more than a fleeting moment. In such circumstances, surgery should not be delayed in the hope of obtaining a better response, though transfusion should continue during the course of an operation that is performed.

Nearly all those who are seriously exsanguinated require a transfusion of large volume and at rapid rate, at least so far as the first two or three pints are concerned. With certain types of injury transfusion may be ineffective. With all types considerable clinical judgment is required, whilst with some the procedure may indeed be contraindicated. For example, with injuries to the brain or central nervous system the response may be poor; with thoracic injuries great caution is required, whilst if the clinical signs of fat embolism (inexplainable pulmonary or cerebral symptoms) arise when transfusing cases of bony injury, it is dangerous to continue the administration. Myocardial failure, coronary occlusion, hæmopericardium and pulmonary embolism are other examples of cases which should not be transfused or of complications requiring the cessation of the transfusion.

Many aspects of the highly individual problem of transfusion in the injured are discussed in a fairly recent number of the British Medical Bulletin, which is devoted to the subject of the "Reaction to Injury." Therein may be found consideration of such all-important factors as choice of fluid, volume and rate, indications for and against the procedure, and the different treatment of injuries due to trauma, crush, and blast.

Suffice it here to summarize the position by saying that most of those who have been seriously injured need to be transfused, and usually with a considerable volume at a fast rate for the first two or three pints. With such cases, when in doubt, it is better to transfuse than to withhold. Blood, fresh or stored, is the ideal when the injury has obviously caused loss of blood, but either plasma or a so-called plasma-expander can save life by restoring blood volume, and in cases of moderate hæmorrhage may be all that is required.

The same principles apply in acute hæmorrhage, such as may occur at childbirth, but with continuing hæmorrhage a non-oxygen carrying fluid will not suffice; blood must be supplied.

### Anæmia.

Certain chronic anæmias, which are refractory, need to be treated by transfusion. Such treatment becomes necessary when the primary cause cannot be controlled, as with leukæmia or malignant disease, or cannot be determined, as with so many of the hypoplastic or almost aplastic states. In these, the patient has to lead a transfusion life because his hæmopoietic system is quite unable to keep pace with the ordinary daily wear and tear of the circulation. When, however, an anæmia is likely to respond to treatment with hæmatinics, iron or vitamin $B_{12}$ or folic acid, it is quite unjustifiable to transfuse unless the anæmia is of such a serious order that life is in danger.

Transfusion, however carefully matched, carries a risk, of either a reaction or a sensitization, which may endanger life or lay up trouble for the future. I emphasize

this point because a transfusion is often prescribed as a tonic or as an accelerator to recovery or for some trivial reason when nature, given time, or medical treatment intelligently applied, would achieve the same result at no risk whatever. It is perhaps some temptation to prescribe a relatively unnecessary transfusion in the convalescent period of recovery from injury.

In principle, patients with chronic anæmia who need to be transfused require nothing more than corpuscles to restore the oxygen-carrying power of the circulation. The blood volume, plasma volume in particular, is usually relatively normal, whereas the cardiac muscle of such patients may be in poor condition and unable to stand the rapid addition of a large volume to the circulation. The rate of administration needs, therefore, to be carefully regulated, and should be such as to allow time for the circulation to adjust itself to the increased volume and to excrete the unwanted plasma portion if whole blood be used.

But in order to reduce the volume of the transfusion and, at the same time, contribute the maximum amount of oxygen-carrying capacity, a concentrated suspension of corpuscles is to be preferred. This consists of blood from which the supernatant plasma has been decanted, and no trouble arises from the viscosity of the suspension, provided a minimum amount of plasma remains. Such a technique is particularly suitable for cases of aplastic anæmia who need to have a transfusion at regular intervals, or in leukæmia, though here, unhappily, the survival of the transfused cells may not be long. In my own experience, with the blood dyscrasias, the transfusion of fresh corpuscles has many advantages over the administration of those which have been stored or salvaged from a blood bank.

It is perhaps a happy circumstance when one can introduce a patient with hæmachromatosis to one suffering from aplastic anæmia. The former can be bled, his corpuscles separated by centrifuge or gravity for administration to the aplastic patient, and his plasma readministered to himself to restore his own blood volume, and this to the mutual advantage of both sufferers.

Restoration of oxygen-carrying power is also required when the circulating hæmoglobin has been immobilized by carbon monoxide poisoning or with acute benzol poisoning when oxyhæmoglobin is converted into methæmoglobin. In such cases venesection, followed by transfusion, is a valuable form of treatment. Some 20-50 per cent. of the effective hæmoglobin may be immobilized as carboxy-hæmoglobin in cases of poisoning; the volume of the transfusion, therefore, needs to be large, and likewise with acute benzol poisoning.

### Other Elements of the Blood.

Transfusion may be used to transfer elements of the blood, other than red corpuscles, such as leucocytes, platelets, immune bodies, as well as the clotting elements which may be deficient in certain hæmorrhagic states. It is salutory to remember that the natural life of a red corpuscle is some one hundred and twenty days, whereas the normal existence of a neutrophil leucocyte is certainly not more than a few days, and it would seem that transfused platelets may not survive for longer than three to five days, though this greatly depends upon the manner in which the blood is collected. Collection by negative pressure with frothing appears

to be very destructive to platelets. In these circumstances, whenever it is desired to transfuse any of the ephemeral elements, fresh blood is essential, and there is much to be said for a direct transfusion with an appropriate two-way syringe.

Even though the transfusion of leucocytes can hardly be more than temporarily successful, there is always the chance that other, perhaps inestimable, elements in fresh blood may have a therapeutic effect in cases of toxic or idiopathic agranulocytosis. Platelets also may be transfused and appear to be effective sufficiently long to tide a patient over the acute phases of essential thrombocytopenia.

There are a number of methods for concentrating platelets for this purpose. The development of this aspect of transfusion, the precise differential transfusion of material appropriate to each individual case, began to be a practical proposition with the brilliant work of Cohn and his team of experts who separated various fractions of blood according to the physico-chemical properties of the plasma proteins. The specific substances so far available include albumen (used as a volume-restoring fluid) immune bodies in the globulin class and fibrinogen.

So far it has not been possible to obtain antihæmophilic globulin which separates with the fibrinogen fraction, in amounts sufficient to make it generally available for the treatment of the disease. The only effective way, therefore, of treating the bleeding in hæmophilia is the intravenous administration of the antihæmophilic globulin which is contained in very small amount in fresh whole blood or fresh plasma. Large volumes are necessary, several pints of blood or plasma being required for an adult, and as antihæmophilic globulin is somewhat labile the blood or plasma should be as fresh as possible; in any case, not more than twenty-four hours old.

Lyophilized fresh plasma or plasma frozen immediately after collection may also be used, provided they are used as soon as they are reconstituted. Alternatively, the fibrinogen fraction of plasma may be administered if it is available, since it contains antihæmophilic globulin in concentrated form. Antihæmophilic globulin is not found in serum.

The Christmas factor, absence of which is responsible for the inherited hæmophilia-like disease known as Christmas disease, is, however, stable, and is therefore present in stored blood. It is also found in serum.

### Special Procedures.

In certain circumstances, a special transfusion technique is employed. There is no better example than in the case of hæmolytic disease of the new-born, which calls for judgment in respect of action and skill in execution.

Many factors govern the treatment of a case of hæmolytic disease of the new-born, and appropriate planning should begin quite early in pregnancy. With a previous history, or with knowledge in advance, everything should be prepared for the immediate transfusion or the exchange-transfusion of the infant, and since this demands a high degree of practice and skill, which, in itself, may greatly influence the outlook, it is advisable for delivery to take place in an institution where such skill is available.

In principle, investigations have clearly shown that exchange transfusion is the treatment of choice in all cases of prematurity and in full-term infants when the cord hæmoglobin is less than 11 g. per 100 ml. But ideas differ about the exact indications for exchange transfusion, and most now argue that it should be employed whenever there has been a previous pregnancy ending in hydrops or kernicterus, whenever the infant weighs less than five and a half pounds and, perhaps, whenever the cord hæmoglobin level is less than 15.5 g. per 100 ml. in a full-term infant.

The risk of kernicterus appears to run somewhat parallel to the serum bilirubin level in the first few days after birth, and such infants as are not transfused should be carefully watched for the onset of jaundice. If the serum bilirubin rises above 20 mg. per 100 ml., or if early signs of brain damage occur, then exchange transfusion should be carried out.

Exchange transfusion has the advantage of raising the hæmoglobin level without increasing the blood volume, and it reduces to the minimum the destruction of Rh-positive cells during the critical first four days of life, at the same time providing the infant with such a concentration of Rh-negative cells at one operation that no further transfusions are required.

The volume of the transfusion is usually based on the assumption of a blood volume of 40 ml. per lb. of body weight or about 300 ml. for a normal 7 lb. infant. Various methods are used and a really efficient exchange requires the provision of about 60 ml. of blood per pound of body weight. Some use Diamond's plastic catheter introduced into the umbilical vein, whilst others use the saphenous vein. The exchange is usually made with a 20 ml. syringe which, by means of three-way stop-cocks, permits alternate withdrawal of infant's blood and infusion of donor's blood to an amount of 400-500 ml. The donor's blood should be adjusted by removal of plasma to have a red-cell content of 5-6 million per cmm. This achieves an exchange of the order of 80-90 per cent. The blood should be warmed, but not over-heated. The umbilical vein route is only practicable during the first forty-eight hours, whilst the vein is patent.

The selection of suitable donors is sometimes difficult, but complete investigation of the red-cell and plasma factors of the mother and child indicate the ideal type of blood to administer. Even so, direct compatibility tests should always be performed.

As a general rule, when the disease is known to be caused by anti-Rh antibodies, the child should be transfused with Rh-negative blood of Group O, or its own group. Suitable donors are more likely to be found among maternal than paternal relatives; in cases of great urgency a maternal group O relative involves the least risk, though, even so, such a risk is large. The father should never be used.

### Difficulties and Dangers of Transfusion.

If one is to speak of the abuse of transfusion, as well as its use, it is as well to appreciate at the outset that most of the abuses arise from over-use, or from failure to realize the risks which the operation carries. Some of the risks are

always inherent in a biological fluid which itself is an excellent culture medium, as well as one whose qualities can rapidly degenerate.

In these days, when almost every civilized community has a blood bank from which stored blood is freely available day and night, there is considerable temptation to transfuse for even the smallest reason. To some extent, this attitude existed in some of the armies in the war, so much so that it was commonly said that a wounded man was lucky to escape a transfusion, whilst those who successfully survived the surgical toilet often had their convalescence unduly hurried, one might almost say harried, by transfusions, so that apparent somatic recovery occurred before the mental trauma associated with wounding had been repaired.

Simple mild pyrexial reactions, though not serious, are at least unpleasant, and occur with not less than 10 per cent. of transfusions, whilst allergic reactions, especially urticaria, have an incidence of about 1 per cent. A rigor, on the other hand, is more difficult to assess. It may be the first indication of an incompatible transfusion or no more than a sign that the patient cannot tolerate the speed at which the transfusion is being administered. Fast rates are sometimes necessary in an emergency, as after a large hæmorrhage or serious injury. A rigor due to this cause rapidly subsides, if the rate be slowed.

An ever-present hazard is the fact that blood, and to a lesser extent its products, always carry the chance of immunization, and in this respect, the female sex is exposed to a particular risk. This is especially the case if a wife receives a transfusion from a husband, for there is no surer way of sensitizing the wife to a future pregnancy if such is genetically possible.

Deaths from incompatibility occur even at the present time, despite the fact that careful cross-matching is usually the rule, and this because even the most stringent laboratory tests cannot eliminate the clerical or the human error.

Blood which is too old is almost as lethal as incompatible blood, and similarly with blood which has been improperly stored. Trouble may occasionally arise with Group O universal donor blood, if administered in large amount, and especially if the agglutinin content is of high titre.

Infected blood may be fatal in very small amount, with symptoms similar to those occurring with intravascular hæmolysis, particularly when it is contaminated with *œrobacter* or *pseudomonas*, which not only do not reveal their presence by hæmolysing the blood, but also are not restrained at refrigerator temperature (4°-6° C.) by which some are even encouraged. The transfusion of as little as 50 ml. of such blood may be fatal. Blood which has been removed from the refrigerator and allowed to warm up should never be refrigerated again for use at some future time, since the lifting of the restraining influence of refrigeration for even a short period allows any chance bacterial contaminant to multiply rapidly.

An incalculable risk is the transference of infective hepatitis, as well as other diseases, some of which are also due to viruses. The type of hepatitis caused by transfusion, particularly of plasma, appears to have a considerable mortality. The risk of this complication is reduced by using blood or plasma from individual donors, rather than plasma obtained by pooling the blood of several donors.



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With patients whose cardiovascular system is feeble, such as the poor cardiac musculature in chronic anæmia, the danger of overloading the circulation is considerable unless great care is taken to restrict both the volume administered and the rate at which it is given. Cardiac failure and pulmonary œdema can readily be produced.

Air embolism and fat embolism are also definite risks, the former whenever blood is being administered at high speed under positive pressure, and the latter whenever there have been extensive bony injuries. With regard to air embolism, it is well known that a surprisingly large volume of air can be tolerated by a healthy subject, but no more than a few ml. may precipitate death in a patient who is gravely ill; this complication may arise from faults in the apparatus such as ill-fitting or perished rubber-tubing, or from the level of fluid falling below the exit-tube of the vessel after positive pressure has been applied. Fat embolism should be suspected when pulmonary and cerebral symptoms associated with petechiæ supervene in the course of the transfusion of a patient with bony injuries.

Transfusion in the acquired hæmolytic anæmias carries a special risk, since many have a circulating hæmolysin which has almost panagglutinating properties, and it may be extremely difficult to find a donor with which the recipient's serum is compatible by the direct test. At times it has been my experience that it may be necessary to examine as many as a hundred samples before all criteria can be satisfied.

Should trouble occur, that is, should significant intravascular hæmolysis develop owing to frank incompatibility of orthodox type, or, as the result of the more complex problems of the hæmolytic anæmias, or from the use of aged and ageing blood, what can be done to avert disaster?

In the first place, on the occurrence of suggestive symptoms, of which the most significant is violent pain in the back, the transfusion must be stopped. Other signs and symptoms include rigor, respiratory embarrassment, circulatory collapse and those which may be attributed to the small hæmorrhages or emboli found at autopsy in the brain, mesentery, endocardium and gastrointestinal tract. Later features include hæmoglobinuria, hæmalbuminæmia, jaundice, urticaria and, eventually, oliguria or anuria with renal failure.

With any marked degree of intravascular hæmolysis, there is always a considerable deposition in the renal tubules of a pigment of hæmatin type, and this was for long considered to cause oliguria, anuria and death from uræmia, owing to blocking of the renal tubules. In that the pigment was not deposited in an alkaline urine, the long-practised treatment of incompatible transfusion was the administration of alkalis, especially potassium citrate. The uræmia of incompatible transfusion is now thought to be due, not to the blocking of renal tubules, but to renal damage caused by arterial spasm and ischæmia giving rise to a lower nephron nephrosis. In such circumstances, the uncontrolled administration of potassium may at times contribute to, rather than relieve the pathological state.

Apart from a cerebral catastrophe, the immediate danger is death from shock, hypotension and peripheral-circulatory failure. With more moderate reactions, a

fatal issue from renal failure with oliguria or anuria may occur at any time within a few days or weeks. The main renal lesion is a lower nephron nephrosis, but the damage affects the whole nephron to some extent.

During the periods of onset, and duration of the renal damage, as well as in the recovery phase, there are usually profound and serious changes in the body chemistry, particularly in water-balance and electrolyte distribution, and these changes may range from one pathological extreme to another. Thus, at one time the patient's life may be in danger from pulmonary œdema and water intoxication, and this state may later pass into one of dehydration, or, the level of blood potassium may vary from excess to deficiency, and likewise with sodium or chloride. Apart from the initial acute phases, it will therefore be obvious that proper treatment demands strict and constant biochemical control, since such observations will provide the information vital for the appropriate prescription of life-saving requirements, particularly in relation to the intake of water, potassium, chloride and protein.

At the outset, the transfusion having been stopped, immediate stimulants may be needed to overcome gross collapse. Otherwise, there is much to be said for the immediate transfusion of a small quantity of compatible blood, as this may minimize the renal ischæmia. This is especially so if the blood volume has been significantly reduced by hæmorrhage or continuing hæmorrhage. The critical period during which benefit from such treatment can be expected is some six to eight hours. After this time, the renal damage is not reversible without epithelial regeneration.

The second stage, the stage of renal failure with oliguria or anuria, is apparent within twenty-four hours, and may last from one or two days up to three weeks. A critical period is often from the seventh to the fourteenth day.

During this period the blood urea rises, perhaps to 100 mg. per 100 ml. at the end of twenty-four hours and may reach a peak of 500 mg. per 100 ml. or more before death or diuresis occurs. During this phase the main dangers are over-hydration, pulmonary œdema, water intoxication and hyperkalæmia. The principles of treatment are to balance water intake against output and to reduce protein breakdown and potassium release as much as possible by a high-calorie non-protein diet; at the same time any intake of potassium is avoided and electrolyte disturbances are corrected as they occur, having been revealed by biochemical control estimations.

As to water-balance, the insensible loss by all routes is approximately 1,000 ml. in twenty-four hours, and this is increased by about 500 ml. when there is visible perspiration as the result of pyrexia or a hot and humid atmosphere.

The amount of urine excreted (if any), or of vomit, should be added to whatever estimate is made of fluid loss. In principle, the intake of fluid should be from 700 to 1,500 ml. per day; the amount may be increased if clinical signs of dehydration are present. As to a high-calorie non-protein diet, this should contain glucose, fat and vitamins, especially fat soluble vitamins. Bull's diet, best administered by intranasal gastric tube on account of nausea, is as follows: glucose 400 g. and arachis (peanut) oil 100 g.; emulsify in acacia and make to 1 litre with water;

add 15 minims of halibut oil, 600 mg. of vitamin C and some ten powdered tablets of any multi-vitamin preparation.

The alternative is the intravenous administration of dextrose solutions of 20 or 40 per cent. at a rate of about 1 litre a day. The only method of overcoming an uncontrolled rise in blood potassium or gross over-hydration is by peritoneal dialysis.

The third stage, the stage of diuresis, requires meticulous biochemical control and bedside observation of fluid intake and output, since over-hydration may pass rapidly to dehydration and incipient hyperkalæmia may change suddenly to hypokalæmia. Sodium and chloride loss may also be considerable and require replacement with appropriate fluid.

Hypokalæmia is accompanied by weakness, lethargy, tremor, ataxia, shallow breathing and a definite change in the electrocardiogram. With potassium depletion in association with good diuresis, potassium should be administered as 4 g. of the chloride as a 25 per cent. solution in 5 per cent. dextrose for every three litres of urine excreted. With gross deficiency the amount may need to be as much as 8 g. and sometimes administration may have to be made by the intravenous route. During the stage of diuresis any salt deficiency can be corrected by adding 5 to 10 g. of salt to the diet.

The fourth stage, the stage of convalescence, during which renal function returns to normal, lasts from one to nine months, during which the diminished renal blood flow returns to normal. The daily fluid intake should be adequate and a high-carbonhydrate, low-protein, low-salt diet should be maintained as in the case of chronic nephritis. This should be maintained until renal function is normal.

These, then, are some of the uses, some of the abuses, and some of the hazards of transfusion as practised to-day. If I were asked to name the greatest use, I should say replacement of loss or deficiencies, since this is, in fact, a physiological tissue graft. If I were asked to name the greatest abuse, I should say over-use, unhesitatingly. This is mainly due to the great facilities now available for the free supply of blood, but it is also influenced by public opinion and by the deep-rooted instinct urging that something should be done.

The hazards increase yearly. Gone are the days when the satisfying of the simple compatibilities of the Landsteiner groups would suffice. Massive transfusion and especially multiple transfusion has opened a tremendous vista of incompatibilities due to immunization, since mankind can now be divided into at least 792 types by various components of the red cell.

One day we may find that we all have the individuality of our finger-prints, and are quite incompatible with each other. When that is so, there will be neither use nor abuse for transfusion.

# The Importance of Population Fertility and Consanguinity Data being available in Medico-Social Studies

## Some data on consanguineous marriages in Northern Ireland

*By*

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IN recent years increasing use has been made of studies in the community as a means to better understanding of ætiology. At first the techniques used were essentially those developed in work on the epidemiology of infectious disease, but there have been developed more specific methods designed to illuminate the patterns of "constitutional" or degenerative disorders. The interpretation of the findings in work of this kind is often severely limited by the lack of adequate background data relating to the community from which the sample studied was drawn. Such considerations apply with peculiar force to studies in human variation where hereditary factors are of importance, because knowledge of the static and dynamic aspects of the mating and reproduction behaviour of the population is essential to an understanding of the pattern of such conditions. There is no doubt that the need for such studies is increasing and that they will constitute an essential part of balanced medical research activities in the future.

As the mean age of populations increases a higher proportion of disabling conditions than ever before is caused by the disorders present at birth, and by those determined by premature degeneration of tissues and organ systems which is the result, in considerable part, of inherited constitution. Further, appreciation of the size and nature of the potential problems in populations (and in specific populations) exposed in part or whole to radiation is handicapped at present by a lack of factual data relating to human populations. Finally, however carefully such an appreciation may be made, even with more knowledge of the population genetics of man, there will remain the necessity to observe by precise methods what changes in fact take place in exposed populations. Unless much preliminary knowledge is accumulated, the period of uncertainty about the effects of radiation from warlike or peaceful use of atomic energy may be unnecessarily prolonged. The data from population census figures and from the registration of births, deaths, and marriages is published in the United Kingdom by the Registrars General for England and Wales, Scotland and Northern Ireland.

From census data in the whole of the United Kingdom, reasonably accurate distributions in each county and in administrative areas are available every ten

years in respect of age, sex, marital condition, religion, occupation, and social class. From the registration procedures in all the countries information is available each year concerning births, marriages, and deaths during the year. Basic tabulations give (1) live births by sex and legitimacy, (2) marriages by age of partners, (3) deaths by age and certified cause.

In England and Wales and in Scotland stillbirths are also registered and the data published. Even more important in the present context, these countries also record and publish (as a result of the Population (Statistics) Act of 1938) much detailed information on fertility. This information about stillbirths and fertility is not available in Northern Ireland.

The purpose of the Population (Statistics) Act of 1938 was primarily to give data which would facilitate study of the trends of the age and sex compositions of the population, but it has had much additional value in illuminating the biological effects of age on fertility and in helping to understand the genetics of communities. In none of these countries do the Registrars General collect information on inbreeding in the population, or in other words, of the numbers of marriages where the partners are related in varying known degree.

It appears to us that such additional information on stillbirths, fertility, and inbreeding should be collected and made available in Northern Ireland for the reasons which we set out below. It seems to us that, from some points of view, it is even more important that the information should be available for Northern Ireland than for the rest of the United Kingdom. This is because it is possible, with a population of the size of Northern Ireland, to carry out studies in population genetics and human variation, which could only be done by an immense and largely impersonal organization in the rest of the United Kingdom. It may be noted that there are good precedents for innovations by Registrars General in Ireland, particularly in respect of census information. The remarkable collection published in each census from 1851 to 1911 of data relating to the deaf, blind, mentally affected, and physically handicapped is unique, and if similar information had been available for the United Kingdom in 1945 it would have simplified and improved much social planning.

### The Value of Fertility Data and the Kind of Information Needed.

One of the fundamental conceptions in the modern theories of evolution is that differential fertility of persons of particular genetic types ultimately determine, at any given time, the genetic constitution of populations. Thus mutations which are unfavourable to survival are prevented from increasing in the population or fall in numbers to a low level at which they are part maintained by new mutations. Most expressions of new mutations in man take the form of what are biologically defects or deformities, or of a characteristic so bizarre that the possessor is, as a result, looked at askance in society. Whether the mechanism be biological or social, such individuals as a group tend to reproduce themselves less frequently than "normal" individuals. There are many examples from direct observation of such phenomena in populations. For example, boys with sex-linked progressive Duchenne type muscular dystrophy all die before reaching adult life and have a

zero fertility (Stevenson, 1953). Even in a condition such as hereditary deaf mutism, the fertility of affected subjects in Northern Ireland is probably only about one-third of that prevailing in the population as a whole (Stevenson and Cheeseman, 1956). The reverse situation, whereby favourable genes determine greater fertility in the group of those possessing them than that prevailing in the population as a whole, is less frequently observed; indeed, it seems likely that genes of positive evolutionary value seldom have a definite individual expression such that they may readily be recognised. In view of the socio-psychological pressures which tend to determine that people who are markedly "different" are not liked, this is understandable.

An example has recently been recognised which is of very great interest where there is good evidence that persons heterozygous for a particular gene have a better chance of survival in certain circumstances than the general population, although the homozygous expression of the gene is very unfavourable. Allison (1954 (a)) has shown that of the children with the sickle cell trait in endemic areas of subtertial malaria in tropical Africa a much smaller proportion than those with no sickling trait have the malarial parasites in their blood. Further injection of malarial parasites into adults who had not primarily been affected showed that those with sickle cell trait showed a very marked resistance to infection. It has been known for some time that those with sickling trait only were heterozygous for a recessive gene and that those who showed hæmolytic crises and sickle cell anæmia were homozygous for this gene. In large populations it would be expected that there would be a relationship between the frequency of the heterozygote and the homozygote and further, that as the condition is genetically determined the frequency of the two genotypes would vary little between separate populations. It has been demonstrated (Allison, 1954 (b)) that there are great variations in different areas and that these are related to the incidence of malaria. It is estimated that the proportion of descendants who reach maturity of the offspring of those heterozygous for a sickling gene is one and a quarter times that of the general population.

Recent observations that an undue proportion of persons who suffer from cancer of the stomach have a particular genotype determining a particular blood group (Aird, Bentall and Fraser Roberts, 1953) are also relevant to these considerations. A further example is the work of Struthers (1951) which suggests that an undue proportion of children with chronic bronchitis and asthma are of blood group A. Indeed it is generally agreed that no gene is entirely neutral in evolutionary value.

It is important to be able to estimate the rate at which known genes are lost to a population by the mechanism of diminished relative fertility. Estimates of this kind are essential to any indirect calculations of mutation rates in man, and as a majority of harmful genes are recessive, only indirect methods are available for human studies. In essence, such methods equate the number of genes lost to the number of new mutations needed to replace them and maintain a stable incidence of expression of the trait. Further, in any situation where an excess number of harmful genes arise in a population, an effect which could follow exposures to

radiation, the rate at which these genes would be eliminated is of fundamental importance. To estimate the speed of elimination, the fertility of the specific genotypes and that of the general population must be directly comparable and the information about each must therefore be available in the same form.

There are a few points about the assembly and interpretation of fertility data which are of particular importance in this important matter of determing the relative fertility of specific genotypes. In collecting information in a specific investigation the individuals whose fertility is of importance will be of varying ages and, if married, of different durations of marriage. In short, the information which can be collected will be (1) the numbers married and not married in each sex at each age, (2) the duration of marriage, (3) the number, condition, and ages of offspring of those married.

The information at present available in Northern Ireland concerning the whole population is not sufficient for direct comparison. Information comparable to (1) is available at each census, but there are no comparable data to (2) and (3). The information published by the Registrars General of England and Scotland coming from the data collected under the Population (Statistics) Act, 1938, is much more complete and parallels most of the information which can be collected in studies. There is no need to elaborate the range of this information, as the matter is fully considered in the Registrar General's Statistical Review for England and Wales for the years 1938 and 1939 (Text).

## Consanguinity.

Consanguinity is of importance mainly in respect of the recessive gene determined conditions which constitute almost all the grave single gene expressions in man. Genes are said to be recessive when there is expression of the trait or characteristic determined by the gene in the homozygote but not in the heterozygote. The heterozygote, having only one "abnormal" gene, will have received it from only one parent while the homozygote having the two abnormal genes must have received one from each parent.

The frequency of persons homozygous for any unfavourable gene in man is always low and an undue proportion of affected subjects have parents who have had, within a few generations, a common ancestor. The explanation is, of course, that if a given person is heterozygous for a given gene any of his relatives descended from a common ancestor whom he marries is much more likely to be heterozygous for the same gene than a mate chosen at random in the general population.

Suppose, for example, that in a rare condition one in a thousand of the population was heterozygous for a particular gene. If a given man who was heterozygous for that gene married at random in the population the chance of his marrying another heterozygote would be one in a thousand. If, however, he married any full cousin, as he and his cousin must have had one pair of common grandparents, the chance of his cousin being heterozygous for the gene would only be $\frac{1}{8}$. (The probability of a gene being derived from the parent through whom the cousin relationship occurs is $\frac{1}{2}$ (either father or mother). The chance of the sib of the heterozygote parent (the uncle or aunt) having the gene is $\frac{1}{2}$. The chance of each of his or her

offspring (the cousin who may be married) having the gene is $\frac{1}{2}$. The chance of any given cousin being heterozygous is therefore $\frac{1}{2} \times \frac{1}{2} \times \frac{1}{2} = \frac{1}{8}$.)

A little consideration of the above will make clear the four following propositions :

1. *That the less common the gene the higher will be the proportion of affected subjects having related parents.*

Logically, if a completely new mutation occurs for the first time in the population, it would never occur in the homozygous state and therefore be manifest until there occurred a marriage of persons descended from a common ancestor.

2. *That there should be a numerical relationship between the frequency of the recessive gene and the proportion of homozygotes who have related parents in a given degree, e.g., full cousins.*

This numerical relationship will, however, be varied by the number of consanguineous marriages which take place in the population. There will be three "bands of frequencies" of cousin marriages in a community. In the first no such marriage will occur—for example, in a strict Roman Catholic community. In the second, cousin marriages would occur no more frequently than by mere chance, so that if a man had x female cousins his chance of marrying one would be no more frequent than x multiplied by the inverse of the number of potential spouses in the whole community. Such a situation would make cousin marriages very uncommon. The third, which is in practice what is always observed, is a frequency of cousin marriages which probably varies considerably in different communities, but it is in all considerably greater than would occur by mere chance. This is because of physical isolation of small communities, because opportunities for meeting spouses are not unlimited, and because religious and economic cleavages limit choice. Various social pressures, some, for example, connected with land holding and inheritance customs in rural communities, may also limit choice of a partner. It follows that, in relating the frequency of a gene to a cousin marriage rate, the prevailing cousin marriage rate in the community concerned must be taken into account.

The numerical relationship between the frequency of the recessive gene determining the trait, the proportion of affected homozygotes who have full-cousin parents, and the prevailing full-cousin marriage rate in the community concerned is conveniently expressed in a formula derived by Lenz (1919). Dahlberg (1929) has subsequently produced a more sophisticated version, but the principle is more easily explained by considering Lenz's original formula, which is

$$F = \alpha / ( \alpha + 16q)$$

where F is the proportion of cousin marriages in all marriages which would be expected to give rise to homozygous affected offsprings, $\alpha$ is the chance of an individual in the community marrying a first cousin, and q is the gene frequency of the abnormal gene. (For those interested, the derivation of this formula is adequately explained in Penrose (1948)).

It will be apparent, therefore, that F can be estimated by knowing the frequency of the condition and the prevailing cousin marriage rate. A value can also be

obtained by direct observation of the proportion of the parents (matings) of affected persons who prove to be full cousins.

Comparison of the two values for F will enable confirmation or otherwise that the condition being studied is probably determined by a single gene fully recessive. It will also be clear that the value of $\propto$ is critical in determining the estimated value of F, and that for the formula to be of value, cousin marriage rates must be accurately determined.

3. *That the relationship in 2 above is also a test of the specifity of one gene to the condition.*

There are a number of conditions where the characteristic or trait may be the expression in the homozygote in some instances of one recessive gene and in others of entirely different recessive genes. If it is impossible clinically to differentiate these homozygous expressions it might never be suspected that more than one gene could be responsible for the condition. The situation would be suspected if, when two homozygotes married, sometimes all and sometimes none of their offspring showed the trait. However, marriage of homozygotes (except in recessive deaf mutism) is a phenomenon of extreme rarity. Yet, as has been noted, if the prevailing cousin marriage rate in a community is known, and the frequency of the homozygote is also known, then the expected proportion could be estimated of subjects showing the trait whose parents were full cousins. If, however, more than one homozygote genotype was causing the condition, then the frequency of the separate genes would each be lower than if only one gene was involved, and the observed frequency of full-cousin parents would exceed that expected in the single gene hypothesis. Such reasoning leads us to expect a parent cousin marriage rate, based on the frequency of albinism of about 6 per cent. The observed parent cousin marriage rate is, in fact, about 20 per cent. (Roberts, 1940).

An interesting observation of the same kind has recently been made in Northern Ireland, where the evidence from similar calculations that more than one gene can cause deaf mutism is reinforced by study of the marriages of hereditary deaf mutes which sometimes results in deaf and sometimes hearing offspring. The cousin marriage rate in Northern Ireland from the inadequate data available is estimated as 1 per cent. The incidence of deaf mutism is 0.00023. The expected frequency of full-cousin parent marriages on a single gene hypothesis would be 4.23 per cent. The observed frequency was 9.5 per cent.

It is not unlikely that other supposed single recessive gene determined conditions are really heterogeneous in genetical origin, and it is important to have as accurate knowledge as possible about the distribution in the population of recessive genes in man. Such information is essential both in calculation of the possible effects of harmful radiations and in the recognition of their effects. Failure to appreciate that more than one recessive gene could determine the same inherited traits could be very misleading. PUBLISHED DATA ON CONSANGUINITY.

We cannot trace any published figures relating to consanguineous marriage rates in Ireland and, as is well known, only Bell (1940) has recorded any considerable body of data for England and Wales.

It is likely that the whole trend in countries which have undergone social revolutions with accompanying industrialization, and improvements in communication is for the frequency of marriages of those related in ascertainable degrees to fall. The effect of breakdown of isolated communities so determined will be to make more homogeneous the consanguineous marriage rates in different districts in given countries. Nevertheless, such differences persist and are of importance.

Table 1 illustrates that the range of variation between and within countries is large enough to invalidate the kinds of calculation mentioned previously in this paper.

TABLE 1.

ESTIMATES OF THE FREQUENCY OF COUSIN MARRIAGES IN VARIOUS POPULATIONS MADE IN THE LAST 25 YEARS.

| Reporters | Population | Years of Study | Number of Marriages | Cousin Marriages per cent. |
|---|---|---|---|---|
| Dahlberg, 1929 ... | Bavaria ... | 1926-1933 ... | ... | 0.20 |
| | 40 Parishes, rural Bavaria... | 1925 ... | 16182 ... | 0.6 |
| | 1 Community, Switzerland... | 1931 ... | 270 ... | 1.9 |
| | 1 Community, Obermatt, Switzerland ... | 1934 ... | 52 ... | 11.5 |
| | Sample, Island Bornholm, Denmark ... | 1938 ... | 399 ... | 1.3 |
| Böök, 1948 ... | Sample, Copenhagen, Denmark ... | 1941 ... | 498 ... | 1.2 |
| | 1 Rural District, Northern Sweden ... | 1948 ... | 843 ... | 0.9 |
| | I Rural District, Northern Sweden ... | 1948 ... | 281 ... | 2.8 |
| | 1 Rural District, Northern Sweden ... | 1948 ... | 191 ... | 6.8 |
| Neel, Kodani, Brewer, and Anderson, 1949 ... | Hiroshima, Kure, and Nagasaki ... | 1949 ... | 24000 ... | 4 (approx.) |
| Bell, 1940 ... | Parents of 10,236 children in general hospitals | 1925-1939 ... | 10236 ... | 0.4 |

Additional information on consanguineous marriage rates in different countries have been published by other authors. However, in these countries the complete data showing the size of the population and mode of the selection of the sample are not given and/or the proportion of the consanguineous marriages where the parents were full cousins is not stated. (Bartels (1941), quoted by Lindenov (1945), referring to the Netherlands.)

It will be seen that there is a great dearth of good recent data and that such as is available is heterogenous, in that it deals with marriages which occurred at different periods of varying length in different countries. What is needed is continuously recorded data, from different countries, in each case the sample being of such size and nature that isolate effects can be detected, and trends observed. Further, in every instance, the precise consanguineous relationships of the partners to the marriages should be stated.

### The Northern Ireland Data.

Table 2 sets out some data which have been collected in recent years in Northern Ireland.

TABLE 2.

The Available Information on Consanguinity in Northern Ireland.

| | No. of Marriages | $C_1$ | $C_2$ | $C_3$ | $C_\chi$ | % $C_1$ | % All C |
|---|---|---|---|---|---|---|---|
| County Fermanagh, 1954 | 350 | 1 | 1 | 4 | – | 0.28 | 1.71 |
| County Londonderry, 1954 | 717 | 10 | – | 12 | 1 | 1.39 | 3.3 |
| County Tyrone, 1954 | 3000 | 6* | 4 | 4 | – | 0.20 | 0.47 |
| County Armagh, 1954 | 560 | 3 | 1 | 3 | – | 0.54 | 1.25 |
| City of Londonderry, 1955 | 162 | – | – | – | – | – | – |
| Registrar General's Return of Marriages, 1954-55 | 5333 | 7 | – | 28 | – | 0.13 | 0.66 |
| Mathers, 1952 | 670 | 1 | 1 | – | – | 0.15 | 0.30 |
| Medical Students (Q.U.B., 1953-54) | 116 | – | – | 1 | 1 | – | 1.72 |

*One of these was closer than first-cousin relationship. This is included in preceding figure.

Note. $C_1$, $C_2$, and $C_3$ refer to matings of first cousins, first cousins once removed and second cousins respectively, as defined in the Oxford Dictionary. $C_\chi$ refers to degrees of relationship less close than above but where the partners had a common ancestor.

The information referred to the counties was collected in 1954 by the health visitors when paying visits to the homes where there were new-born children. It may be assumed that the great majority of the marriages took place in the preceding ten years.

The medical student's data refer to two classes where the students were invited to complete a card detailing any known relationship between their parents. One of us (J. D. M.) assembled his data by questioning 670 successive married persons coming to the Casualty Department of the Royal Victoria Hospital, Belfast, with minor injuries and superficial sepsis.

The Registrar General's data were collected by the co-operation of about half of the Protestant clergy and ministers, over the year 1954, when questioning persons about to be married to ensure that they were not within illegal degrees of relationship. The information relates to areas scattered fairly uniformly over

the Six Counties. It seems likely to be the most intrinsically reliable of the sources and it also relates to the most recent marriages which is of particular interest.

It is unlikely, in view of the independent evidence from these scattered sources, that the full-cousin marriage rate in recent years is as much as 1 per cent. It may, however, have been higher in the past, and this has to be taken into account on appropriate occasions.

As will be seen from Table 3, which is derived from the data in the four counties, the proportion of full-cousin marriages is significantly less in Roman Catholics. This low proportion has presumably prevailed for a long time so that the decline in rate which is probably occurring is entirely in the Protestant population. It is noticeable, however, that there is a greater proportion of first cousin once removed ($C_3$) marriages in Roman Catholics. It is difficult to interpret this observation.

TABLE 3.

CONSANGUINEOUS MARRIAGES IN PARENTS OF NEW-BORN CHILDREN IN COUNTIES ARMAGH, FERMANAGH, LONDONDERRY, AND TYRONE, 1954.

| RELIGION | Consanguineous Marriages in each Degree of Relationship and Percentage in each Case of Total Marriage | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $C_1$ | | $C_2$ | | $C_3$ | | Cx | | TOTAL | |
| | No. | % | No. | % | No. | % | No. | % | No. | % |
| Protestant - - - | 12 | 1.60 | 2 | 0.27 | 6 | 0.80 | 1 | 0.13 | 21 | 2.80 |
| Roman Catholic - - | 2 | 0.23 | – | – | 13 | 1.51 | – | – | 15 | 1.74 |
| TOTAL - - | 14 | 0.87 | 2 | 0.12 | 19 | 1.18 | 1 | 0.06 | 36 | 2.23 |

It is clear that better data are required and that only constant careful collection will disclose trends and ensure accuracy when relating incidence of recessive gene determined conditions in young children to consanguinity rates.


SUMMARY.

This paper presents arguments in favour of accumulation of data on fertility and "inbreeding" in the population of Northern Ireland. The reasons advanced are that such data are essential as a background to population genetic studies. It is suggested that such studies are of increasing importance in two ways. Firstly, the understanding of many chronic disabling disorders, and, secondly, in providing some of the information, at present scanty or missing, which is necessary for an understanding of the extent of the problem of exposure of populations to radiations. It is pointed out that the data available from the Population Statistics Act (1938) and the recording of consanguineous marriages would meet all needs at present.

Some data on prevailing consanguineous marriage rates in Northern Ireland are recorded.



We are indebted to Dr. J. C. Paisley, Dr. B. O. Moore, Dr. J. H. Kitson, and Dr. W. Bamber for the information from Counties Armagh, Fermanagh, Londonderry, and Tyrone respectively, and also Dr. W. R. Abernethy and Dr. H. P. Swann for the information from Londonderry City. Mr. L. C. Mulligan was responsible for suggesting the method and making possible the assembly of data relating to the Protestant marriages. Finally, we are most grateful to Miss H. Johnstone for her help in assembly and typing of this paper.

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# Impalement Injuries of the Rectum

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It is proposed to present a case of impalement injury of the rectum and to review briefly the diagnosis, prognosis, and treatment of such cases. From a study of the literature, it appears that these injuries are not very common. One of the earliest reviews of this subject was in 1896, when Van Hook of Chicago analysed fifty-eight cases, two of which were his own. Stiassney and Tillman added further cases in 1905, but the most extensive early survey was done by Habhegger of Wisconsin in 1912, when he analysed one hundred and seventy-five injuries of this type. Of this total, there was penetration of the peritoneal cavity in seventy. Spencer (1912) and Roquès (1931) recorded further cases. In 1938 Hambly reported a case in which a steel tube penetrated to a distance of eighteen and a half inches. His patient was a boy aged fifteen years, and the rod, after penetrating the perineum, entered the peritoneal cavity, passed through the transverse mesocolon and small intestine, coming to lie under the skin of the chest wall, in front of the sixth and seventh costal cartilages. Other cases have been published by Conway (1938), James, Powers, and O'Meara (1939), and Crymble (1943). In Professor Crymble's case the handle of a hayfork penetrated through the ischio-rectal fossa, perforated the levator ani, and left the pelvic cavity through the great sciatic notch without damaging any important structures. O'Regan (1947), in an excellent review of the subject, was able to account for two hundred reported cases and he, himself, added four more. Thomas (1953) recorded three further cases, two of whom had peritoneal involvement and recovered following operation.

The following case is interesting in that a metal tube not only penetrated the perineum and peritoneal cavity, but also passed through the left dome of the diaphragm into the left pleural cavity. Having examined the literature on the subject, I can find reference to one similar case only—that reported by Roquès (1931) in France. Unfortunately, the thesis in which this case was reported is unobtainable.

## Case Report.

A boy aged sixteen years was admitted to the Downe Hospital, Downpatrick, on 8th May, 1953. A history was given that one hour previously, while jumping over a tubular metal crossbar ($\frac{1}{2}$ in. diameter), he accidentally landed on it. The crossbar collapsed, and part of it, turning into the vertical position, penetrated his perineum. The boy's father removed the tube and his doctor had him transferred to this hospital.

On admission, the patient was extremely shocked, semi-conscious, with an imperceptible pulse, very shallow respirations, and a blood pressure that could not be recorded. An intravenous drip was started and three pints of blood run in under

pressure. This resulted in some improvement, as the patient was now conscious, with a pulse of 146 per minute and a blood pressure of 85/45. Examination showed a ½ in. circular laceration of the skin on the anterior anal margin. Rectal examination showed that the anterior fibres of both external and internal anal sphincters had been divided, that the rectum was almost empty, and that there was a tear of the anterior rectal wall, with damage to the adjacent part of the prostate. The abdomen was slightly distended, rigid, tender, and dull on percussion. The patient's condition did not further improve in spite of another three pints of blood and, as an intra-abdominal hæmorrhage was suspected, the abdomen was opened under general anæsthesia, through a lower mid-line incision. A 1 in. tear in the left external iliac vein, just distal to where it is crossed by the ureter, was identified and plugged with a finger. Several pints of blood were sucked out of the peritoneal cavity, the vein separated from the artery, clamped on either side of the tear and ligated with linen thread. The tear in the anterior rectal wall was repaired with interrupted catgut sutures, as was the tear in the peritoneum on the lateral pelvic wall. Apart from several small areas of subserous hæmorrhage in the small bowel surface, no gross damage to other viscera was noticed. However, the patient's poor general condition did not permit a thorough search being made. The abdomen was closed with drainage. An intravenous drip was continued until a total of eleven pints of blood had been given and penicillin and streptomycin therapy commenced.

The following day the boy's father was interviewed and, after questioning him and examining the rod, it was estimated that penetration to a depth of 18 in. had taken place.

Thirty-six hours after operation the patient developed marked respiratory distress and a marked cardiac shift to the right. Ten ounces of blood was aspirated from the left pleural cavity, giving considerable relief. There was no history or clinical evidence of chest injury, and repeated X-rays during the next few days failed to show any evidence of fractured ribs. During the next thirty-six hours a further ten ounces of brighter blood was aspirated from the chest to relieve respiratory distress, and it was now suspected, towards the end of aspiration, that the material was semi-purulent. Further aspirations through a needle were now impossible, and a nasal type of catheter was inserted under local anæsthesia into the sixth left interspace. Aspiration through this produced foul smelling B. coli pus and laboratory examination showed the presence of pus cells, Gram negative bacilli and coliforms, sensitive to chloromycin, streptomycin, and sulphamethazine. The catheter was connected to an underwater drain and streptomycin injected daily into the chest. In spite of this, it was necessary, two months after admission, to transfer him to the thoracic surgical unit in Belfast, where Mr. Smiley, F.R.C.S., operated on him and reported as follows: "I was surprised to find a piece of tissue which, unmistakably, had hairs upon it. Unfortunately, the laboratory were not able to identify it as skin, but there seemed no doubt that this was in fact so. The explanation can only be that he carried a piece of his skin from the perineum on the point of the crossbar, right up through his diaphragm into his chest."

Following this, his chest condition steadily improved, but while in hospital he developed calculi in his right kidney. An intravenous pyelogram at the beginning of October, 1953, showed that both kidneys were functioning, but there was some degree of hydronephrosis on the left side with dilatation of the left ureter above the point where the ureter crosses the pelvic brim. The calculi were removed from the right kidney by Mr. Loughridge on 19th October, 1953, and he was discharged from the Royal Victoria Hospital on 26th December, 1953.

However, on 4th January, 1954, he was readmitted to the Downe Hospital with severe right-sided pain, vomiting, headache, and a temperature of 102.6°. He stated that he had not passed urine during the previous forty-eight hours, but, in spite of this, he had no demonstrable bladder enlargement. There was, however, a history of "watery diarrhœa." Blood urea on admission was 154 mg. per 100 ml. A catheter could not be passed beyond the prostatic urethra and a diagnosis of recto-urethral fistula was confirmed by an intravenous injection of methylene blue. With treatment, his condition improved, and seven days after admission he, spontaneously, passed thirty-six ounces of urine per urethra. Two weeks later his blood urea was 27 mg. per 100 ml., and an intravenous pyelogram now showed "Good function on the right side with a normal right renal tract, but no evidence of function on the left side." Repeated X-rays confirmed this finding and, on 6th July, 1954, the late Mr. Woodside explored the left ureter and found that the lower end was embedded in a mass of fibrous tissue. It was found that the kidney was secreting urine. Under considerable tension the proximal end of the ureter was anastomosed to the bladder. This fibrous obstruction of the left ureter below the pelvic brim was obviously of slow onset and was apparently due to infection, as there was no evidence of injury to the ureter before or during operation.

The boy, a bright student, is now back at school and feeling well. His empyema is closed, his general health is good; but there is still no evidence of return of function to the left kidney.

*Analysis.* Analysing this case in retrospect, it is felt that the metal tube, after passing through this boy's abdomen, entered his left pleural cavity. The following facts support this claim: (1) the absence of any other cause for the left-sided hæmothorax; (2) the Father's statement and the fact that the rod was stained to a depth of 18 in.; (3) the presence of a B. coli pleural infection, and (4) the finding of a section of skin-like tissue in the chest.

The course of metal tube is shown in Figures 1 and 2.

## Discussion.

*Types of impalement injury.* Probably the simplest classification is as follows: (1) impalement without penetration of peritoneal cavity; (2) impalement with penetration of peritoneal cavity but without visceral damage, and (3) impalement with penetration of peritoneal cavity and visceral damage.

*Common objects causing this type of injury.* Shooting-sticks, pitchfork handles, steel rods, spiked railings, billiard cues, broken chair legs, mop handles, and home-made bougies.

*Diagnosis.* Early diagnosis of peritoneal perforation is of paramount importance. This may very occasionally be easy, for Morley cites a case where omentum actually prolapsed through the anus. Abdominal examination may not reveal much in the early stages unless there has been damage to major pelvic or abdominal blood vessels or viscera. If, however, there has been much soiling of the peritoneum with fæces from the rectum a virulent peritonitis with abdominal rigidity will develop within a few hours. If possible, an estimate should be formed of the depth and direction of penetration. The rectum should be palpated and, if empty, the presence and position of tears noticed. The presence of a tear may be confirmed by proctoscopy, but sigmoidoscopy is of doubtful value and, if the bowel is inflated

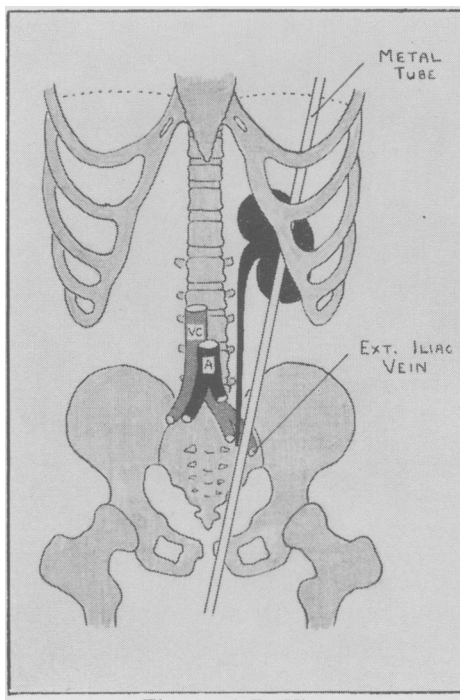


Fig. 1—A.P. View.

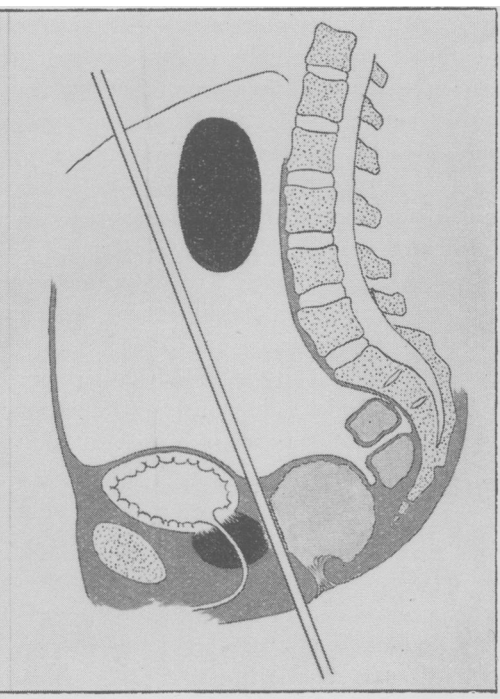

Fig. 2—Lat. View.

during the latter procedure, harm can be done by forcing fæces or fæcal gas into the peritoneal cavity. A straight X-ray of abdomen may help by showing the presence of gas and cystoscopy has been advised to exclude bladder damage.

*Treatment.* (1) The extra-peritoneal type of injury requires no special treatment apart from exploration, possibly excision and adequate drainage of the perineal wound. If the urethra is damaged it should be repaired over a urethral catheter; (2) if the peritoneum has been penetrated early laparotomy has been advised. The rectal tear should be carefully sutured and the peritoneum closed over it. Other abdominal viscera, especially the bladder, should be examined for possible damage. In cases where the bladder has been perforated, supra pubic drainage has been

advised, but it would seem sufficient to repair the bladder tear and tie in a urethral catheter. The abdomen should always be drained and a colostomy is generally advised, but with modern chemotherapy it is probably unnecessary in cases where there has not been gross peritoneal contamination and where the rectal tear can be satisfactorily repaired.

Thomas (1953) advises a colostomy in the following circumstances :—(a) A large laceration of rectum which is difficult to close; (b) a wound involving rectum and buttock, where it may be attempted to lessen infection; (c) severe damage involving rectum and bladder.

Surgical toilet and inspection of the perineal wound should be carried out as in the extra-peritoneal type of injury. If the anal sphincter has been damaged, no rectal drainage is necessary, but if the sphincter is intact and a colostomy has not been performed, it is probably safer to fix a tube in the rectum for a few days, in an attempt to reduce rectal tension. It was with a similar idea in view that some surgeons formerly practised splitting the anal sphincter in the mid-line posteriorly.

Intensive antibiotic treatment is, of course, advisable.

*Influence of full bladder and rectum.* O'Regan (1947) suggests that a full bladder at the time of injury is probably beneficial in that it is likely to act as a buffer, thus protecting the peritoneum from contamination. A full bladder also serves to protect the bowel from injury by displacing it upwards out of the pelvis.

A full rectum, however, is a decided disadvantage in that it increases the risk of gross peritoneal contamination by fæcal matter.

*Prognosis.* It is generally agreed that prognosis in cases with peritoneal involvement is serious. Habhegger (1912) reported a mortality of 25 per cent. in cases with peritoneal involvement and no visceral damage and a mortality of 78 per cent. in cases with visceral injury.

In contrast, O'Regan (1947), reviewing a much smaller series of cases (16), had a mortality of 60 per cent. in cases with peritoneal involvement only and no deaths in six cases with visceral damage. He believes that the prognosis is directly proportionate to the interval between injury and operation and that the grosser the injury the easier the diagnosis, and, therefore, the earlier the case comes to treatment.

In recent years there is no doubt that prognosis has improved considerably with the use of modern antibiotics.


## Summary.

In a boy of 16 years a metal tube penetrated through the perineum for 18 inches, tearing the rectal wall and the left external iliac vein, and, passing through the abdomen, it entered the left pleural cavity, where an empyema developed. Despite this, and infection and fibrosis around the left ureter and unilateral loss of renal function, the boy is now well.

The literature is reviewed and the treatment of impalement injuries discussed.



I am indebted to Dr. J. C. Robb, M.D., M.Ch., for his help and advice. I am also grateful to Dr. Ritchie, Dr. Millar, the Nursing Staff of the Downe Hospital, and the various Royal Victoria surgeons who co-operated in the treatment of this case.

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# Can Renal Calculi be Prevented?

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*A paper presented to the Ulster Medical Society on 3rd February, 1955*

RENAL CALCULUS is a common disease in Northern Ireland. In the past fifteen months I have seen 55 cases. In 54 per cent. of these cases calculi have been formed more than once, and in 33 per cent. stones have been formed in both kidneys on more than one occasion, not counting two cases in which there were bilateral calculi when the patient first appeared.

TABLE 1.

RENAL CALCULUS.

| | | No. | Single Episode | Recurrents | Recurrents Bilateral |
|---|---|---|---|---|---|
| Adults | —Male | 28 | 13 | 15 | 10 |
| | —Female | 22 | 9 | 13 | 8 |
| Adolescents | —Male | 3 | 2 | 1 | 0 |
| | —Female | 0 | 0 | 0 | 0 |
| Children | —Male | 1 | Bilateral | 0 | 0 |
| | —Female | 1 | 0 | 1 | 0 |
| TOTAL | | 55 | 25 | 30 (54%) | 18 (33%) |

The high incidence of recurrence of stones after operative removal makes it important to search for some efficient method of prophylaxis. It would also be of great interest if it were possible to discover a method for dissolving even small stones by medical means. Dissolution of stones is not an impossibility, and there have been rare reports in the literature of the spontaneous dissolution of calculi; about sixteen cases in all have been reported, mostly recumbency stones (Elliot, 1954). It has been shown by the use of radio-active calcium that the ions on the surface of the stone are continually passing into solution and fresh ions are being deposited again (Cristol, Bothe, and Grotzinger, 1948; Benjamin, Newman, Thompson, and Waterhouse, 1950). These reports point to the possibility of dissolution of stones, if the solubility of the stone-forming substances in urine could be increased. There have been attempts to do this in cases where direct access to the stone could be obtained via a nephrostomy tube, but I do not wish to discuss these because such cases form only a small fraction of stone patients.

I will mention briefly some of the factors which have been suggested as a cause for stone formation, and will confine myself in the main to stones in which the inorganic substance is a calcium salt, since these are by far the commoner type of stones. The causes usually suggested for stone formation are shown in Table 2.

TABLE 2.

CAUSES SUGGESTED FOR STONE FORMATION.

1. Urinary infection.
2. Urinary stasis.
3. Vitamin A deficiency.
4. Excess excretion of stone-forming substances.
5. Change in the urinary colloids.

1. Urinary infection frequently accompanies renal calculi, and many workers in the past have regarded this as being of great importance in the formation of stones, especially infection with urea-splitting organisms. Hellström (1938) claimed to have identified Staphlococci in the matrix of a large number of calculi, but it is difficult to see how he could have detected their presence after the treatment to which he had subjected the stones.

TABLE 3.

RENAL CALCULUS.

| Type | No. Cases | Infected Urine | % Infection |
|---|---|---|---|
| Single Episode - - | 25 ... | 13 ... | 52 |
| Recurrent - - - | 30 ... | 18 ... | 60 |
| Recurrent bilateral - - | 18 ... | 12 ... | 66 |

Many cases of renal calculi occur without an infected urine, and in my series 24 out of 55 (44 per cent.) did not show evidence of infection at any time. The series contains six cases of recurrent bilateral calculi in which infection has not been demonstrated, and there are also four cases of recurrent unilateral stone without infection. Another fact which suggests that infection is probably not an essential factor in the pathogenesis of renal calculi is that pyelitis and pyelonephritis are very common diseases in comparison with stone, and although similar organisms are frequently found in both diseases, many patients with chronic urinary infection never develop stones. However, infection probably plays a part in aiding the growth of stones in patients already in some way predisposed to them.

2. Many people have suggested that an obstructive lesion in the urinary tract may cause the formation of calculi, and some have postulated that stones never form in the absence of obstruction. It is obvious that obstruction would favour the retention of any minute deposit of organic or inorganic material around which a macroscopic calculus could be formed, but few cases of calculi are associated with gross obstructive lesions, probably because the urine from an obstructed kidney is very dilute (Woodside). In cases where there are recurrent unilateral stones there might be some physiological obstruction on the stone-forming side. Urinary stasis appears to play a part in the formation of recumbency stones, but again, many patients are confined to bed for long periods, yet do not develop stones.

3. Vitamin A deficiency has often been evoked as a cause for calculus formation, mainly because diets deficient in vitamin A have been used for the experimental production of calculi in rats. These diets are also unbalanced in mineral elements,

and stones can be formed in rats on diets which contain ample amounts of vitamin A. The relationship of these findings to the human disease is uncertain. The hyperkeratosis seen in the renal pelvis in the experimental avitaminosis is not a feature of the human calculus containing kidneys. A number of series of human cases has been surveyed for evidence of vitamin A deficiency, and usually no evidence of this has been found. Sobel (1952) has suggested that there might be a localised deficiency of vitamin A in the kidneys of stone patients, due to poor transportation of the vitamin across cell membranes. A vitamin A depleted animal, when given small amounts of vitamin A, stores it first in the kidneys. Two of Sobel's patients who had histories of repeated stone formation were given 40,000 units of vitamin A daily for two years. No new stones formed during this period, and stones present at the beginning have shrunk. It is difficult to see how this hypothesis could be proved, but it is an interesting possibility.

4. Some stone patients excrete greater amounts of the stone-forming elements than do normal individuals. This is true of cystinurics, who tend to form cystine stones. However, the relatives of the patients with cystine stones are sometimes found to excrete abnormally large amounts of cystine yet never form demonstrable stones. Another group of patients who excrete the stone-forming substances in greater amounts than normal are patients with hyperparathyroidism, and these patients are considered to account for anything up to 20 per cent. of all cases of renal calculi (Pyrah, 1955). It may be that hyperparathyroidism is an even more common cause for renal calculi than this suggests, because the condition is often not looked for. It is noteworthy that not all patients with hyperparathyroidism form calculi; in Hellström's series (1954), 30 per cent. did not have calculi. Others have tried to show that even in the cases without hyperparathyroidism there is an increased output of calcium in the urine. Sutherland (1954) claimed to find an increased output in nearly 60 per cent. of his cases, but his criteria for increased excretion are not sufficiently rigid. In my series I have estimated the urinary output of calcium on a basal diet containing 154 mg. calcium, and have found 7 out of 28 patients (25 per cent.) who had an excretion of over 200 mg., while none of my 10 normal control subjects exceeded 150 mg. on the same diet. These, with increased output, have all, except one, had recurrent calculi, and it may be that they include some patients with a minor degree of hyperparathyroidism, but although several cases are suspect, I feel that there is not sufficient evidence to justify exploration of the neck in search of a tumour or hyperplastic parathyroids. Six cases who persistently form stones have an excretion of under 100 mg. calcium per day.

5. The urinary colloids have been involved in the theories of calculi formation in two ways. Some have suggested that there might be a deficiency of colloids, and therefore less surface area to which the stone-forming elements could be absorbed, and hence prevented from precipitation. Others have postulated that in stone patients the colloids may alter in some way to form a gel around which, and in which the mineral salts are deposited to form stones. The latter theory has been brought into prominence in the recent past by the work of Butt on the injection of

hyaluronidase for the prevention of calculi. He claimed great success with this, but others have not been able to repeat his good results, and have even suggested that hyaluronidase therapy appears to increase the rapidity with which stones are reformed (Prien, 1954). Butt claimed that the injection of hyaluronidase caused a reduction in the surface tension of the urine, presumably due to the excretion of hyaluronic acid. If this is so, hyaluronic acid ought to be present in normal urine, and I have been unable to demonstrate its presence by incubating urine with hyaluronidase, and looking for the reducing compounds that ought to be produced by its hydrolysis. Other workers have been unable to show any reduction in the urinary surface tension after the injection of hyaluronidase into normal individuals (Smiddy, 1954). Narins, Simon, and Oppenheimer (1948) reported that when stones were incubated *in vitro* with hyaluronidase, they underwent fragmentation, but I have been unable to find any such effect, even after prolonged periods of incubation up to a week. It has also been reported that hyaluronidase will not prevent the formation of stones around foreign bodies introduced into the urinary tract of rats (Smiddy, 1954).

There does not appear to be any common factor which would serve to link these causes for stone formation, and it is noteworthy that stones are not always formed when any of these conditions are present, and stones can be formed in the absence of all of them. It seems reasonable to suppose that there might be some underlying condition which predisposes to stone formation, and factors such as urinary infection, stasis or increased urinary output of calcium only make such a tendency more marked. With this idea in mind, I became interested in how the inorganic salts are kept in solution in normal individuals. It has long been recognised that urine is supersaturated with regard to the major stone-forming substances. Why do we not all have stones? It has been considered that the solubility of these stone-forming substances depends on: (1) the pH; (2) the presence of other electrolytes; (3) the so-called hydrotrophic action of urea; (4) the protective action of the urinary colloids. I will consider the first three factors together. I have prepared a solution containing all the major cations and anions in the proportions in which they are usually present in the urine. Physiological amounts of urea and uric acid were added, and the pH was adjusted to 6.0, at which point all the calcium would have gone into solution if it had been urine. After shaking the mixture and leaving it to sit for several hours, it was found that only 30 per cent. of the expected calcium was in solution, and after five days 47 per cent. was in solution. At this point the addition of amino acids in physiological amounts brought another 22 per cent. into solution. I will refer to this point again later. It was necessary to take the pH down to 5.3 before all the calcium was held in solution, whereas normal urine will hold a similar amount of calcium in solution at a pH of 7. This suggests that there is some substance acting in normal urine other than the electrolytic effect of other salts, and the hydrotrophic effect of urea, since these were both present in my synthetic urine. I find that calcium tends to precipitate from the urine of my stone patients at a lower pH than in the normal controls.

A consideration of the other substances normally present in urine in amounts that make them likely to account for the large amount of calcium that can be held

in solution pointed to the amino acids, of which over 6 gms. are excreted daily. It was thought that these might form a soluble compound with the calcium and hence hold it in solution. It is known that amino acids form soluble chelation compounds with such cations as zinc, cobalt, nickel, and copper; but there is little in the literature about their behaviour with calcium. These chelation compounds are interesting, because, if they are formed in urine, they might bind the calcium in soluble form so that it would not be available for precipitation as calcium oxalate or phosphate. I was able to show that in a simple solution at physiological pH the addition of amino acids could prevent the precipitation of calcium as a phosphate, but it required relatively large amounts of the amino acids to do this. Glycine, alanine, hippuric acid, glutamic acid, and glycylglycine all had appreciable effect, but the other amino acids normally occurring in urine were much less active. This prompted me to add amino acids to normal urine to see if this increased the amount of calcium that could be held in solution. It is sometimes possible to demonstrate that this is so, but the magnitude of the effect varied from urine to urine, and occasionally no increase at all can be detected. These experiments are difficult because they require an exact control of the pH. However, in the synthetic urine the addition of a mixture of amino acids increases the amount of calcium held in solution by 22 per cent. It may be that the inconsistent results obtained with urine may be explained by the possibility of a balance existing between the various amino acids, because in the synthetic urine a mixture of amino acids seems to have greater effect than a single amino acid. This is as far as I have progressed with this side of the work up to the present.

If the amino acids are part of the mechanism which prevents the precipitation of calcium salts in the urine of normal individuals then stone patients might excrete less amino acid than normals. On chromatography of their urine many of them appear to have a reduced output of all amino acids. Some patients who are known to form calcium stones have a marked cystinuria, and this does not appear to be due to renal tubular damage. The significance of this finding is as yet unknown, but further work on this point is in progress.

A further test of the amino acid theory is being carried out on rats. A large batch of rats are being fed on a diet which is known to produce stones. These are divided into groups, one of which acts as a control. The other groups are being fed various amino acids. If the amino acids are effective there should be a lower incidence of stone formation in the treated than in the control group, but the results of this experiment will not be forthcoming for several months yet. The next step would be to try the effect of feeding additional amino acids to a group of patients who are known to form stones fairly rapidly. A number of patients are known who would form a suitable group. A difficulty is the fact that amino acids are very expensive. A possibility that suggests itself is to feed a high protein diet, and several patients have been started on a diet containing 200 gm. protein per day. This. too, is expensive, and it may be that the protein metabolism of these people differs from that of normal individuals in some essential way, and I may not succeed in altering their urinary amino acid output towards a more normal picture. It is

intended to repeat the chromatograms on these people after they have been on the high protein diet for a few months and to note any change that may have occurred.

Can renal calculi be prevented? My work on amino acid is not sufficiently advanced for its value to be assessed. What can we do for these patients at present? First of all, we ought to exclude hyperparathyroidism as a cause of recurrent stone formation. Those patients who excrete abnormal amounts of cystine ought to be given alkalis in the attempt to keep the urine alkaline, as cystine is more soluble in alkaline solutions (Dent, 1955). Every effort ought to be made to clear up urinary infection where it exists. Since most stones are mixtures of calcium oxalate, phosphate, and sometimes carbonate in varying proportions, it is more likely that the calcium is of greater importance than the anion, and therefore special diets would not seem to be of much help, as it is practically impossible to feed a low, or even a moderately low calcium diet in these days of calcium fortified flour. When the stones are predominately calcium phosphate it would appear logical to give aluminium hydroxide to lessen absorption of phosphate. It also seems reasonable to encourage them to take as high a fluid intake as possible. I ask them to drink sufficient fluid in the evening to necessitate them passing urine once during the night.

This work is being carried out with the aid of a grant from the Medical Research Council, under the guidance of Professor Bull. I am also indebted to the Northern Ireland Hospitals Authority for facilities made available in the Royal Victoria Hospital and the Royal Belfast Hospital for Sick Children. I owe a particular debt to the surgeons who have provided me with the clinical material, especially to the late Mr. Woodside, from whose wards much of it has come. I am grateful to Mr. D. W. Neill and the Department of Biochemistry of the Royal Victoria Hospital for help with biochemical determinations.

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# Neonatal Respiratory Obstruction due to Hygroma Colli Cysticum

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As long ago as 1843, Werntier described cystic hygroma as a new growth, but its cause is now generally accepted as due to maldevelopment of the lymphatic system. In the neck, according to Sabin (1912), this begins in mammals in the two jugular sacs on either side, near the junctions of the internal jugular and subclavian veins. Small veins branch off the internal jugular vein, lose their connections with the vein, and coalesce to form sacs. At a later period, the lymphatic vessels join the veins again, into which they empty. Finally, the primary groups of lymph glands develop from these primitive vessels. In man, two jugular and two subclavian sacs are joined into one structure on each side; this fact explains the extension of many cystic hygromas upwards into the neck and downwards under the clavicle.

The association of serious respiratory obstruction with cystic hygroma in the newborn infant is uncommon. Cases have been reported by Goetsch (1938) and by Sarason and Roberts (1953), and, from the point of view of the anæsthetist, by Eckenhoff (1951). Respiratory obstruction is probably due to several factors, among which are (a) the infiltrative nature of the condition, which, in some cases, has been found to extend as far as the frenum linguæ, and the critical sub-mylohyoid region, (b) macroglossia, and (c) the effects of hæmorrhage, possibly as a result of birth trauma, causing enlargement of the cysts leading to an increase in tension and pressure on the trachea. Post-operatively, the clinical picture may become even more complex.

## Case Report.

Baby McA. was admitted to the City and County Hospital, Londonderry, on 11th July, 1954, delivery having occurred normally at home some twelve hours before admission. On examination she was in acute respiratory distress, and there was gross swelling and deformity of the neck. On first inspection this was considered the cause of the dyspnœa, but it was nevertheless considered advisable to carry out urgent radiological investigation of the thorax to exclude the presence of other congenital abnormalities such as a malformed diaphragm, which could, of themselves, have rendered survival impossible. No such abnormalities were, in fact, found. The infant exhibited gross deformity of the thoracic region and neck, which latter area appeared to be the seat of a very large hygroma cysticum extending upwards into the region of the angles of the mandible, the submandibular region, and even into the cheeks. There was associated macroglossia and macrocheilia. The thoracic deformity was apparently due to the strong respiratory

efforts of an otherwise healthy infant acting on a pliable and elastic thoracic skeleton. While the upper thorax was completely obscured, the inspiratory activity produced an elevation and protrusion of the sternum, the chest assuming an exaggerated "pigeon-breast" appearance on inspiration.

*Treatment.* As a first measure, a size 00 endotracheal tube was passed, laryngoscopy being rather difficult due to the macroglossia and extreme anterior position of the larynx—even further forward than in the normal infant. The larynx itself appeared normal. When the tube was in situ, the infant's condition improved remarkably, and the thoracic outline lost its deformity.

Further treatment now became a matter of comparative urgency, in view of the certainty of the endotracheal tube causing laryngeal sepsis if it were left in unduly long, and operation was decided upon.

Premedication of atropine sulph. gr. 1/200 was administered, and anæsthesia was induced via the endotracheal tube using nitrous oxide, oxygen and minimal ether. Through a collar incision suitably placed, the more superficial portions of the loculated mass were easily removed, but as dissection proceeded, it became manifestly impossible to accomplish total removal. The deeper dissection progressed, the more cysts were uncovered, extending deeply into the floor of the mouth, the region of the styloid process, and downwards at least to the superior mediastinum. Nevertheless, it was hoped to accomplish sufficient "decompression" of the neck to relieve the respiratory obstruction. To this end, as many of the cysts as possible found in relation to the trachea were removed, but many in the deeper planes of the neck, the sub-mylohyoid and styloid regions, had perforce to be left. After removal of as many of the cysts as possible, the incision was sutured with drainage.

At the end of the operation, the endotracheal tube was removed, and the airway now seemed satisfactory. The infant was returned to an oxygen cabinet, but soon, however, respiratory obstruction was again in evidence, and was not relieved by traction on the tongue. Convulsions and pallor (signs of anoxia in the neonate, which can be grossly anoxic without cyanosis under these conditions) were not noted. Repeat laryngoscopy confirmed the presence of early œdema of the base of the epiglottis and ary-epiglottic folds, but, at this stage, no involvement of the vocal cords or narrowing of the airway had taken place. Re-insertion of the endotracheal tube would only have increased the risk of laryngeal sepsis, and tracheotomy was decided upon. This measure restored the airway, and the infant was again returned to the oxygen cabinet breathing easily and giving no further cause for alarm. The oxygen cabinet proved ideal for nursing an infant with a tracheotomy, as no clothing was required. The oxygen was cut off, and ventilation was by fan only. There was provision for head-down tilt, which facilitated clearing of the tracheotomy tube—frequently necessary for the first few days. For this, we used a simple mouth operated mucus extractor, a short piece of fine rubber tubing being passed into the tracheotomy. The infant progressed very favourably, and was later even able to feed normally from a bottle, though intragastric tube feeding was necessary in the early post-operative days.

Unfortunately, about three weeks after operation, the wound, which had healed well, began to ooze serous fluid near the tracheotomy opening (which had been maintained with a view to possible radiotherapy for the remnants of the tumour in tongue and cheeks) and signs of sepsis in the neck now appeared which did not respond to penicillin. The infant's condition deteriorated, and death occurred on 7th August.

*Pathology.* About two-thirds of the cystic tumour excised was unruptured and in one mass. This was examined by Dr. J. E. Morison of the Central Laboratory, Belfast, who reported as follows :—

"The specimen after fixation is roughly spherical and measures 5.0 by 3.5 by 3.0 cm. The surface is coarsely irregular and only a few tags of adipose tissue are adherent to it. The mass is made up of multiple small vesicles which vary in size from the largest of diameter 1.5 cm. to minutely small cysts. The walls of these are sometimes thick and opaque and sometimes almost translucent. The cysts contain slightly opalescent fluid, but a few contain brownish fluid resembling altered blood. The cysts do not communicate freely with one another, and gentle pressure fails to empty one cyst into another.

Histology shows a complex arrangement of cyst walls. These are composed of connective tissue and vary in thickness. The spaces are lined by a thin layer of endothelium. There is no growth of granulation tissue into the spaces. No lymphocytic aggregates are present.

The formation is a cystic hygroma."

## Discussion.

The treatment of hygroma colli cysticum is a subject of considerable difference of opinion. Thus, Sawyer and Woodruff (1951) state that conservative methods are unwise, and advise early operation, before fibrosis occurs. They state that the tumour is inherently radio-resistant. Callister (1941), after his experience of a particularly extensive infiltrating lesion, believes that surgical excision may sometimes be impossible. Ward, Hendrick, and Chambers (1950) report excellent results from surgical excision in all their twenty cases. Hygromas are said by some to undergo spontaneous disappearance, or to disappear following infection, but Figi, quoted by Pfahler and Pulman (1950), stated that, in his experience, acute infection did not cause the growth to disappear spontaneously; rather, it proved fatal in seven of thirteen cases.

Sarason and Roberts (1953) suggested swabbing the remnant with tincture of iodine, but this is obviously inapplicable to cysts that could not be exposed, as in the case under review. As regards macroglossia, Lierle (1944) describes an anterior amputation of the tongue with wedge resection which he has practised successfully in a few of these cases. Pfahler and Pulman (1950) report a case successfully treated by radiotherapy, without interference with growth, and without affecting the skin. This measure, indeed, had been our hope post-operatively, but it was advised against by the radiotherapist.

In this hospital a similar respiratory obstruction occurred in a newborn infant from a thyroid tumour, and death occurred eight hours after operation. In this

infant, however, tracheotomy was not done until it was moribund, and until irreversible anoxic damage had occurred. It would appear that several factors may be operating in the causation of post-operative respiratory obstruction following cervical surgery in the neonate. Œdema may arise following not only intubation, but also dissection close to the larynx and trachea—this latter factor being held to be responsible in the fatal case reported by Hanlon and Seybold (1950), where the lesion was a thyroid tumour. A reflex laryngeal spasm arising from the operation site may also occur, especially when such site involves the cervical region and the external surface of the trachea. It seems to us that early tracheotomy is essential in this type of case where the insidious onset of œdema in the immediately post-operative period may escape attention until it has produced serious respiratory obstruction. There can be no doubt that anoxia, however slight, is of the greatest possible danger to these infants, and its correction should be undertaken with the utmost urgency. A healthy child, when first submitted to anoxia, will show the cyanosis with which all are familiar, but one in poor condition, shocked or already the victim of anoxia, may only respond by convulsions or gross pallor. With full oxygenation, the neonate is extremely tolerant of surgical interference, and it should, therefore, be our aim to place respiratory function first in our evaluation of such neonatal pathology as is here described.


## Summary.

A case of hygroma cysticum colli causing respiratory obstruction in the newborn infant is described.

The causation and treatment of respiratory obstruction after extensive cervical surgery is discussed.

A plea is made for earlier prophylactic tracheotomy in these cases to avoid the obstruction caused by œdema of the larynx and the progressive development of anoxia in an already shocked child.


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# The Application of Modern Techniques to the Detection of a Typhoid Carrier

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THE search for satisfactory methods of isolation of *Salmonella typhi* and *Salmonella paratyphi B* from water, contaminated with sewage, was greatly advanced when Wilson and Blair (1927) introduced their glucose-sulphite-iron-bismuth brilliant green medium. Further help came with the development of the selenite F medium of Hobbs and Allison (1945a). The next great advance was the description by Moore (1948) of a successful method of sampling sewage and sewage polluted water during a search for carriers of *Salm. paratyphi B*. This consisted in placing a gauze swab in the sewers for two to five days and then culturing the entire specimen in selenite F medium and subculturing on to Wilson and Blair's medium. Soon after this Moore (1950) extended the use of his technique to a search for *Salm. typhi,* and Lendon and Mackenzie (1951) further demonstrated the great value of the method in the search for enteric carriers.

The present paper describes the prolonged, but finally successful, search for a typhoid carrier, who proved to be the source of infection of nine cases of typhoid fever over a period of four years, using the methods outlined above, and it tries to show how easily errors and misinterpretations of results can cause confusion and delay in finding the carrier.

In 1951 three cases of typhoid fever were notified in and around Belfast, all in boys aged 11 to 15 years. After questioning these boys, it was thought that they had probably been infected while playing in the vicinity of Stream I (see sketch map). Many samples of this stream and the effluents from the septic tanks which discharge into it were taken by the Moore swab technique. All were negative for *Salm. typhi.* Six weeks later a further case of typhoid fever came to light. This patient had been working in the wood through which Stream I flows. Enquiries of this man revealed that there had been, working in the same gang, a labourer who was known to have had enteric fever in 1945. Latrines were not provided for the workmen, and it was felt, at the time, that this known, old case of typhoid fever was the probable source of infection. One sample of fæces was obtained from him, but after that he refused to co-operate. This one sample proved, however, to be negative for *Salm. typhi.* Blood for Vi antibody tests could not be obtained. There the matter rested, apart from the fact that it was shown that the strains of *Salm. typhi* from the three boys and the infected workman were all Vi-phage type C.

In 1952 there were no known cases of typhoid fever connected with this area.

In 1953 there occurred, in the late summer, three more cases referable to the same source. Enquiries from these patients again indicated that Stream I was the probable source of infection. Further repeated samples from this stream and the septic tanks were taken, and again the results were negative. Once again, each of these cases was infected with *Salm. typhi* Vi-phage type C. No other related cases occurred that year.

In 1954 two more cases of *Salm. typhi* Vi-phage type C infection occurred, and both boys had, according to their statements, been playing in and around the suspected Stream I. Samples were taken from the stream and septic tanks, and once again the findings were negative for *Salm. typhi*. When these two boys were discharged from hospital they were taken to the area where they had been playing and were asked to retrace their movements. It was then revealed that they had, in fact, also played around and drunk water from Stream II. Enquiries were reopened with the boys infected in previous years, and two boys of those involved in 1951 and one in 1953 admitted that they also had drunk water from Stream II.

Swabs were placed in Stream II at the relevant position (point E) and *Salm. typhi* Vi-phage type C was isolated.

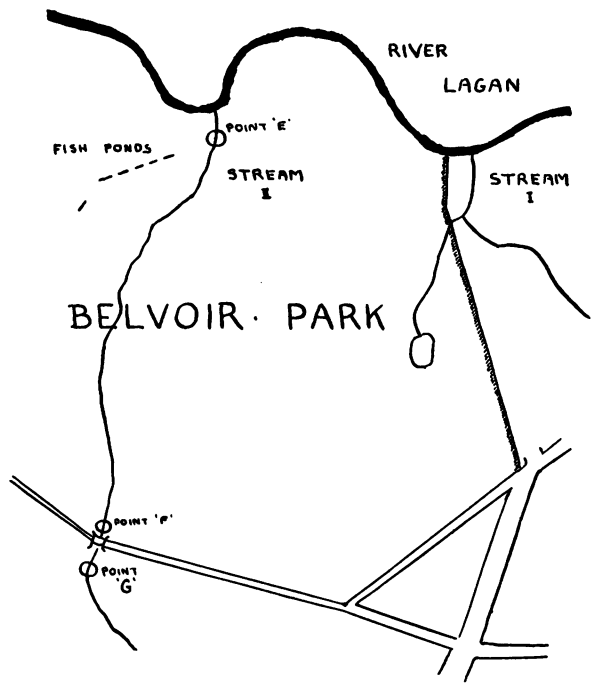
It remained for the source of this contamination to be traced. Swabs were laid upstream from point E and in the fish ponds. Point E and above continued to be positive on almost all occasions when sampling was done and there was also one isolation from the disused fish ponds. This, too, was a strain of *Salm. typhi* Vi-phage type C. As all further swabs taken from the fish ponds have been negative, it seems probable that the result was unconnected with the continuing source of pollution. Swabs were laid in Stream II and its tributaries, and as the stream was progressively examined towards its source it continued to yield *Salm. typhi* until a swab from point G upstream from the bridge was found to be negative. Near this bridge there were the outlets of pipes carrying the effluents from different septic tanks in the neighbourhood. These effluents were examined, and one (F) yielded *Salm. typhi* Vi-phage type C. Enquiries were made at each of the houses served by this pipe, and at one a woman was found who had had typhoid fever in 1936. Samples of fæces were obtained from this woman and the other members of the household. Only the old case of typhoid was found to be positive, and the strain from her was found to be of Vi-phage type C. Colour tests with fluorescein were carried out and it was confirmed that the effluent from the septic tank used by this household discharged through the pipe F.

To exclude the possibility that there was a second excreter of *Salm. typhi* Vi-phage type C in the area, individual samples from all the residents whose sewage discharged into Stream II at this point were examined. None yielded *Salm. typhi*.

## Methods.

Moore (1948) swabs were used throughout the investigation except when fæcal samples from individual suspects were being examined. The swabs were left in situ for seventy-two hours and then placed in wide necked honey jars for transport to the laboratory. Fifty ml. of the "liquid" expressed from the swab was added to

50 ml. double strength selenite F medium (Hobbs and Allison, 1945a) and incubated at 37° C. After 24 and 48 hours incubation, subcultures of the undiluted selenite culture and serial dilutions of it at 1 in 1, 1 in 5, and 1 in 25, in sterile saline were made on the modified bismuth sulphite medium of Hobbs and Allison (1945b). This dilution method had been suggested to us by Dr. Moore in a personal communication and it proved to be a most helpful refinement in that colonies of *Salm. typhi* might be present or absent in any of the four dilutions employed in a haphazard and entirely inexplicable distribution. The additional labour involved in carrying out this procedure was fully justified by the greatly increased numbers




of isolations achieved by the method. Dr. Moore had suggested that a 1/125 dilution might also help, but it was found that *Salm. typhi* was never isolated from this dilution alone, and in the examination of later samples this was dropped.

All isolates of *Salm. typhi* were confirmed serologically and phage typing of the strains was carried out when necessary.

## Discussion.

It is apparent that correct history taking, in relation to the possible place of infection of a case of enteric fever, is of the greatest importance. In the present instance the source of infection might well have been traced years earlier if only it had been discovered that the boys had been playing in and around Stream II as well as Stream I. We feel that, when it is possible, the patient should be asked

to demonstrate all the places which he has visited in addition to the usual verbal descriptions.


## Summary.

The successful search is described for a source of *Salm. typhi* indirectly responsible for nine cases of typhoid fever over a period of four years. The usefulness of the Moore swab technique of sampling is demonstrated. More accurate identification of the scene of the patients' activities might have prevented the later cases occurring.



## Acknowledgments.

We are grateful to Dr. Felix and Dr. Anderson of the Central Enteric Reference Laboratory and Bureau, Colindale, for phage typing the strains of *Salm. typhi,* and we acknowledge our thanks for the help we have received from the Sanitary Officers of No. 3 Division, Co. Down, and the technical staff of Central Laboratory, especially Mr. J. E. Carleton and Mr. Norman McDonald, A.I.M.L.T.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Since this investigation was completed and the source of infection demonstrated one further case of typhoid fever has been traced to this source. We understand that the Rural District Council for the area is putting work in hand to provide a pumping station to raise the sewage from this area into the main Belfast sewage system.

# Tuberculin Sensitivity in Town and Country Dwellers

## *A Survey in Co. Fermanagh, Northern Ireland, 1949-1951*

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THIS survey was carried out at Enniskillen, the county town of Fermanagh. The 2,029 Fermanagh subjects tested can be divided into three groups :—

1. Attenders at Enniskillen Chest Clinic—1,429.
2. School boys from Co. Fermanagh homes, aged 8-18 years, attending a public school in Enniskillen—169.
3. Employees of a local textile factory—431.

### METHOD OF TESTING.

For all, except a few who are specially mentioned, this was the Mantoux test. Owing to the impossibility of recalling all the clinic attenders for a second test, the Mantoux test using .01 mgm. of Old Tuberculin (O.T., 0.1 ml. in 1/10,000 dilution) had to be accepted in these. All others were tested with 1 mgm. O.T. (0.1 ml. in 1/100 dilution).

Tuberculin jelly (3 per cent. O.T. in a jelly base) was used as a preliminary test early in the series, on those under 10 years at the clinic, and under 12 at the school, but was soon abandoned. For the reasons given below, the entire clinic results of the jelly test were discarded, but as only three of the Fermanagh school boys had the jelly test, the figures for them were retained.

### INFLUENCE OF TEST USED.

The Mantoux test using .01 mgm. O.T. was found to be very accurate in young children. Under the age of 10 years only 3 per cent. of 368 children negative to this test proved to be positive to 1 mgm. O.T. Between the ages of 10 and 14 years, 12.2 per cent. of negatives to .01 mgm. became positive to 1 mgm. O.T. These percentages vary in different communities (Deeny, 1954). In older groups the percentage of the negatives becoming positive to the stronger test increased so that .01 mgm. O.T. alone was not reliable in these. Thus 15.2 per cent. of 59 factory workers average age 23, and 36 per cent. of 200 police recruits average age 20, both groups negative to .01 mgm. O.T., became positive to 1 mgm. These recruits were from all parts of Northern Ireland.

About 10 per cent. of false "positive" reactors, often impossible to distinguish from the true, was found in this survey to occur with the tuberculin jelly test (Caplin, *et al.*, 1954). Thus 248 clinic children under 10 years of age showed 29 per cent. positive to the jelly test, whereas 209 clinic children of the same age Mantoux tested with .01 mgm. O.T.—a highly sensitive test at this age in our series—showed 21 per cent. positive. This meant that some 15 children in the first

group missed the chance of vaccination with B.C.G. More obvious was the discrepancy in 28 twelve-year-old public schoolboys jelly tested, of whom 17 (64 per cent.) were "positive," a figure 15 per cent. higher than that for the entire school at all ages and Mantoux tested with 1 mgm. O.T.

## Results.

*Pre-School Children (clinic children age 0 to 5 years).* The results from the jelly test were discarded for the reasons given, leaving 209 children Mantoux tested with .01 mgm. O.T., of whom 12.4 per cent. proved positive. Of these, 48 in their fifth year contained 7 (14.5 per cent.) positive reactors. As in this age group less than 3 per cent. of those negative to .01 mgm. O.T. became positive to 1.0 mgm., these figures can be calculated to represent about 15.3 and 17 per cent. positive to 1 mgm. O.T. These results may be compared with those given in Table 1. In making the comparison, the high tuberculin reactor rate ordinarily encountered in clinic attenders, apart from contacts, must be borne in mind (Clarke, 1952).

TABLE 1.

| Age | Survey | Per cent. positive to 1 mgm. O.T. Mantoux |
|---|---|---|
| 5 years ... | Belfast | ... 21.4 to 26.4 (Sherrard, 1952) |
| 5 ,, ... | Rural Northern Ireland | ... 26.6 ,, ,, ,, |
| 5 ,, ... | Rural England and Wales | ... 20.3 (Daniels, 1952) |
| 5 ,, ... | Co. Fermanagh (town and country) | ... 17.0 (Present survey) |
| 0-5 ,, ... | Co. Fermanagh (town and country) | ... 15.3 ,, ,, |

*School Children (clinic attenders, aged 10-14 years).* All clinic children aged between 6 and 10 years were jelly tested and the results were therefore discarded. Among 307 children, aged 10-14, and Mantoux tested with .01 mgm. O.T., 21.5 per cent. were positive. Since 12.2 per cent. of the negatives at this age become positive to 1 mgm. O.T., the figure positive to the latter test would probably be 24.4 per cent.

*Public School Boys, aged 8-18 years.* These were tested when necessary with 1 mgm. O.T., and the results in different groups are given :—

Boys from Enniskillen town 40, positive 20 or 50 per cent.
,, ,, small country towns 73, ,, 21 or 29 ,, ,,
,, ,, Fermanagh country 56, ,, 8 or 14 ,, ,,

These and the clinic results may be compared with those in Table 2.

TABLE 2.

| Age | Survey | Per cent. positive to 1 mgm. O.T. Mantoux |
|---|---|---|
| 8-18 years ... | Rural England and Wales | ... 45 (Daniels, 1952) |
| 5-15 ,, ... | Rural Northern Ireland | ... 48.8 (Sherrard, 1952) |

*Young Adults (the Clinic Survey).* This included 502 persons aged 15-35 years, of whom 38 per cent. were contacts or had a family history of tuberculosis. Most of the remainder were suspects with symptoms, referred by their family doctors. Of these 53.4 per cent. were positive to the Mantoux test using .01 mgm. O.T.

*The Factory Survey.* These were 248 men of average age 26 years, and 183 women of average age 20 years. The Mantoux test was employed, using 1 mgm. O.T. when necessary. The results were : males 62.5 per cent., females 36 per cent. positive. The proportion of rural dwellers amongst them was stated by the factory medical department to be 70 per cent.

The clinic group could not be compared with surveys employing 1 mgm. O.T. Mantoux.

In rural England and Wales males, aged 19-20 years, showed 68.7 per cent. positive to 1 mgm. O.T. Mantoux (Daniels, 1952). MacFarlane and Jones (1953) Mantoux-tested 148 English girls, aged 20 years, of mixed rural and urban extraction, and found 75 per cent. positive to 1 mgm. O.T. The County Fermanagh figures are lower than either of these, and the female figures much lower.

Boys, aged 15, in rural Northern Ireland, contained 64.8 per cent. positive, and girls of the same age—the oldest group tested—54.4 per cent., using the Mantoux test with 1 mgm. O.T. on those negative to a preliminary tuberculin jelly test (Sherrard, 1952). Experience at Enniskillen indicates that the use of the tuberculin jelly may have increased the percentages positive, but taken as they stand, the factory figures are considerably lower, even at the much higher age group.

*Those aged 35 years and over.* These numbered 183 persons in the clinic survey, of whom 62.8 per cent. were found to be positive to .01 mgm. O.T. Mantoux. Contacts and those with a family history of tuberculosis numbered 70, and the remainder, with few exceptions, were suspects with symptoms and referred by the family doctor. Clarke (1952) gives Myren's figures for persons aged 40-50 years in rural Norway in 1950 as 69.1 per cent. positive to the Pirquet test. This test is known to be approximately equal to our Mantoux with .01 mgm. O.T. (Clarke). Rich (1950) quotes Aronson as finding 76.4 to 83.3 per cent. positive to 1 mgm. O.T. in persons aged 40 years and over in rural areas in America between 1933 and 1935. Norway possesses a tuberculin reactor rate lower than many European countries. Our figures for older subjects do not conflict with the finding in the younger age groups, and suggest a low degree of tuberculin sensitivity in County Fermanagh at all ages.


## Summary.

Pre-school children, school children, and young adults have a lower tuberculin reactor rate in County Fermanagh than in other parts of rural Northern Ireland so far tested, and lower than the average for rural England and Wales. At the age of 35 and after, the rate is also low, and is presumed to be in keeping with the figures for the younger age groups.

The results for the public schoolboys suggest that, were rural dwellers considered separately, much lower reactor rates would be found in these.

My warmest thanks are due to the Tuberculosis Health Visitor, the school matron, and the nursing sister at the factory for their willing help, and to the clinic secretary for most of the calculation and for the typing of this paper.

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## REVIEW

AIDS TO PSYCHIATRY. By W. S. Dawson, M.A., D.M., F.R.C.P.(Lond.), F.R.A.C.P., D.P.M. Seventh Edition. (Pp. viii + 314. 8s. 6d.) London: Baillière, Tindall & Cox, 1955.

THIS useful handbook, which has been popular for thirty years, has been revised and brought up to date without increasing its size. The chapters on personality and child psychiatry, which were additions in the sixth edition, have been retained, but otherwise there are many alterations. The section on differential diagnosis has been omitted, and a short one on mental mechanisms is new. The names and sequence of certain chapters are changed, and some subjects are dealt with under different headings. For instance, psychiatric examination is described earlier in the book, and narcoanalysis is more fittingly included in the concise section on treatment, while certification leaves this and is considered with legal aspects of mental disorders. This difficult subject is clearly treated for England and Scotland, but no mention is made of Northern Ireland, where it differs in many respects.

This edition will be welcomed by medical students and workers in many fields in which it is necessary to have a practical knowledge of psychiatry. D. M. G.

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# A Case of Placenta Prævia Increta

*By* M. R. NEELY, M.B., F.R.C.S.Ed., M.R.C.O.G.
Consultant Obstetrician, Daisy Hill Hospital, Newry

By placenta accreta is meant an abnormal adherence of the whole, or part, of the placenta to the uterine wall due to partial or complete absence of the decidua basalis, especially the spongiosum layer. Placenta increta is an uncommon variant of this condition when, in addition, the placenta invades the uterine musculature. The incidence of placenta accreta varies from observer to observer, and is reported as ranging from one in 1956 to one in 40,000 deliveries. Irving and Hertig (1937) in their summary of cases in the literature found only about one out of six cases of placenta accreta to be situated in the lower segment. The incidence of placenta prævia increta is rarer still. Chisholm, in 1948, could find only three recorded cases in the previous ten years. The ætiological factors have been classified by McKeogh and D'Errico (1951). They divide them into two groups, uterine and placental. It is interesting that in this case a cause from each group is present, the uterine factor being previous trauma in the form of two Cæsarean operations and the placental one being its situation in the lower segment.

The patient, aged 36 years, a small woman of height 4 feet 9 inches and dystrophic appearance, was first seen in the thirty-first week of this, her fourth, pregnancy. In her first pregnancy in 1947 she had a classical Cæsarean operation for disproportion. An early abortion two years ago was followed by curettage. One year ago she had an elective lower uterine segment Cæsarean section. Apart from a transverse lie, no abnormality was noted at the first ante-natal examination in the present pregnancy. At the 36th week the lie was still transverse and she was admitted a few days later for elective Cæsarean section in view of the clinical findings and her obstetric history. At no time had she any vaginal bleeding.

It had been intended to perform another lower segment operation, but, while the bladder was being displaced with gauze dissection, the uterus ruptured with almost explosive violence, producing very copious hæmorrhage and exposing the placenta. The rupture seemed to have commenced in the region of approximation of the two previous uterine scars. The infant was rapidly extracted by the breech through the placenta. It was now discovered that the body of the uterus was attached only behind, and only by about one inch of tissue. The placenta extended almost to the internal os. It was intimately attached in the vicinity of the classical scar, this region of the uterus being extremely thin, but separated easily from the lower segment. A subtotal hysterectomy with conservation of one ovary was performed, following which recovery was uneventful.

The infant, a female, weighed 6 lbs. 14 ozs. at birth, and on discharge along with the mother on the fourteenth day weighed 7 lbs. 1 oz., being artificially fed.

The following is an extract from the pathological report for which I am indebted to Dr. J. E. Morison, Central Laboratory, Northern Ireland Hospitals Authority :—

"The placental tissue lies in the lower part of the uterus. Much of it lies within the anterior wall of the uterus. There it forms a mass which has greatly thinned out the uterine wall in its lower part and led to its rupture at one point. This mass of placental tissue lying within the uterine wall is continuous with more placental tissue lying in the lower part of the uterine cavity. The site of this partly buried placental tissue would correspond to a classical Cæsarean scar, but the scar itself cannot now be recognised. It is possible that the placental tissue has herniated into the site of the scar, but it has grown as a mass within the wall which is greatly thinned. There is no decidual reaction at this point, but decidual tissue is present within the uterine cavity. There is a heavy invasion of the wall by syncytial cells of the trophoblast but this is not a malignant change.

"One ovary was submitted. This shows only a few simple follicular cysts. The corpus luteum of the pregnancy would appear to be in the other ovary.

"I think this is to be regarded as a form of incomplete placenta increta."

In placenta increta there is disagreement concerning the significance of the variation in the histological changes reported (Herbut, 1953). The picture in this case would tend to agree with the statement made by Burke (1951) that the villi are not attached to uterine muscle but instead exert a destructive effect.

One cannot avoid feeling that this patient might well have developed a spontaneous rupture of the uterus if her pregnancy had continued for another two or three weeks—but placenta prævia and placenta accreta have only rarely been recorded as associated with rupture of the uterus. Concerning the etiology of rupture following previous uterine trauma, it is generally agreed that the healing of a uterine wound occurs mainly by the deposition of fibrous tissue and that such a scar predisposes to subsequent rupture. It is also generally agreed that the predisposition is aggravated when the placenta overlies the healed scar. There is little agreement, however, between various writers concerning the actual changes in the uterine wall at the site of rupture.

There is evidence that previous uterine trauma is an important etiological factor in placenta accreta, and in view of the gross example of the present case it is suggested that when rupture follows a previous Cæsarean section, the histological study should exclude the presence of any placental elements embedded in the myometrium at the site of rupture.


## Summary.

A case of placenta prævia increta is described in which uterine rupture occurred through a previous Cæsarean scar at the time of an elective Cæsarean section. A suggestion is made that perhaps placenta increta plays a bigger part than is generally acknowledged in the causation of uterine rupture following previous uterine scarring.


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# REVIEWS

## AN ATLAS OF REGIONAL DERMATOLOGY. By G. H. Percival, M.D., Ph.D., F.R.C.P.(Ed.), and T. C. Dodds, F.I.M.L.T., F.I.B.P. (Pp. viii + 264; figs. 475. 100s.) Edinburgh and London: E. & S. Livingstone, 1955.

This atlas will be generally welcomed as providing a comprehensive collection of colour photographs of skin diseases at a cost which, if not exactly low, is probably as low as it could be made to-day. The authors have chosen to group the photographs regionally so that one can easily compare two separate diseases affecting the same area. This will be of great help to students, and though at first it might be thought to have unfortunate disadvantages yet, since this is an atlas, the scheme works well. The slight disadvantage of duplication of certain photographs is, if anything, probably an advantage to junior students.

The quality of photography and reproduction is exceedingly high—admittedly there are a few "duds," for example, figs. 35, 147, 162; but some of the photographs are outstandingly good, for example, figs. 10 to 13, 27, 42, 65, 164, 176, 247, and 344. The reviewer does feel, however, that quite a few of the photographs are superfluous, for example, figs. 32 to 35 (two could be omitted), figs. 44 to 45 (one could be omitted), figs. 91 to 95 (two or three could be omitted).

If one is to criticise this atlas then the main criticism will fall on the text matter. This is short and dogmatic and open to misunderstanding by junior students. The statements made in the captions are frequently of opinions held only by Professor Percival and the Edinburgh School of Dermatology, yet no indication is given anywhere as to what is solely Professor Percival's opinion and what is generally accepted teaching. There are no references at all to other work. Since the majority of the photographs in the atlas are of common conditions the reviewer presumes that the atlas is primarily for the use of junior students. It is certainly going to be extremely difficult—and rather trying—for orthodox dermatologists in other teaching centres to explain to their student class that in a great many cases Professor Percival's opinions cannot be accepted. The greatest confusion occurs in the section on the eczema-dermatitis group of skin diseases. The terms "seborrhœic" and "nummular" are not used, instead there are "flexural infective" and "post-traumatic infective" eczemas. Indeed, "nummular eczema" does not appear in the index. It would appear too that varicose eczema (hypostatic eczema) is a variety of "post-traumatic infective eczema," but no explanation is given of this change in terminology.

It would appear, from some of the statements made in the captions, that if the pemphigus blister is subepidermal then the diagnosis is that of dermatitis herpetiformis, the insinuation being that before one calls an eruption pemphigus one must have an intra-epidermal blister. This is certainly not current teaching. One caption suggests that lichenification occurs only with Besnier's prurigo—but this may be "loose" writing.

The reviewer deeply regrets having to criticise a collection of photographs of this quality because of the unfortunate terminology and opinions expressed in the small text-matter available, but the junior student who learns his dermatology from this atlas will be hopelessly confused by the teaching which he receives in our medical school (and indeed in most other schools).

Molluscum sebaceum is not mentioned, though fig. 126, labelled "squamous cell carcinoma," looks extremely like it.

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section on the diagnostic approach to each symptom is included in the chapter, and this will be found of value in sizing up the relative points of importance in reaching a conclusion.

This method of approach to clinical medicine is, in the reviewer's opinion, of considerable importance, and medical students will find it a most valuable aid in their clinical studies. Not only will students be helped, but every doctor who practises the difficult art of diagnosis will find his knowledge widened and senses sharpened.

This book can therefore be highly recommended to doctors and medical students alike as a stimulating and practical guide to bedside diagnosis, and Dr. Seward is to be congratulated on writing what deserves to be a medical best seller. D. A. D. M.

## PROFESSIONAL NEGLIGENCE. By J. P. Eddy, Q.C. (Pp. xii + 140 + vi. 13s. 6d.) London : Stevens & Sons, 1955.

IMPERITIA culpæ adnumeratur—Unskilfulness is counted as negligence. So said Justinian the law-giver in 565 A.D., and he went on to cite as an example of professional negligence the case of a physician carelessly giving the wrong medicine. The negligent surgeon is even older : the code of Hammurabi of 2084 B.C. says : "If a doctor has opened a man's tumour with a metal knife and destroyed the man's eye, his hands shall be cut off." And throughout the history of our own common law the negligent doctor has appeared not infrequently as a defendant, though it is only in the past five or six years that actions against medical men have become increasingly common. The exact numbers are difficult to ascertain, but some indication can be gathered from statistics of the amounts paid out by hospital authorities in the way of damages. In 1948 the figure was £7,500 : by 1953 it had risen to £153,000.

No one who is acquainted with the true facts imagines for a moment that doctors are becoming more careless : indeed, one has only to chat with an aged practitioner who can describe the conditions of fifty years ago to realise that standards of exactness and thoroughness have risen throughout the present century and continue to rise. The real explanation is that the present situation is partly a by-product of the nationalisation of the medical service and partly the result of the introduction in Great Britain of the Legal Aid system. Instead of the surgeon and physician of the old days whose work in hospitals was voluntary or rewarded merely with a token honorarium, we now have hospital officers who are employees of the hospital authorities. It is no wonder that the attitude of the public towards practitioners has changed, and the slightest suspicion of negligence suggests an action against the hospital in which the damages will be paid out of the limitless coffers of the State. Add to this the fact that Legal Aid comes to the assistance of the potential litigant and we can at once account for the spectacular increase in this type of action.

The limit of a doctor's duty is clear. He does not undertake to cure you, any more than a lawyer undertakes that he will win your case or a clergyman guarantees to procure your salvation. He is expected to bring to the exercise of his craft a reasonable degree of care and skill, but such have been the advances of medical science that what is a reasonable degree becomes a higher standard each year.

The book under review does not deal exclusively with doctors but with professional men generally. Lawyers, bankers, architects, surveyors and many other professional men are under a similar liability and are targets for the same type of action. Nor does the book pretend to be a text-book on the subject. It is a reprint of the Travers Memorial Lectures which Mr. J. P. Eddy, Q.C., delivered at the City of London College early in 1955, and in 140 pages the author has not been able to do more than sketch an outline of the position. That part which deals with the liability of doctors, dentists and hospitals is the most interesting because here the author has had a wealth of modern cases on which to draw for examples. In addition to noting the increased incidence of actions against medical men and medical bodies, he also draws attention to what is undoubtedly a most significant trend, and that is the increased reliance on the maxim *res ipsa loquitur* in actions arising out of medical treatment. This maxim is, in effect, a presumption that because something has gone wrong someone has been careless. It is, perhaps, a tribute to the advances of medical science and the perfecting of techniques that the patient has come to expect complete satisfaction

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No one who is acquainted with the true facts imagines for a moment that doctors are becoming more careless : indeed, one has only to chat with an aged practitioner who can describe the conditions of fifty years ago to realise that standards of exactness and thoroughness have risen throughout the present century and continue to rise. The real explanation is that the present situation is partly a by-product of the nationalisation of the medical service and partly the result of the introduction in Great Britain of the Legal Aid system. Instead of the surgeon and physician of the old days whose work in hospitals was voluntary or rewarded merely with a token honorarium, we now have hospital officers who are employees of the hospital authorities. It is no wonder that the attitude of the public towards practitioners has changed, and the slightest suspicion of negligence suggests an action against the hospital in which the damages will be paid out of the limitless coffers of the State. Add to this the fact that Legal Aid comes to the assistance of the potential litigant and we can at once account for the spectacular increase in this type of action.

The limit of a doctor's duty is clear. He does not undertake to cure you, any more than a lawyer undertakes that he will win your case or a clergyman guarantees to procure your salvation. He is expected to bring to the exercise of his craft a reasonable degree of care and skill, but such have been the advances of medical science that what is a reasonable degree becomes a higher standard each year.

The book under review does not deal exclusively with doctors but with professional men generally. Lawyers, bankers, architects, surveyors and many other professional men are under a similar liability and are targets for the same type of action. Nor does the book pretend to be a text-book on the subject. It is a reprint of the Travers Memorial Lectures which Mr. J. P. Eddy, Q.C., delivered at the City of London College early in 1955, and in 140 pages the author has not been able to do more than sketch an outline of the position. That part which deals with the liability of doctors, dentists and hospitals is the most interesting because here the author has had a wealth of modern cases on which to draw for examples. In addition to noting the increased incidence of actions against medical men and medical bodies, he also draws attention to what is undoubtedly a most significant trend, and that is the increased reliance on the maxim *res ipsa loquitur* in actions arising out of medical treatment. This maxim is, in effect, a presumption that because something has gone wrong someone has been careless. It is, perhaps, a tribute to the advances of medical science and the perfecting of techniques that the patient has come to expect complete satisfaction

every time, and though every intelligent man knows that in all medical treatment there is an element of risk the plaintiff often thinks it worth while trying to convince the court that because there has been a mishap there must necessarily have been negligence. To rebut any such presumption is difficult, and often impossible. But though one has full sympathy with a patient who has met with further injury when in fact he was expecting a cure, yet it should not be forgotten that a verdict of negligence against a medical man, or any professional man for that matter, carries consequences reaching far beyond that particular case. In his foreword to this book Lord Justice Denning thinks that this fact makes the courts more tender towards such a defendant. "They realise that a finding of negligence against a professional man is a serious matter for him. It is not so much the money, because he is often insured against it. It is the injury to his reputation which a finding of negligence involves." Twenty years ago Lord Justice Denning would have been unquestionably right, but there is ground for suspicion that the last few years have seen a change, and it is a change which no professional man can view with anything but alarm. F. H. N.

## THE PHYSIOLOGICAL BASIS OF MEDICAL PRACTICE. By C. H. Best and N. B. Taylor. Sixth Edition. (Pp. 1357. £4. 11s. 6d.) London: Baillière, Tindall & Cox, 1955.

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## HANDBOOK OF PEDIATRICS. By H. K. Silver, M.D., C. H. Kempe, M.D., Henry B. Bruyn, M.D. (Pp. 548; figs. 33. $3.00.) Los Altos, California: Lange, 1955.

This handbook endeavours to give the practitioner and student a concise digest of the diagnosis and management of pediatric disorders. Within the limits of its condensed form it covers the subject very adequately, dealing not only with the clinical findings and treatment, but also with the basic physiology and pathology; a useful section with some household poisons and their antidotes, and there is also an index of drugs and doses. The end papers contain normal blood chemistry values.

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After a historical introduction, present-day ideas are given of mind and body, emotions and ætiology. Development and child psychiatry follow, and various conditions are described as psychiatric syndromes, psychoses of unknown origin, or disorders of histogenic and chemogenic origin. Excellent sections on treatment and the technique and use of electro-encephalography include a consideration of psychopathy and epilepsy. Many case-histories are presented, and the bibliography and suggestions for further reading at the close of each section should be of much value to the practitioner and the student. A few pages are devoted to clinical psychology, mental deficiency, and forensic psychiatry. Unfortunately, no mention is made of the latter, as it is applicable to Northern Ireland.

The grouping into sections is a model of clarity, though some may regret that page-numbering has been replaced by decimal subdivision.

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The substances dealt with all occur naturally. The neurohypophysical hormones, oxytocin and vasopressin, are octapeptides for which it is now possible to write structural formulæ; their physiological rôles are partly understood. Cholecystokinin, which is possibly identical with substance P, is another polypeptide extractable from tissues, and probably of physiological importance. The other polypeptides dealt with are formed by the action of enzymes on the $\alpha_2$-globulin fraction of the plasma proteins. This group includes hypertensin and angiotonin (which are probably identical), and kallidin, bradykinin and substance U (which may or may not be identical). Hypertensin may well have a physiological rôle, but of the other substances it can only be said that the ease with which they are formed from plasma, their presence in secretions and tissue extracts, and the very great potency they display suggest that they have a function, though this has not yet been defined.

Other active substances considered are darmstoff, an organic acid present in the wall of the gut, which stimulates intestinal motility, the hepatic vasodepressor, VDM, which has been identified as the iron containing protein, ferritin, and the renal vasoexcitor, VEM, which is a protein of unknown composition.

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## FRACTURES AND JOINT INJURIES, Vol. 2. By Sir Reginald Watson-Jones, B.Sc., M.Ch.Orth., F.R.C.S., F.R.A.C.S.(Hon.), F.A.C.S.(Hon.). Fourth Edition. (Pp. viii + 445-1073; figs. 710-1613. 120s. per set.) Edinburgh: E. & S. Livingstone, 1955.

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The clearness of thought and completeness of expression of the author, which runs throughout the entire book, is no better exemplified than in the pages on Colles fracture. This common and important fracture is dealt with completely and clearly in seven pages and its description is an example for all, who would write, to follow.

The chapter on fractures of the spine includes an appreciation of the difference between stable and instable fractures, and it is clearly pointed out the types of case which should and must be immobilised and those which require no immobilisation. In this connection, the author rightly and strongly stresses the necessity for first-class radiological technique in dealing with spinal injuries. This should be noted by all orthopædic surgeons, especially by those who, through no fault of their own, have to put up with incomplete X-ray examination of their spinal cases.

The article on fracture dislocations of the spine with paraplegia has been completely rewritten in view of the recent work of F. W. Holdsworth, and this chapter is an extremely useful addition to the book.

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Such names as Brock, Paul Wood, Maurice Campbell, and Tubbs are just a few of the list of distinguished contributors.

There is still a divergence of opinion as to the relative merits of hypothermia and the artificial heart. The artificial heart-lung is now being used successfully at the Mayo Clinic by Kirklin and his colleagues, and Cleland and Melrose, in London, have successfully used one of British design at Hammersmith Hospital. Brock is successfully doing open cardiac surgery with hypothermia, the main feature of this method being the extra corporeal cooling of the blood in a special refrigerator. The advantage of this method is that it need not be started until the heart has been inspected and a decision made as to whether it is required.

In the past cardiac surgeons have been chiefly concerned with relieving obstructions. It would seem that, with the help of either the artificial heart-lung or hypothermia, they will also be dealing with other congenital deformities, e.g., auricular or ventricular septal defects, as routine operations.

This Bulletin is highly recommended to those wishing to obtain an up-to-date review of cardiac surgery and also a glimpse into the future in this rapidly developing field.

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TUBERCULOSIS AND THE INDIVIDUAL, by J. S. Campbell. (Pp. 92, with 12 photos. 5s.); WHYS AND WHEREFORES IN TUBERCULOSIS, by G. Day, M.A., M.D. (Pp. 44. Price not stated); REHABILITATING THE TUBERCULOUS IN ENGLAND AND WALES, by M. Owen-Davies, A.M.I.A., S.R.N., S.C.M. (Pp. 71. 5s.); TUBERCULOSIS IN SCOTLAND: A SOCIAL STUDY, by J. F. Wilson, M.A., A.M.I.A. (Pp. 120. 5s.) London: National Association Prevention Tuberculosis, 1955.

Too little attention is paid to a very important page in most reports which deal with tuberculosis. On it are first tabulated, and then described the "unco-operative" patients, the patients who have "discharged themselves against advice" and those few who are discharged for "disciplinary" reasons. Now that waiting-lists are shortening, these patients represent an increasing threat to the community, for many are "open" and "resistant" cases. In a way, they represent a failure in our public relations, for there is evidence that they, and the many other sufferers who are reluctant to seek early treatment, are ignorant of the nature of the disease itself and of the many arrangements which exist for their care. The booklets by Mr. Campbell and Dr. Day are popularly written accounts of tuberculosis and of its social aspects. They will go a long way to allay the fears of patients and to indicate the services that are available to them and to their families. *Rehabilitating the Tuberculous in England and Wales* and *Tuberculosis in Scotland* are reports of careful studies of the adequacy of services for the tuberculous patient. They reveal deficiencies throughout Great Britain, particularly in the extent to which existing legislation is applied and in the efforts made to get the tuberculous back to work. In drawing attention to the patchy and inadequate nature of services and in suggesting remedies these N.A.P.T. booklets are a useful contribution to the social medicine of tuberculosis. E. M. B.

OLD AGE IN THE MODERN WORLD: Report of the Third Congress of the International Association of Gerontology, London. (Pp. vii + 647. 35s.) Edinburgh and London: E. & S. Livingstone, 1955.

THE Third Congress of the International Association of Gerontology was held in London in July, 1954. Papers and discussions were grouped in four sections and members of the Association often found that two or more papers that they wished to hear were being read at the same time. This comprehensive report, therefore, will be greatly appreciated by many of those who attended the Congress and will be welcomed for reference by all those whose interests or responsibilities relate to old people. Instead of presenting a verbatim report of the proceedings of each section of the Congress, the Editorial Committee wisely decided to group papers "containing original work, opening up new avenues of thought, or presenting authoritative views" in a series of symposia, and the seventeen chapters give an international picture of recent progress, research, and initiative in the clinical and social medicine of old age, and in related state and community activities.

It is not possible in a brief review to do justice to the many contributions, and one would have liked to refer in more detail to the eloquent public oration by Miss Marjory Fry, Dr. J. H. Sheldon's philosophical presidential address and, perhaps, to some of the highlights of the proceedings such as Professor Titmuss' provocative paper, Sir Geoffrey King's practical outline of the policy towards state pension schemes, the excellent section on considerations influencing employment of older workers (including some reference to the experimental studies in changes in performance with age), and several of the worthwhile contributions to the clinical sections particularly in neuropsychiatry and general clinical problems.

The printing and binding of the book are beyond reproach, there is a detailed index, and although the price may deter those without a direct interest in this work, the report should be made available in every reference library. G. F. A.

TUBERCULOSIS AND THE INDIVIDUAL, by J. S. Campbell. (Pp. 92, with 12 photos. 5s.); WHYS AND WHEREFORES IN TUBERCULOSIS, by G. Day, M.A., M.D. (Pp. 44. Price not stated); REHABILITATING THE TUBERCULOUS IN ENGLAND AND WALES, by M. Owen-Davies, A.M.I.A., S.R.N., S.C.M. (Pp. 71. 5s.); TUBERCULOSIS IN SCOTLAND: A SOCIAL STUDY, by J. F. Wilson, M.A., A.M.I.A. (Pp. 120. 5s.) London: National Association Prevention Tuberculosis, 1955.

Too little attention is paid to a very important page in most reports which deal with tuberculosis. On it are first tabulated, and then described the "unco-operative" patients, the patients who have "discharged themselves against advice" and those few who are discharged for "disciplinary" reasons. Now that waiting-lists are shortening, these patients represent an increasing threat to the community, for many are "open" and "resistant" cases. In a way, they represent a failure in our public relations, for there is evidence that they, and the many other sufferers who are reluctant to seek early treatment, are ignorant of the nature of the disease itself and of the many arrangements which exist for their care. The booklets by Mr. Campbell and Dr. Day are popularly written accounts of tuberculosis and of its social aspects. They will go a long way to allay the fears of patients and to indicate the services that are available to them and to their families. *Rehabilitating the Tuberculous in England and Wales* and *Tuberculosis in Scotland* are reports of careful studies of the adequacy of services for the tuberculous patient. They reveal deficiencies throughout Great Britain, particularly in the extent to which existing legislation is applied and in the efforts made to get the tuberculous back to work. In drawing attention to the patchy and inadequate nature of services and in suggesting remedies these N.A.P.T. booklets are a useful contribution to the social medicine of tuberculosis. E. M. B.

OLD AGE IN THE MODERN WORLD: Report of the Third Congress of the International Association of Gerontology, London. (Pp. vii + 647. 35s.) Edinburgh and London: E. & S. Livingstone, 1955.

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## THE HOUSE PHYSICIAN'S HANDBOOK. By C. Allan Birch, M.D., F.R.C.P. (Pp. vii + 160; figs. 5. 10s. 6d.) Edinburgh and London: E. & S. Livingstone, 1955.

This small book has been written by Dr. Birch to provide, in small compass, information and guidance on many of the difficulties and problems which house physicians meet in their day-to-day work. It is particularly valuable for those working in non-teaching hospitals who do not always have the immediate guidance of a more experienced colleague.

The book consists of several sections. In the first the house physician's duties are described and useful information regarding death certificates, notification of the coroner, medico-legal notes, infectious diseases in general wards, etc., are given. Sections 2 and 3 deal with clinical procedures and clinical pathology, and provide general information which covers most aspects of the day-to-day work in a medical ward. Section 4 is a long one on medical treatment and covers most of the commonly used drugs. Methods of treating urgent conditions such as acute ventricular failure, asthma, hæmatemesis, etc., will be found useful for the inexperienced doctor confronted with a seriously ill patient requiring immediate attention. A helpful section on fluid and electrolyte therapy will give confidence in the handling of this important aspect of modern treatment. Diabetic ketosis and poisoning are two other subjects covered in this section.

It is obviously impossible in a book of 160 pages to cover everything, but Dr. Birch has been amazingly successful in providing information on the majority of problems likely to vex the newly qualified house physician. In all, he has provided a most readable and helpful book, and those who possess it will find it a reliable guide for their work in the ward. D. A. D. M.

## CLINICAL PATHOLOGY IN GENERAL PRACTICE. Specially Commissioned Articles for the British Medical Journal (October, 1953, to July, 1954). (Pp. x + 321; illustrated. 21s.) London: British Medical Association, 1955.

Many practitioners are insufficiently aware of the facilities which to-day enable them to have laboratory examinations carried out. If these examinations are to be of value and, if the time of laboratory workers is to be employed to best advantage, it is essential that the practitioner should know the value and limitations of modern clinical pathology. The thirty-nine articles, contributed by an equal number of well-known workers, indicate the place of laboratory investigation in medical practice. Some articles, such as that on post-mortem technique, probably attempt too much. Many laboratory workers will not agree with some viewpoints expressed, but all should welcome the book. It is somewhat alarming to the pathologist to be told that "while a biopsy report must be truthful, it should also be tactful, so that an intelligent patient would not be unduly alarmed." Surely other, and more suitable, bedside reading might be provided.

In general, these articles describe the techniques necessary for obtaining specimens, review the assessment of renal and alimentary function and of metabolic and endocrine disorders and discuss the diagnosis of infections and the recognition of blood disorders. No space is wasted describing how tests are done, but the practitioner, whether in consultant or general practice, will benefit by the clear and positive guidance in almost all articles. J. E. M.

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NEURO-VASCULAR HILA OF LIMB MUSCLES. By James Couper Brash, M.C., M.A., M.D., D.Sc., LL.D., F.R.C.S.(Ed.), F.R.S.E. (Pp. xvi + 100; plates 30. 30s.) Edinburgh: E. & S. Livingstone, 1955.

An atlas and text on the sites and mode of entry of the principal arteries and nerves supplying the limb muscles has been compiled from new observations carried out at Edinburgh, Aberdeen, Leeds, and Glasgow on dissecting-room material, and from special dissections and radiographs. The present volume replaces the original brochure on the upper limb issued to Peripheral Nerve Centres in 1945. In all, some seventy upper limbs and about the same number of lower limbs were examined on a uniform scheme. Diagrams showing the more usual modes of entry of nerves and arteries have been prepared for the main muscle groups, and detailed information for each muscle is given in the accompanying text. The most frequently occurring pattern of supply, the percentage incidence and the number of observations are recorded for each muscle. The findings of previous workers are also recorded, and a very useful comparative table showing the levels of nerve entry is given at the end of the book. An excellent and authoritative work which is highly commended as a source of accurate information to those dealing with problems of the nerve and blood supply of the limb muscles.

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SHOULD THE PATIENT KNOW THE TRUTH? Edited by S. Standard, M.D., and H. Nathan, M.D. (Pp. 160. 15s. flexible covers, or 22s. bound.) London: Interscience Publishers, 1955.

This book, first published in America, is by twenty-four contributors, of whom all but one are American. There is of necessity much overlapping and much emphasis on the obvious, but, in the wide diversity of views and discussion of practice, there is much of value to every doctor. The authors are surgeons, physicians, psychiatrists, nurses active in various fields, clergymen representing different faiths, and experts in law. At least four are of international standing in their speciality. Discussion is mainly concerned with whether the patient should be told the truth about his cancer and about a fatal outcome in any disease, but other aspects are also discussed, and one of the most useful articles is by Alan F. Guttmacher on "An Obstetrician Meets Adversity." A balance of many widely conflicting views may be expressed in a quotation from the article by Dr. Bernard C. Meyer: ". . . a humane physician, devoting as much time to the patient as to the lesion, can mostly discern a proper course of action."

STAMMER IS NOT NERVES. (Pp. 67. Price not given.) STAMMERING: ITS CAUSE AND CURE. (Pp. 17. Price not given.) By H. V. Hemery, L.R.A.M. London: The School for Functional Speech Disability, 110 Daneby Road, Catford, S.E.6, 1955.

Stammering is regarded as a physiological bad habit and inheritance, left-handedness and neurosis are not considered significant. The author's method is not explicitly described, but is apparently based on singing and speech-training techniques. Like all enthusiasts, Mr. Hemery implies that his method is the only successful one, but for assessment the serious worker will require facts and figures which are omitted.

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