President of the Ulster Medical Society

1955-56

Presidential Opening Address Ulster Medical Society 20th October 1955

THE TRAGEDY OF MAN-MADE DISEASE

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 1750 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 1920 to 58 in 1955 in Northern Ireland, and in England and Wales from 117 in 1900 to 08 in 1920 and 27 in 1955.

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 1955 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.

President of the Ulster Medical Society

1955-56

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 anaemia 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 anaemia 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

President of the Ulster Medical Society

in "intoxication" when administered in large doses or for prolonged periods. Serious conditions have arisen from massive transfusions of citrated blood and hypocalcaemic tetany and cardiac depression have occurred. Even oxygen can cause disease, as we know from our experiences 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 septicaemia.

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

President of the Ulster Medical Society

1955-56

approximately 10,000,000 have been injured. Every day 45 people die, 10 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 haemolytic 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.

Unfortunately, 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 diarrhoea; anal pruritus; vestibular and auditory disturbances; aplastic anaemia; 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

President of the Ulster Medical Society

1955-56

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 *haemophilus* respond to chloramphenicol and that the haemolytic *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 anaemia; 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 anaemia which converted to aplastic anaemia 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 potency miracles of the century. The 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

President of the Ulster Medical Society

1955-56

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; gonorrhoea 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 sulphaaemoglobinaemia 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 anaemias 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 role 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 haemoglobin. 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 anaemia 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 gastrointestinal perforations (with two deaths), three "psychotic episodes" and one case of steroid diabetes.

President of the Ulster Medical Society

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 oedema, 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:-

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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.

President of the Ulster Medical Society

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 anaemia, 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 hypercalcaemia 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 methaemoglobinaemia 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 haemorrhage 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."

1955-56