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THE ULSTER MEDICAL JOURNAL

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Modern Surgical Anæsthesia

By I. W. MAGILL, M.B., D.A.
Senior Anæsthetist, Westminster Hospital
Senior Anæsthetist, Brompton Chest Hospital

The Robert Campbell Oration
delivered in the Whitla Medical Institute, 23rd March, 1939

I FEEL that I should open my remarks to you this evening by expressing sincere appreciation of the honour conferred upon me by the Robert Campbell Memorial Committee in inviting me to address you. It is particularly gratifying to be accorded this honour in the city where I obtained my qualification.

This oration has a two-fold purpose: its more important function is the commemoration of the man whose name it bears. To many of you Robert Campbell is not merely a name. The memory of his personality and work remains, to those who knew him, as vivid as it was at the time when his life was cut short in its prime. To the younger generation, and to some others, he is one of the famous men who have passed on, leaving behind him the heritage of a noble example which all would like to follow.

I count myself fortunate in that, twenty-five years ago, I was his pupil at the "Royal," and during my term in residence learned much from personal association with him. I remember well the impression he made upon me by the quiet strength of his personality. His surgical decisions were carefully weighed, and his cool, deliberate dexterity filled me with frank admiration; while his keen sense of humour and kindliness showed, at many an unexpected moment, that he was a very humane man at heart.

At the Children's Hospital his pioneer work on congenital hernia must have proved a blessing to many a grown patient alive to-day. It is probable that the statistics he collected in this branch of surgery alone remain unsurpassed at the

present time. No doubt the single fatality attributed to chloroform intoxication in this series of cases stimulated him to anticipate similar complications wherever chloroform was used, and here we have a link with the subject of this oration—namely, that the importance of anæsthetics did not escape his eager perception.

I cannot but feel that Robert Campbell would have been one of the first to appreciate the advances that have been made in anæsthetics in recent times and to encourage still further efforts towards improvement. Some account of what has been accomplished in this field should, therefore, be a fitting tribute to his memory.

It is obviously impossible to go deeply into all branches of anæsthesia in a short lecture. The main object in this paper is to deal with some important factors which have already proved their worth. In this respect it will be understood that I am more at home with an endotracheal tube than a fountain-pen, and if this paper falls short as an oration, it is a reasonable hope that when I have finished, you will have heard something of value on the practical side of anæsthesia. First of all I must say a few words about the past.

Early Developments.

No conception of the present day status of surgical anæsthesia can be arrived at without a brief reference to the history of its development.

It is well known that attempts to alleviate or even abolish the pain associated with operations date back to the very beginnings of surgery, and the potions and applications used for this purpose through the ages would probably fill a volume in themselves. In a recent paper, General MacArthur[1] refers to one of these methods as described by Guy de Chauliac in the fourteenth century. The patient inhaled the fumes from a mixture of opium, hemlock, hyoscyamus, and some other ingredients, and while under the influence, incisions could be made without pain. As MacArthur points out, this is probably one of the earliest references to general anæsthesia.

Mixed as it may have been with other ingredients, alcohol has, of course, been known since the earliest times as an anæsthetic. Even medical students may occasionally have experienced a return home with a black eye with no knowledge of how they got it and no recollection of any pain. Small wonder, therefore, that alcohol has enabled many a patient to withstand the ordeal of the knife.

It was not until the nineteenth century, however, that surgical anæsthesia in the modern sense was truly discovered. After some controversy, Morton's claim to priority appears to have been established by his use of ether for general anæsthesia in America in 1846. In the same year a dental extraction under ether was made in London; two days later it was used in surgical operations at University College Hospital, and from then onwards its fame spread like wild-fire. J. Y. Simpson of Edinburgh soon followed with chloroform.

Davy had suggested the possibility of nitrous oxide as an anæsthetic when he discovered it in 1800, but the profession was slow to appreciate its possibilities, and it seemed to achieve a merely frivolous reputation as a potential intoxicant. Poor Hickman, a young country practitioner who died in 1830 at the early age of 29, devoted the best part of his professional life to a fruitless endeavour to persuade

the medical fraternity that operations could be performed painlessly under the influence of gases including CO_2. He had performed several operations on animals, using this gas as an anæsthetic with considerable success, and his letters show that he had a clear conception of the possibility of painless operation on the unconscious human subject. It is a strange reflection that the work of these men failed to stimulate further investigation by contemporary scientists. But the fact remains that some fourteen years elapsed after Hickman's death before Morton proved that an operation could be performed without pain under the influence of ether, and that it was not until 1870 that nitrous oxide was established in general use in Great Britain.

To surgeons, the new-found boon of anæsthesia provided such a contrast to the pre-existing operative conditions that they remained complacent and contented. Herein lies the cause of the long period of stalemate in development which followed. Controversies arose from time to time over the relative merits and disadvantages of chloroform and ether. Nevertheless, these two drugs have held the field as the most widely used general anæsthetics. They continue to be employed because they are capable of producing good operative facilities when used by simple methods. This brings me to a consideration of the conditions existing to-day.

The Modern Status.

Here I must refer, unfortunately, to a lack of consideration evident in some surgical colleagues. Too long has the surgeon been oblivious to the side-effects produced by anæsthetics. "I do not care what you give, so long as you get the patient deep enough," is a phrase with which anæsthetists are familiar, and if the anæsthetist be in a junior position—as he frequently is—he will proceed to obtain that depth of anæsthesia regardless of any but its immediate effects. It is clear, therefore, that co-operation between the surgeon and anæsthetist is essential. When it is practised in the case of patients who are gravely ill, we are frequently surprised by the unexpected success of our efforts.

Deep ether anæsthesia, amounting practically to saturation, is the standard to which anæsthetists and surgeons have been bound in the past for the majority of operations. Where efforts have been made to break away from this tradition, post-operative results show definite improvement. This has been accomplished in one or two progressive hospitals in America and in at least one in England. In these institutions, the limitation of ether or the substitution for it, as far as possible, of less toxic agents such as N_2O and O, has resulted in shorter convalescence, fewer post-anæsthetic complications, and a reduction in mortality-rate. The economic aspect of this improvement is at once apparent. It means, in hospital, more available beds per annum and a reduction in cost per case.

Again, in the public mind many disagreeable factors are associated with anæsthesia. If we can modify this attitude by increasing our skill, patients will be encouraged to submit more readily to operations when a cure can reasonably be expected, instead of postponing the day until a hopeless stage of a disease, such as cancer, has been reached.

A surgical operation is not merely an exercise in applied anatomy; rather is it an exercise in applied biology in its widest sense. The need for improvement is unquestionable, for in spite of the high standard of surgical skill existing to-day, comparatively simple operations such as appendicectomy and tonsillectomy are still attended occasionally, not only by complications due to the anæsthetic, but by a definite mortality-rate.

The next question which arises is : how can the improvements of which we are in search be obtained? The advances which have been made are not due, as some are inclined to believe, solely to the discovery of the new drugs (which I shall deal with later) and to the swing over from what has been called "rag and bottle anæsthesia" to complicated apparatus.

Blomfield,[2] incidentally, has some trenchant remarks to make on this point. He suggests that, nowadays, the anæsthetist must have as good a working knowledge of pressure-gauges, flow-meters, valves, stopcocks, and manometers of all kinds as he must of the respiratory and circulatory system of the patient. He is pictured assessing the latter's condition by observing dials and scales and bags rather than by noting the colour, pulse, and breathing of the shrouded and often invisible figure who lies at the end of a piece of tubing. One sees the justice of this indictment. Apart from anything else, machines are not foolproof, nor are human beings infallible.

The keynote of successful anæsthesia, whatever the agent, drug, apparatus, or mode of application, is an accurate estimation of the patient's condition coupled with sound technique. Every individual has what for lack of a better term I must call a *physiological balance*. In youth and health this balance is elastic within a certain range. In the presence of disease, on the other hand, and in old age, interference with this balance may turn the scales against him. Moreover, unlike the standard laboratory animal, the human being is an unknown quantity in whom, even in health, the effect of environment and habits of life must be carefully considered before the make-up of the individual can be dissected into its different components and the influence of these gauged in relation to the anæsthetic.

The majority of the agents employed in anæsthesia are depressant in their effect. Some are actually destructive. It is essential therefore to judge beforehand, as far as possible, the capacity of the patient to withstand this action, superimposed as it is on necessary operative manipulation. At the present time this precaution is more imperative than ever, owing to the tendency to elaborate the anæsthetic prescription with drugs which are irrecoverable once they have been administered.

One further point may be mentioned here in connection with assessing the patient's condition—namely, blood-pressure estimations. The American custom of keeping an "anæsthetic chart" throughout the operation has now found its way to the British Isles. I have for several years made the practice of having regular blood-pressure estimations done at five-minute intervals during thoracic operations. In operations where severe surgical interference occurs, the information obtained by this means is invaluable, as it may enable the anæsthetist to say when certain surgical steps can be taken with safety. In any operation, observation of such

changes and of alteration in the pulse-rate give the greatest possible information on the state of the patient, and though the elaborate nature of the transatlantic method of recording these is in many cases impracticable, there is no doubt that much may be learnt from their study, in relation to the surgical procedure undertaken, that is both instructive and valuable.

Factors in Successful Anæsthesia.

At the risk of over-emphasising elementary principles, I must state that the first physiological consideration in anæsthesia is the maintenance of normal respiratory function, without which no agent can be considered satisfactory or safe. The airway must be kept free in all circumstances, and a good general maxim to bear in mind is that the administration of drugs should entail no greater diminution of respiratory rate and excursion than that which occurs in normal deep sleep. The importance of a free airway can hardly be exaggerated, but the chief point to remember is, not that it must be secured, but that it must be maintained.

Observation alone has taught me how frequently this is forgotten. Not only is it more difficult to maintain even or smooth anæsthesia in the presence of a partially obstructed airway, but the whole syndrome produced is a vicious circle which hampers the work of the surgeon and exhausts the patient. The resulting congestion is in itself a sufficient predisposing cause of post-operative pneumonia. Often in these circumstances an oxygen cylinder is brought into use. Oxygen is certainly valuable, but *only* when there is a free airway.

Endotracheal Anæsthesia.

This brings me to what is perhaps the most outstanding technical advance in modern anæsthesia—the endotracheal method in which Kuhn played such an important part. Intubation provides an airway which is patent in all circumstances. It does not imply complicated machinery either in getting the tube into position or in delivering the anæsthetic. Once the patient is intubated, anæsthesia can be maintained with an ordinary mask on inhalation principles, and connection to an apparatus is merely a refinement. Originally applied chiefly to certain operations on the head and neck, the success of endotracheal anæsthesia in this field has caused its extended use to other branches of surgery — particularly abdominal. There is, in fact, a growing tendency among anæsthetists to intubate at every opportunity. With this practice I emphatically disagree, since it is obvious that the airway can be kept free in many cases by simple means. At the same time, irrespective of the nature of the operation, there are certain types of patient, particularly the stout thick-necked variety, in whom control of the airway may become an increasing source of anxiety during the anæsthetic. In these there should be no hesitation in anticipating trouble by using the intubation method. Of the two methods of intubation—oral and, as I call it, "blind nasal"—the latter has particular advantages.

The curved rubber tube which I have devised for this technique and the method of passing it blindly through the nose,[3] constitute, I believe, a material advance in preventing trauma and ensuring ease of application. The basis of "blind" intuba-

tion lies in the fact that the human being normally breathes through the nose, and that there is one position of the head in relationship to the trunk in which the course of the airway from nose to larynx is at its maximum patency. The position is simply that of a soldier standing properly at attention, or of a plumber trying to locate an escape of gas.

With the head so held, the tube is passed along the floor of the nose. Administration of a little CO_2 at this time is useful, in order to abduct the vocal cords before insertion. The proof that the tube is properly *in position* is in the *breath-sounds,* which may be clearly heard at the end of the tube.

Intubation can, of course, be performed through the mouth with the aid of a laryngoscope, and contra-indications such as nasal sepsis, or deformity, or the site of operation, may indicate the oral route only. But when there is a free choice, the blind nasal method claims preference on account of the ridiculous ease with which it can be used in the majority of patients. Intubation puts an end to the grim old struggle we have sometimes seen between the surgeon trying to get his operation done under a handicap and the anæsthetist doing his best to keep the patient anæsthetised and alive at the same time.

It is in thoracic surgery that the most spectacular advances have been witnessed in recent times, and to these advances the endotracheal method has made a striking contribution. The removal of portions of the chest-wall under a local anæsthetic has long been an established procedure, but the extirpation of the whole or part of a lung has only been made practical, with reasonable safety, through improvements in anæsthetic technique.[4] Endotracheal anæsthesia *per se,* whether by inhalation or insufflation, gives no protection against the spread of secretions to the sound lung. Factors which contribute to this are the position of the patient on the table and the manipulation of the diseased lung by the surgeon. In such circumstances positive-pressure anæsthesia appears to be both useless as a protection and an actual danger in itself. Not only is it possible to open the chest with safety, but anæsthesia can be confined to one lung by means of an endobronchial tube, thereby protecting the sound lung from cross-infection during the operation. Endotracheal suction can be applied during operation when necessary. Further, by application of the principles of controlled respiration, the pulmonary excursion can be reduced to such an extent that in pneumonectomy the surgeon is enabled to sever the main bronchus when its movement has been brought to a standstill. When lobectomy for bronchiectasis is contemplated, the bronchus on the affected side can be blocked by a gauze tampon or by a balloon, thereby confining the secretions to the affected area.

A final application of endotracheal anæsthesia is cleft palate and hair-lip operation, even in infants it has proved itself to be an important contributory factor to surgical success. This is readily acknowledged by Kilner.[5] Again, Cade has come to regard endotracheal anæsthesia as a *sine qua non* for successful operations on the tongue.[6] It is easy to understand the advantage of being able to give N_2O and O through the endotracheal tube with a larynx under control and no respiratory obstruction, in contrast with the rather clumsy and Victorian method

of giving chloroform through a hooked tube, with the attendant difficulties of not being able to secure an even and light level of anæsthesia, and also adequate protection from the entry of blood, etc., into the trachea.

A certain amount of criticism has, however, been levelled against nasal intubation, on the grounds of trauma and the possibility of introducing septic material into the bronchial tree. Trauma which is, after all, avoidable is likely to arise with any form of instrumentation. In a twenty-year experience I have yet to record a single instance of pulmonary complications which can reasonably be attributed to this method.

I have just spoken of the importance of a free airway in maintaining satisfactory anæsthesia, and of the advantages offered by the endotracheal method. This seems to be a suitable moment for a few words on carbon-dioxide, already referred to in connection with intubation. It is only in the last few years that the value of this agent has been fully recognised. Owing to its specific action on the respiratory centre it can be used to accelerate induction, to stimulate sluggish breathing during the maintenance of anæsthesia, to hasten the return to consciousness after the operation, and to assist the aeration of the base of the lung during the post-operative period, thus minimising the possibility of post-operative pneumonia.

The proper control of CO_2 is, however, not always so simple as it sounds. In the closed system, so frequently used nowadays, unless some method of removing CO_2 is arranged for, accumulation occurs, giving rise to hypernœa, increase in systolic blood-pressure, and a greater tendency towards oozing of blood in the operative field. The incorporation of a soda-lime canister remedies these defects, and, if it can be cut out or in at will, enables proper control to be exercised and physiological conditions imitated. In addition it prevents loss of heat and water from the body.

A specially valuable application of this principle can be exercised in certain operations where the surgeon may require the breathing to be damped down or even stopped—so-called "controlled respiration." This can be achieved for short periods by squeezing the bag. The effect of this is to hyper-ventilate the lung with oxygen, and remove through the canister the greater part of the CO_2 from the lungs. There being no stimulus to natural respiration, voluntary breathing now ceases. Oxygenation must, of course, be maintained by occasional pressure on the bag. Natural breathing will recommence only when the CO_2 has been allowed to accumulate again to the threshold necessary to stimulate the respiratory centre.

Basal Anæsthesia.

The practice of trying to allay the patient's apprehension before operation by means of sedatives must be as old as surgical history. Some fifteen years ago a rather striking advance was made when drugs began to play an important part in the anæsthetist's stock-in-trade. Where formerly little else than a sedative effect was the rule, something more dramatic seemed called for, and nowadays patients commonly demand to be made completely unconscious before the anæsthetic proper is administered. The use of drugs to this end came to be termed basal narcosis, and we know how attractive it is from the patient's point of view. To the anæsthetist

also the smaller amount of the subsequent anæsthetic required by this system is an added advantage. Basal narcosis is still looked upon by some as not entirely devoid of danger. In fact I know of some surgeons who continue to refuse it to their patients. But I know also of many patients who have gone to other surgeons on account of such refusal!

No doubt the drugs which are powerful enough to produce coma must be considered dangerous—but the same may be said of chloroform, or even alcohol. When we consider the psychological aspect of anæsthesia, it cannot be denied that basal narcosis has proved to be a valuable asset, especially in operations upon children. The nightmare of a mask is a definite entity to a nervous child who has previously undergone the ordeal of a "straight" anæsthetic badly administered, and the same may be said of many an adult patient. But when a new drug or technique is discovered, in anæsthetics as in other branches of medicine, there is a tendency to apply it to every case regardless of indications or consequences. So also with basal narcosis. The patient's wish to be made unconscious in bed is an ever-increasing demand to which anæsthetists are tempted to submit, sometimes against their better judgment. A simple example will show how impracticable this may be: An extensive pelvic operation requires a low spinal anæsthetic, and the patient asks to be put to sleep before the injection. Here a firm line must be taken. A low block is best done with the intelligent co-operation of the sitting patient and on the operating-table. The spinal must be given first—it can be quite painless—and this can be followed by an intravenous barbiturate, such as evipan or pentothal, which induces unconsciousness pleasantly and quickly. Another difficulty arises when intravenous anæsthetics are used alone but are demanded before the patient, who is often aged and gravely ill, is in the theatre. In this instance delay during the journey to the theatre and from the ensuing preparations may cause loss of valuable anæsthesia and require a higher total dosage than is desirable.

I must now say a few words about the actual agents employed. Most of the drugs used for basal narcosis are, with the notable exception of avertin, barbiturates. Practically no limit exists as to the number of derivatives which can be produced, so that to the many which are already familiar continual future additions are to be expected. It is worth noting, that although evipan and pentothal are more effective than nembutal during induction, the former drugs are detoxicated so quickly that they contribute little to subsequent anæsthesia and practically nothing at all as sedatives in the immediate post-operative period. Both these drugs will be mentioned again in connection with intravenous anæsthetics. The oral use of barbiturates for basal narcosis is not to be recommended owing to their erratic absorption. This is particularly important in children, where difficulty in assessing the correct dosage also comes into the picture.

Apart from paraldehyde, the veteran basal hypnotic, avertin (given by rectal injection) requires special consideration. Avertin is perhaps the most popular basal hypnotic at present in use. Its value is undisputed. The peculiar virtue of avertin lies in its possession of considerable anæsthetic properties even when given in safe doses. As it readily induces muscular relaxation, it is the agent of choice

in certain abdominal operations when there is no contra-indication to rectal injection. It must be remembered that general muscular relaxation is often accompanied by a tendency towards obstruction of the airway. A constant watch for this must be maintained. Avertin is a most powerful drug, and the greatest care should be exercised in regulating the dose. It is not advisable in elderly or gravely ill patients.

When a basal narcotic has been administered, certain precautions are necessary in the immediate post-operative period. Much of the calumny which has been showered on these drugs is due to neglect of the airway at this time, and the nurse must be instructed to pay particular attention to this, also to withhold the administration of further sedatives as long as possible. If respiration is lagging, coramine or lobeline should be injected, and inhalations of carbon-dioxide and oxygen given at intervals.

The Anæsthetic Proper.

Having considered the basal hypnotics, I can now pass to the anæsthetic proper which supplements it, and will very naturally turn to nitrous oxide and oxygen as the most innocuous combination known. It causes no interference with metabolism or any destruction of tissue. It is also non-inflammable. Within the last decade, however, there has been a growing tendency among surgeons, physicians, and some anæsthetists to speak casually of "gas and oxygen" for any and every operation. It would be well, I think, if the position of this combination were put on an honest basis. Gas and oxygen means gas and oxygen, and nothing else. We should bear in mind that the potency of nitrous oxide and oxygen is limited, and honest anæsthetists will admit the use of an adjuvant such as ether in small quantities—but nevertheless ether. It is true that with the help of adequate basal narcosis, the scope of nitrous oxide and oxygen has been extended, but to press for muscular relaxation without these aids involves a degree of suboxygenation to my mind more dangerous than the use of a small amount of ether, and certainly less satisfactory from the standpoint of muscular relaxation.

By all means, then, let us employ nitrous oxide and oxygen as far as we can, but let us not delude ourselves into thinking that we are using nitrous oxide and oxygen for major surgery when in reality we mean nitrous oxide and oxygen plus something else.

Of course some may be ambitious to follow McKesson's secondary saturation technique. McKesson was reputed to be something of a magician with nitrous oxide, but I know definitely that he worked with a surgeon who was content to operate on a rigid abdomen. Secondary saturation practically amounts to periodic asphyxia. One experienced anæsthetist who saw McKesson in action described the physical signs of the patient as approximating those of impending death.

Having mentioned evipan and pentothal in connection with basal narcosis, it is now necessary to describe them under the heading of total anæsthetics given intravenously. This procedure must be considered as definitely established, as in addition to other advantages these drugs fill a gap which previously existed when an anæsthetic was required for short operations—particularly those in the region

of the head and neck, such as excision of eye, extraction of teeth, etc. Again, they have proved valuable in patients who are "difficult" under N_2O and in cases where muscular relaxation is required for a brief period for orthopædic manipulations.

Pentothal is in my experience the outstanding drug. Its forerunner, evipan, has some disadvantages which make it relatively unreliable—namely, failure to induce satisfactory muscular relaxation. With evipan there is frequently rigidity. With pentothal, muscular relaxation is the rule, and on this account a careful watch must be kept for respiratory obstruction through the tongue falling back or depression of the lower jaw. This is all the more important when it is remembered that respiratory depression with pentothal is more marked than with evipan. To combat respiratory depression with pentothal, Organe[7] has recently devised a technique in which N_2O and O is used to supplement the preliminary injection. The needle is kept in position in the vein, and as the demand for deeper anæsthesia arises from time to time a further injection of 1 or 2 c.c. of pentothal is given. The value of this method is that owing to re-breathing, an accumulation of CO_2 is obtained which acts as a respiratory stimulant, while the N_2O and O acts as a supplementary agent and enables economy in total pentothal dosage to be made.

It is worth while noting that, owing to its containing sulphur, pentothal should not be used when the patient is under treatment with prontosil or allied compounds.

Despite the advantage of these intravenous drugs, it is unlikely that they will ever entirely replace inhalation anæsthetics, in which the control of respiration is easier and attention does not have to be divided between two different parts of the body—the head and the arm.

Cyclopropane.

Among the gases which have been tried out as anæsthetics in the laboratory and afterwards used successfully on the human subject, cyclopropane has come into striking prominence since it was first used by Waters[8] in 1934. This gas is an isomer of propylene and is represented by a close-ring formula, in virtue of which it is reputed to cause no interference with metabolism. Cyclopropane has the advantage that in concentrations of ten to twenty per cent. with oxygen it will produce surgical anæsthesia with good muscular relaxation. This secures quiet respiration with ample oxygenation. Cyclopropane does not cause irritation of the respiratory tract, or damage to liver or kidneys. It is expensive, and on this account administration is only practicable in a closed apparatus using the carbon-dioxide absorption technique. This, coupled with the fact that cyclopropane is not a respiratory stimulant, necessitates a close watch for respiratory depression. As with other new agents which have proved successful experimentally, there was at first a tendency to over-estimate the value of cyclopropane. In practice, for instance, it is found that although recovery is rapid following a short administration, it is retarded after a major operation of some duration, and is accompanied by nausea in almost the same percentage of instances as in the case of ether. Further, in deep cyclopropane anæsthesia cardiac irregularities of obscure origin and significance are liable to occur. These irregularities disappear when the concentration is diluted by adding more oxygen.

The most practical method of making use of the advantages of cyclopropane is to use the gas as an adjuvant to N_2O and O in place of ether. With such a combination, adequate oxygenation is provided for. The percentage of cyclopropane in the mixture is never sufficiently high as to depress respiration unduly or to cause the cardiac irregularities referred to. Cyclopropane has now established itself as a most useful adjunct to our anæsthetic resources, especially in "bad risk" cases. In the hands of experts it gives us, when used as an adjuvant to nitrous oxide, about the most innocuous general anæsthetic prescription at the present time. A warning is, however, necessary. As it does not act as a respiratory stimulant, an overdose can easily be administered—even when the patient is a good colour. Thus it is not an agent for a novice to use. The gas is explosive (so also is ether), but the closed system helps to prevent this risk. All the same, caution is essential if diathermy is to be used at the operation. In addition, capillary oozing has been reported in some cases, though it is probably of little significance.

Local and Regional Anæsthesia.

While attention in England and America has been centred chiefly upon general anæsthesia, the trend on the Continent has been towards the development of local and regional analgesia. Finsterer's published reports[9] on regional anæsthesia in abdominal surgery show results superior to those obtained by any other method. More recently in London, Ogilvie[10] indicates equally good results in a paper personally communicated and shortly to be published. His cases are mostly gastric resections. Summing up the advantages of the method, the author states that local anæsthesia makes the operation easier for the surgeon, leading to neater and quicker work, but that it also removes all need for hurry, should extra time be wanted for some refinement. Relaxation is perfect; respiratory movements are slow and shallow; the blood-pressure is not raised nor are the capillaries dilated, while the viscera preserve their tone and movement and do not prolapse from the wound. Local anæsthesia abolishes many of the risks of the post-operative period. The patient is conscious and rational; unlike the subject of spinal anæsthesia, he can sit up; he can breathe, he can move, and he can drink, so that the likelihood of respiratory, vascular, and embolic complications is greatly diminished. Further, he has inhaled no foreign vapour or gas, so that he will not secrete respiratory mucus in excess. These advantages, Ogilvie states, continue over the later stages of recovery.

Another significant fact supporting the value of regional anæsthesia is that at the Brompton Hospital it is tending to replace general anæsthesia in the operation of thoracoplasty. Clearly, when the patient is of suitable temperament, local or regional methods obviate many of the risks associated with inhalation. The chief disadvantage of regional anæsthesia is the time-factor, and the technique must, of course, be carried out with meticulous care if it is to be successful.

Spinal Anæsthesia.

The popularity of spinal anæsthesia has waxed and waned for the last thirty years with the discovery of some new drug or some new theory as to the behaviour

of solutions injected into the subarachnoid space. Without going into details of all the methods, the mention of a few techniques may be of some practical interest.

Spinal anæsthesia has this advantage over regional anæsthesia—that one injection alone is necessary and can be made without any loss of time. There are two definite fields of applications, low (sub-umbilical), and high-reaching as far as the fourth dorsal nerve and therefore giving anæsthesia of the greater part of the wall of the thorax if necessary.

Sub-umbilical spinal anæsthesia is indicated in certain extensive pelvic operations such as excision of the rectum, operations on the bladder, and, in certain cases, hysterectomy. There is no doubt as to its value in such conditions. High spinal anæsthesia, on the other hand, produces such a fall in blood-pressure that there is no excuse for its employment when regional anæsthesia will, as Ogilvie[11] points out, produce equally good operative facilities without the accompanying fall of blood-pressure.

Of the drugs which are available for spinal anæsthesia, percaine is as good as any. The 1 : 200 solution (heavy) is preferable for low blocks in doses of from 1 to 1.3 c.c. The injection should be made in the sitting position if possible, and two or three minutes allowed for the solution to become fixed. After that the patient can be safely placed in the recumbent or "head down" position.

The 1 :1500 solution is preferable for high blocks; in virtue of its low specific gravity in comparison with the cerebro-spinal fluid, considerable controllability is afforded. The Howard Jones technique depended upon volumetric displacement using doses up to 20 c.c. gauged in accordance with the length of the patient's spine. When the patient is able to sit up for one and a half minutes, however, with the head well flexed, doses of from 5 to 10 c.c. will give anæsthesia high enough for surgery in the upper abdomen and lower part of the thorax. The advantage of the sitting position is, that in using a light solution such as 1 :1500 percaine, adequate height of anæsthesia can be obtained with a small dose. If for any reason the patient cannot sit up, Lake's method[12] of making the injection with the patient lying on the face in the reverse Trendelenberg position commends itself.

Unilateral block[13] is in theory an excellent procedure, and an attempt should always be made to obtain it in one-sided operations. In my own experience, notwithstanding every care, anæsthesia has been found to extend to the opposite side more often than not.

I have employed spinal anæsthesia for many pneumonectomies and lobectomies, but I am convinced that the resultant fall in blood-pressure and embarrassment of respiration, coupled with the lack of protection which can be afforded to the opposite lung when endotracheal anæsthesia is used, makes the practice inadvisable for these operations. High spinal anæsthesia should never be used for patients who are too ill to stand a general anæsthetic. Its main indication is the extremely robust person who is likely to prove difficult under a "general"; but here again regional anæsthesia will give all the advantages without the fall in blood-pressure if ample time is available to make the injections.

Local, regional, or spinal anæsthesia with basal narcotics is a tempting proposi-

tion. If, however, it is decided in a given case that the patient is too ill to have a general anæsthetic, it is highly improbable that he is also too ill to sustain the depression of complete basal narcosis. A sedative such as omnopon is allowable, but obviously the patient will not stand avertin except in very special cases. In any event, the effect of the basal narcotic may wear off during the course of the operation, leaving the surgeon with an uncontrollable patient.

Conclusion.

Before passing to a conclusion, I should like to deal with a few oddments which in any review of anæsthetics are difficult to fit in their proper place. These will not, however, include an account of those post-operative effects for which anæsthetics have been given wholesale blame in the past, i.e., vomiting, pulmonary complications, abdominal distension, and retention of urine.

The limitations of machinery have already been referred to, and it has been explained that the possession of an anæsthetic apparatus is no panacea for poor anæsthesia. The chief value of the apparatus is that it secures regular dosage : but the anæsthetist must familiarise himself with the controls of whatever machine he uses, in the same manner as he is expected to do with the controls of a motor-car. To continue the simile, he will be careful to note the difference between the accelerator and the brake. He must keep his eyes on the road and his hands on the wheel. Failing these precautions, he is liable to drive badly and possibly have an accident, even with a Rolls Royce. Success in the use of anæsthetic apparatus can only be attained by a close watch on the needs of the patient—and these needs, like road conditions, are liable to change at any moment.

If an apparatus is used, it should be equipped with a sight-feed of some kind to ensure regular delivery of gases and oxygen in accurately gauged proportions and quantities. Dry-flow meters serve this purpose best. The principle involving carbon dioxide absorption in a closed circuit bids fair to displace other inhalational methods, on account of economy and portability, apart from the physiological advantages already referred to.

Two important points concerning the relation of surgeon to anæsthetist are hæmorrhage and muscular rigidity. If a patient is still able to bleed normally during operation, this should surely be a matter for congratulation to the anæsthetist rather than blame—some of us may remember the days when only praise was heard if a patient, on being incised, revealed tissue as avascular as a slice of bacon.

It is possible to produce general anæsthesia, safe for the patient, by a combination of various agents in harmless, or as we might term it, atraumatic doses. Associated with this anæthesia is immobility, but not necessarily muscular relaxation, which depends on the abolition of intrinsic elasticity and all those complicated factors which maintain muscular tone. If we are prepared to submit our patient to all the risks of ether saturation, immediate and remote, absolute flaccidity can be obtained. Although I sympathise freely with the surgeon who calls for such relaxation in abdominal cases—precisely these cases in which after-effects such as vomiting and bronchitis are most disturbing—I hold strongly that the end does not justify the

means, and would put forward a plea for compromise and collaboration. It must be realised that the muscles are not merely draped upon the skeleton. They have both origins and insertions, and between these points there exists in healthy muscle some intrinsic tone. If the stretch upon a muscle is increased, as it can be by abnormal posture, difficulty of access is often increased.

The closure of the acute abdomen with distended intestine is a common problem which anæsthetists are expected to solve (sometimes unreasonably). In such cases the distended gut in the abdomen resembles the inner tube of a tyre which has burst through its cover. We would not expect to replace the protruding inner tube without preliminary deflation. It is the same with the distended gut. The contents can be let out with the aid of a trocar and canula, and the intestine can not only be replaced easily, but will recover its normal tone more quickly. The extra time and trouble involved in employing local anæsthesia of the abdominal wall will repay the surgeon well both by increasing the comfort in which he will carry out his manipulations and by the improved post-operative condition of his patient.

It is clear, I think, that the attainment of the common ideal of both surgeons and anæsthetists—namely, improvement in operative results—entails some departure from the haphazard routine of the mask and drop-bottle, efficient though the latter may be on some patients who are good risks. But it is too much to expect a newly qualified doctor, equipped with a certificate to say that he has given a dozen anæsthetics, to employ all the refinements which make the difference between good and bad anæsthesia in the hands of an expert. No house surgeon is expected to perform major surgery, except in emergency, although he may be already a good surgical technician. (After all, surgery can be practised in the dissecting-room.) He is expected, however, to give major anæsthetics. Anæsthetists must therefore be trained. However much the general practitioner may regret incursion on yet another of his preserves, it is apparent that anæsthesia, if it is to be efficient, must be a speciality. In this respect the institution of the Diploma in Anæsthetics has already done much to improve the position. In the future it will not be enough for a doctor to say "I am an anæsthetist." He will have to produce the credentials which prove that he has given some attention to the study of the subject, just as the possession of the Fellowship does for the surgeon.

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Pink Disease

By JANE M. FULLERTON, M.B., B.CH.

THE first account of this disease was published in 1903 by Selter of Solengin, who called it trophodermatoneurosis, but not until Dr. Swift of Australia described it was it recognised as a clinical entity. Since then numerous descriptions have appeared, including that of Feer, a German pædiatrician. Several names are still current, e.g., erythrœdema, acrodynia, dermato-polyneuritis, while in Germany the condition is known as Selter-Swift-Feer's disease.

Cases of pink disease are being observed with increasing frequency in Northern Ireland, or perhaps one should say, more frequently recognised and not diagnosed as cases of vague rickets or teething disorders.

The clinical picture is as follows : a child of six months to two years old has become gradually fretful and miserable and refuses food. Insomnia is marked, there is hypotonia of muscles and the mother may offer the information that "the baby's head has become loose." At some stage there appears a fine papulo-vesicular red rash either preceded or followed by marked redness of feet and hands, which remain cold. The tip of the nose is often red, which may be due to the fact that the child burrows into its pillow because of intense photophobia.

The following description of the disease is based on a series of twenty cases admitted to the medical ward of the Belfast Hospital for Sick Children during the period 1933-38.

OCCUPATIONAL AND GEOGRAPHICAL DISTRIBUTION.

There is no definite evidence that the social position or district of residence in the series bears any relation to the incidence of the disease. Seven of the cases were of the labouring or unemployed class, while thirteen were of families of good average class; séven were country children, and thirteen from towns.

From the series of cases under discussion there appears to be a slight increase in cases in the months of April, May, and November; this rise has been noticed by Feer and Rocaz, but as yet its significance is not clearly understood. On the other hand one notices that the disease is rarer in the summer months June to September, which rather suggests that cold wet weather may be an etiological factor.

Age and Sex.—The youngest case observed was a female infant aged three months, and the oldest a male aged two and a half years, the average age over the series was eight months, but cases have been recorded up to the age of fourteen years. A predominance in male children was noted, there being fifteen males and five females.

Family History.—This is of no apparent value in diagnosis, as the cases seen ranged from first-born to seventh.

Etiology.—Two theories as regards the etiology of pink disease are put forward by writers on the subject, but as yet no definite conclusion has been recorded. A

vitamin deficiency has been suggested, but the evidence is not conclusive as no constant dietetic deficiency has been so far discovered, and breast- and bottle-fed children are equally affected. Moreover the supply of all known vitamins fails to promote a cure.

The other thing is, that it is a virus infection, analogous to the causative agent of epidemic encephalitis, of a neurotrophic nature attacking the vegetative nervous system; this idea is strongly held by the French and German writers. To quote Rocaz: "the facts are extremely suggestive that pink disease is an inflammation of the nervous system and bears an intimate relationship to epidemic encephalitis."

Pathology.

Owing to the fact that the majority of cases of pink disease recover, the autopsies are few, and as the nervous symptoms have been but recently recognised, the detailed pathology of the nervous system has been investigated in only about five cases. The best recognised account is that of Paterson and Greenfield, who found diffuse cellular infiltration in the grey matter of the lumbar cord, the peripheral nerves showing similar changes with complete demyelination of nerve fibres; along with this they describe changes in the basal ganglia, oblongata nuclei, and cell chromatolysis on the floor of fourth ventricle, in lenticular nucleus, and the thalmus. Another notable feature was the presence of perivascular cuffing round the vessels and capillaries. That is, the changes found have been of a purely degenerative nature suggestive of a "toxic change on an infectious basis." (Freer).

Symptoms.

Onset.—The onset is insidious, vague symptoms of nasal catarrh and anorexia gradually develop into the complete clinical picture. The symptoms will be described according to the system affected.

Nervous System.—The first thing the mother may notice is the gradual onset of irritability and restlessness associated with insomnia and an increasing look of misery in the child. Sensory symptoms are difficult to investigate in infants, but the presence of irritation is evident from the restlessness, constant scratching, and gnawing of the body and extremities, and the resentment shown to lifting or moving. Some writers have described objective sensory changes in their older patients, e.g., hyperæsthesia and paræsthesia; one older child complained of sensations in limbs "like needles."

Tendon reflexes may be diminished or even absent in the more severe cases, in moderate cases little change is found.

Trophic changes are an essential feature in severe or advanced cases, e.g., loss of hair, falling out of teeth, necrosis or whitlows of fingers are all described, the latter occurring in one case of the present series.

Photophobia, when present, is characteristic; the child keeps its eyes tightly shut and lies in bed with its face buried in the pillow—"burrows"; no abnormality of retinæ is found, occasionally a mild conjuctivitis is present.

Soon after the onset, hypotonia and general softness of the muscles is noted; in the case of the child of two and a half years the gradual inability to walk was the

first symptom noticed. As the disease progresses the child ceases to try to sit up in bed, or when it does, the head falls forward or to the side; he may even lie on his abdomen or in a crouched position for weeks. In babies the mouth hangs open, characteristically described as "gosling mouth."

Occasionally a lumbar puncture is performed owing to the fact that meningismus with head retraction is sometimes seen; the fluid is usually found to be normal. Rocaz describes several cases where this meningismus was associated with a slight increase in cells, the highest recorded being 10/c.m.m.

Cutaneous Symptoms.—There is profuse sweating. Early in the disease a rash of papulo-vesicular erythematous nature usually occurs, and there is characteristic pinkness of feet, hands, and nose, which may show signs of desquamation. The extremities are constantly cold and often œdematous.

There is a tendency for the hair and teeth, if present, to fall out, and necrosis of fingers may be seen, while the liability to secondary sepsis is a complication for which observation should be made.

Digestive Symptoms.—The mouth occasionally shows a stomatitis which may become very severe. Anorexia is constant, with gradual loss of weight, the bowels tend to be constipated; this was recorded in ten cases of the series; occasionally slight diarrhœa may occur. Children over two years of age have been known to complain of colicky abdominal pains as is described by Feer.

Respiratory Symptoms.—At the onset of pink disease there is marked rhinorrhœa occasionally accompanied by mild bronchitis. Later a severe bronchitis or pneumonia may develop and may prove fatal.

Urinary Symptoms.—Not infrequently albuminuria with or without bacteriuria is found accompanied by marked pyrexia. Three cases of this were found in this series.

Circulatory Symptoms.—Tachycardia with slight increase in the systolic blood pressure is described by most writers and is apparently a fairly constant feature. Cyanotic attacks and true gangrene has been described by Feer. The blood, if examined, may show a slight leucocytosis and polycythæmia, the latter being due to dehydration from the intense perspiration. Continental writers also stress the fact that the blood calcium is often increased to 11-12 mg. per cent. with a low inorganic phosphorus content, the chloride remaining normal.

General Condition.—The most marked feature is the gradual deterioration of the child with wasting, associated with its very dejected appearance; a mild pyrexia may be present throughout, which often makes one suspect abdominal tuberculosis. Once convalescence occurs the uphill course is strikingly progressive.

TABLE OF FIRST SYMPTOMS.

	Cases	*Percentage*
Irritability	6	30
*Rash	4	20
Rhinorrhœa	3	15
Anorexia	2	10

Loss of weight	2	10
Mild bronchitis	1	5
Hypotonia	1	5
Cold feet and hands	1	5

* With regards to this, one has to distinguish between the primary erythematous papulo-vesicular rash (recorded above), followed by desquamation of skin of hands and feet, and the pinkness of these which is marked later on in the disease.

INCIDENCE OF SYMPTOMS.

	Cases	*Percentage*
Irritability	20	100
Pink feet and hands	20	100
Cold feet and hands	20	100
Anorexia	16	80
Loss of weight	15	75
Pyrexia	15	75
Rash	14	70
Hypotonia	14	70
Restlessness	13	65
Sweating	11	55
Sleeplessness	9	45
Rhinorrhœa	6	30
Bronchitis	6	30
Photophobia	6	30
Miserable appearance	6	30
Meningism	2	10
Coincident rickets	5	25
Coincident B. Coli infection of urine ...	4	20

THREE SHORT CLINICAL RECORDS OF CASES SEEN IN THE BELFAST HOSPITAL FOR SICK CHILDREN.

Case I.—Male, aged eight months. Bottle-fed. Five weeks before admission there was gradual onset of anorexia, then inclination to cry as if in pain. Head began to sag from side to side, and there was restlessness and free perspiration. Condition on admission: well nourished, child irritable and restless; hypotonia marked in neck muscles, perspiring freely, tips of fingers, palms of hands, and soles of feet bright pink, and tachycardia were present. In four weeks some improvement was noted. Net loss of weight approximately 1 lb. Now normal child doing well. In hospital five weeks. Duration before improvement, nine weeks.

Case II.—Male, aged seven months. Bottle-fed. Five weeks before admission began to cry incessantly, very restless, and cried as if in pain when moved; anorexia was present. Condition on admission: well-nourished infant. Both feet and hands were red and desquamating, and a papulo-vesicular erythematous rash was present on trunk and face; chest showed vesicular breath sounds, while child was per-

spiring freely, and bowels were constipated. Urine showed mild pyuria. Duration in hospital four weeks. Duration before improvement, nine weeks.

Case III.—Female, aged three months. Bottle-fed. Two weeks before admission very irritable, cross, throwing head about, photophobia, and insomnia marked. On admission: child of average nutrition, lying with head retracted and legs extended with very marked photophobia. Anorexia was present as was also a papular eruption on face and trunk. Head retraction and photophobia were so marked that lumbar puncture was performed and the cerebro-spinal fluid found to be normal. Urine showed B. coli and albumen. The course of disease in this case was pyrexial. Total loss of weight 2 lb. Duration in hospital six weeks. Duration before treatment, eight weeks. One week after discharge, readmitted with otitis media, which cleared up in two weeks. Total duration four months. Child now doing well.

Duration of Illness.

In some cases it was not possible to decide the precise date of onset, but the duration has been determined from the first departure from normal noticed by the mother to the date at which the child showed evidence of gaining weight with returning appetite, or, in the two fatal cases, the date of death. The longest duration in the series was five months, and the shortest three weeks, the average being two months. Longer duration has been noted by others, up to ten months; while Feer points out in his cases it was found that the older the child at the onset the longer the disease lasted.

Prognosis.

The prognosis is generally accepted as being favourable except in those cases with marked respiratory symptoms which are liable to develop broncho-pneumonia and prove fatal owing to the fact that the child is debilitated and unable to resist any secondary infection. In the cases under review two died from broncho-pneumonia, giving a death-rate of ten per cent. Others give mortality as high as twenty-five per cent. Rocaz points out that the average mortality recorded (eight to twelve per cent.) is probably too high, owing to the fact that probably only the severer cases are seen in hospitals or by statisticians, and that many milder cases go unrecognised. Complications recorded in the series were otorrhœa, three cases; whitlow of toes in one case; all the other cases cleared up and resumed the existence of normal children. Other complications described are encephalitis, severe stomatitis going on to noma, gastro-enteritis, and septicæmia.

Differential Diagnosis.

Early in the disease the irritability and photophobia may suggest meningitis or teething. The wasting and anorexia suggests tabes mesenterica. The erythematous rash with peeling of hands may lead to diagnosis of scarlet fever, but in all cases of pink disease the rash is followed by the characteristic pink; while the intense itching might suggest scabies or a toxic dermatitis.

The hypotonia, inability to walk and irritability and accompanying stomatitis may suggest rickets, muscular dystrophy, acute anterior poliomyelitis, epidemic

encephalitis or diphtheretic paralysis, while the pinkness of the extremities associated with coldness makes one think of Raynaud's disease or cardiac disease. However, a careful clinical examination will show a variable combination of the more marked symptoms which make a picture easily recognised as a definite disease syndrome; here one could include Bilderback's mnemonic, "Pain, peeling, prostration, paræsthesia, perspiration, posture, Pink."

Treatment.

This largely consists of treating the symptoms with an understanding of the disease syndrome. In the Belfast Hospital for Sick Children the child is clothed with non-irritating material next the skin, e.g., silk, linen, or cotton, with woollens on top. It is put into a large-size cot with pillows around the sides to prevent bruising when restless, no bed clothes are supplied, but the infant is protected from draughts and bright light by a screen which helps to decrease the photophobia; some writers recommend the use of ruby glass for windows. If very restless, sedatives are given, e.g., bromides, chloral, phenobarbitone, trional or one of the newer barbiturates. The skin condition is treated with lotio calaminæ, zinc oxide, and talc powder and frequent baths, while the feet and hands are kept covered so as to prevent scratching and picking of trunk and extremities. Atropine is recommended to combat the intense perspiration. Maintenance of nourishment is essential and forced feeding may be required as increase in food taken and general improvement appear to occur simultaneously; with regard to this, relaxation of the rules in infant feeding may be allowed, taking as a rule "any reasonable form of nourishment at any time."

Hydrotherapy is a method advocated by some writers; frequent baths and cold sponging appear to relieve the patient considerably, and older children definitely like to immerse their hands in cold water. Some authorities also give extra fluids orally to make up for the fluid lost in perspiration.

Treatment with ultra-violet light and vitamin preparations has been tried, but no outstanding benefit from these lines has been recognised.

Acting on the similarity of animal and human disease syndromes raw liver has been given to cases of pink disease with satisfactory results by Wyllie and Stern, basing their treatment on the fact that Finlay and Stern produced a disease syndrome in rats similar to pink disease, and rapidly cured it by the addition of raw liver to the diet. Braithwaite, on the other hand, states that liver may be definitely harmful, as five of his cases treated thus developed severe diarrhœa and rapidly became much worse.

Another line of treatment is one based on the fact that the blood calcium is raised. Sodium citrate is administered intravenously or intraperitoneally in four per cent. solution, or orally in five- to ten-grain doses; this $Ca_3(PO_4)$ and $CaCO_3$ thus decreasing the amount of calcium absorbed and lowering the blood calcium. This produces an immediate beneficial effect in decreasing the restlessness and irritability of the child, although it has not yet been claimed that the duration of the disease is shortened.

So far, no universal line of treatment has been adopted, owing to the fact that the etiology is indefinite, but good nursing combined with maintenance of nutrition, along with the cooling measures of hydrotherapy and light clothing, appear to be the best routine yet known.

Summary.

An account is given of pink disease, dealing briefly with its history, etiology, symptomatology, prognosis, and treatment, with reference to and quotations from notes of twenty cases from the wards of the Belfast Hospital for Sick Children, 1933-38.

For access to their case records I wish to thank Dr. Rowland Hill and Dr. F. M. B. Allen, and to the latter for his advice and criticism; also to Dr. Muriel Frazer for reading the proofs.

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REVIEW

DIETETICS IN GENERAL PRACTICE. By Leslie Cole, M.A., M.D., F.R.C.P. 1938. London: John Bale Medical Publications, Ltd. Pp. 150. Pocket-Monograph Series. Price 3s.

This book is notable for the inclusion and detailed description of diets which are easily followed, simple, and clearly set out.

The first part of the book deals with intestinal disorders, and shows how simple disorders can be effectively dealt with by proper dieting. Menus of special value to the general practitioner are those suitable for the treatment of the patient suffering from incurable carcinoma—to quote the author, "by giving as full a diet as possible much can be done to prolong life and activity and lessen the misery which results from profound weakness and under-nutrition." In dealing with the treatment of gastric and duodenal ulcers, there is a full graduated course of diets, including a description of the Meulengracht treatment of hæmatemesis.

The second part deals with diets suitable for treatment of genito-urinary disorders, metabolic disorders, cardio-vascular disease, etc. The chapter on "Diseases of the Kidney" is well written, and the aim of the diets here is "to relieve the organ of all unnecessary strain and at the same time to give a diet which is sufficient both for recovery and as a high standard of general health as possible."

The general practitioner will find this small book useful not only for refreshing his memory on the dietary treatment of disease, but also for the clearly set out diets which his patients could easily follow and understand.

So far, no universal line of treatment has been adopted, owing to the fact that the etiology is indefinite, but good nursing combined with maintenance of nutrition, along with the cooling measures of hydrotherapy and light clothing, appear to be the best routine yet known.

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REVIEW

DIETETICS IN GENERAL PRACTICE. By Leslie Cole, M.A., M.D., F.R.C.P. 1938. London: John Bale Medical Publications, Ltd. Pp. 150. Pocket-Monograph Series. Price 3s.

This book is notable for the inclusion and detailed description of diets which are easily followed, simple, and clearly set out.

The first part of the book deals with intestinal disorders, and shows how simple disorders can be effectively dealt with by proper dieting. Menus of special value to the general practitioner are those suitable for the treatment of the patient suffering from incurable carcinoma—to quote the author, "by giving as full a diet as possible much can be done to prolong life and activity and lessen the misery which results from profound weakness and under-nutrition." In dealing with the treatment of gastric and duodenal ulcers, there is a full graduated course of diets, including a description of the Meulengracht treatment of hæmatemesis.

The second part deals with diets suitable for treatment of genito-urinary disorders, metabolic disorders, cardio-vascular disease, etc. The chapter on "Diseases of the Kidney" is well written, and the aim of the diets here is "to relieve the organ of all unnecessary strain and at the same time to give a diet which is sufficient both for recovery and as a high standard of general health as possible."

The general practitioner will find this small book useful not only for refreshing his memory on the dietary treatment of disease, but also for the clearly set out diets which his patients could easily follow and understand.

Blood Storage for Transfusion

By J. M. Houston, M.D., B.Sc.
Royal Victoria Hospital, Belfast

This is a preliminary report describing the storage of blood for transfusion, and comparing the results obtained in the first fifty cases transfused with those of fresh blood transfusions.

Blood storage is a definite advance in blood transfusion therapy, the use of such blood having a number of advantages over fresh blood; notably the saving of time, and the fact that the blood may be collected to suit the mutual convenience of the donor and of the doctor responsible for the venesection. Thus its advantage in an emergency, and in war time when many urgent transfusions may be necessary, would be very great. It is also a means of avoiding the waste of blood, as the blood collected from cases where venesection is done as a therapeutic measure need no longer be thrown away, but may be kept until a suitable occasion arises for its use. In addition to the healthy donor and the therapeutic venesection, the source of the blood may be from the placenta or the cadaver. Cadaver blood differs from that from other sources in that it is said not to require the addition of anticoagulant preserving solution. The method has been employed to a considerable extent in Russia, and is still on trial.

Most of the blood which I have stored was obtained from therapeutic venesections, and included cases of hypertension, cardiac failure, and polycythæmia. Albuminuria or an increase in the blood urea do not constitute a bar to the use of the blood, and such blood has been used with similar results to the blood from normal donors. Some of the bloods were from healthy subjects, and a few were placental.

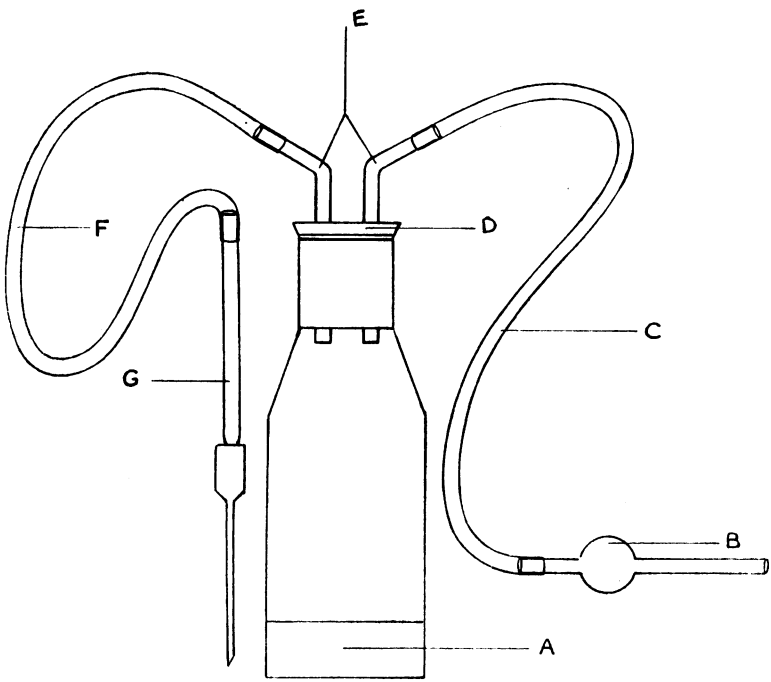
The number of anticoagulant preserving solutions used is large, but after trying many different solutions I have found the following, composed by mixing one part Solution 1 with three parts Solution 2, before use, to give the best results:

Solution 1	Sodium Citrate	3.8 g.
	Bi-distilled Water	100 c.c.
Solution 2	Glucose	5.0 g.
	Bi-distilled Water	100 c.c.

Further trials may require a slight modification of this solution. Experience has shown that adherence to the proportions in which the two solutions are mixed is very important if the best results are to be obtained. The total amount of the preservative used is also important, the blood keeping best when the quantity is large. A fixed quantity of 200 c.c. has been found to be a suitable amount to use, volumes of blood up to 500 c.c. when mixed with this volume of preserving solution keeping in a state suitable for transfusion for many weeks. The method of preparing the solutions is important. 150 c.c. of the glucose solution are sterilized in the collection bottle in the steam sterilizer. Glucose cannot be satisfactorily autoclaved or sterilized with the sodium citrate, 50 c.c. of which are separately

sterilized in a small flask. After sterilization the containers are kept in the ice chest until required for use. While this solution has been found to be the one of choice for keeping blood in storage for long periods, 3.8 per cent. sodium citrate alone has been found quite satisfactory for the preservation of blood for short periods. One part of 3.8 per cent. sodium citrate when mixed with nine parts of blood will keep the mixture in a satisfactory state for transfusion for from one to two weeks.

The method of venesection is similar to that ordinarily used, and the time at which it is done does not appear to be of any significance, though the cases done on a fasting stomach tend to give a clearer supernatant plasma than those done directly following a meal. This, however, did not appear to influence the quality of the blood, its keeping properties, or its sterility. The blood cultures were invariably sterile. The chief factor in the venesection is that the blood should run off easily without any impediment. If any difficulty is experienced in getting off the blood it is unlikely to keep well. Trauma at all stages is to be avoided. The blood collection bottle consists of an ordinary one-pint or two-pint milk bottle (see diagram), according to the amount of blood for collection. This is stoppered with a rubber bung D,



Apparatus for the collection of blood.
(For details see text)

containing two holes. Short pieces of glass tubing E are passed through these holes, a moderate bend being present on the outside portion. The glass tubing is stoppered with cotton wool, and the whole assemblage containing the glucose solu-

tion A, is kept ready sterilized in the ice chest. When required for use the cotton-wool plugs are removed from the glass tubes which are flamed to ensure sterility. To one of them is then attached a piece of rubber tubing F, approximately one foot long. At the free end of this tubing the venesection needle is inserted. This consists of a small needle made of nickel steel, size 14/10, and not exceeding one and a quarter inches in length. Into the hub of the needle is inserted a piece of glass tubing G, approximately three inches long, which may be kept in place with plaster of paris. This glass tubing serves as a handle for the insertion of the needle and also as a sight, blood showing in it immediately following entry of the needle into the vein. To the other piece of glass tubing is attached a rubber tube C, approximately two feet long; at its free end is inserted a glass tube B, about three inches long, and which contains a cotton-wool filter. Before use, the rubber tubes and needle are sterilized by boiling. The citrate solution is drawn into the bottle by applying buccal aspiration to the glass tube B. The resultant glucose-citrate mixture is well shaken, ensuring that all parts of the collection bottle are wet by it. The donor is prepared in the usual way lying down. A sphygmomanometer cuff is adjusted on the arm, and the region of the antecubital fossa is prepared. A pressure of 80 mm. Hg. is maintained by the sphygmomanometer and the needle is inserted in an appropriate vein, no local anæsthetic being required owing to its small size and sharpness. The needle is sharpened before each venesection. In most cases the blood will flow quite freely, intermittent clenching of the donors hand being a help. If the blood does not flow freely this can be brought about by applying slight buccal aspiration. Following collection the blood is stored in the ice chest at a temperature of 4°C., the rubber tubes being removed and replaced by sterile rubber caps. Rubber teats serve very well for this purpose. The blood is tested for its sterility, Wassermann reaction, and type.

On standing, the blood mixture separates into layers which appear in a definite order. Two easily distinguished layers first appear consisting of a lower one of the red blood cells, and an upper one of the plasma. In addition to these two primary layers, a third very thin layer containing the leucocytes appears within a few days at the junction of the other two layers. Should the plasma layer originally be cloudy, this may clear from above downwards. After standing for a varying length of time, but usually subsequent to the third or fourth week, a fourth layer appears as a buff ring directly above the intermediate third layer. This consists of red blood cells which have floated up into the plasma layer, and it finally assumes the clear red colour associated with hæmolysis of red blood cells. This final hæmolysis does not appear for some weeks following the appearance of the fourth layer, and it has been found that no ill effects follow the use of the blood prior to the onset of this hæmolysis. No blood has yet been used subsequent to this stage. The time of appearance of these later stages depends on many different factors, such as the nature of the preserving fluid, and its volume to that of the blood. Also important are the efficiency of the venesection and individual blood variations. Present indications are that the times given here may be extended with further experience.

Prior to use, the blood is heated in a water bath at a temperature of approximately 40°C. for about fifteen to twenty minutes. It does not appear to be essential that the blood should be brought to blood heat, and for a drip transfusion it is not necessary to heat it at all. Also for a transfusion which is given very slowly with blood which has been permitted to stand long enough at room temperature to lose its chill, heating does not appear to matter; but ordinarily where the blood is given soon after removal from the ice chest, I prefer to stand it in warm water as indicated above, while the necessary preparations for the transfusion are being made. The blood is gently mixed and filtered through sterile gauze. Some form of filtering is essential, as even though no clots are present a good deal of fibrinous material may have formed. The actual method of administration does not differ from that of fresh blood. I prefer to give it at the rate of fifteen to twenty cubic centimetres a minute. The actual preparations do not take long, and the blood may be in process of administration to the patient in as short a time as fifteen minutes. In addition to typing the preserved blood and that of the patient, a direct match is also done; the patient's serum being mixed with the preserved red blood cells.

The first fifty cases which were transfused with preserved blood comprised:

Twenty-seven transfusions for shock and hæmorrhage. The majority of these were post-operative cases, and cases of hæmatemesis. The oldest blood used in this group was thirty-five days.

Seven transfusions for symptomatic anæmia, the preservation time of the oldest blood in this group being ten days. Included here were cases of uterine bleeding, melæna, carcinoma of the cervix, and ulcerative colitis.

Five transfusions for leukæmia in which the preservation time of the blood ranged from two to twenty-eight days.

Three transfusions for hæmophilia with blood preserved for fourteen days, seventeen days, and twenty-three days.

Three transfusions for aplastic anæmia in which the blood had been stored for one day, seven days, and twenty-three days.

Two transfusions for microcytic anæmia with bloods preserved for three days and seventeen days.

Two transfusions for pernicious anæmia, one in which the blood had been preserved for six days, and in the other for eight days.

One transfusion as a pre-operative measure, with a mixture of two bloods which had been stored for five days and ten days.

Comparing the results obtained from these transfusions with those of fresh blood transfusions no essential differences were noted. They appeared to be quite as beneficial, the cases of shock and hæmorrhage responding well to them, and the oozing of blood which occurred following certain operations such as those to the gall-bladder was checked. All the seven cases of symptomatic anæmia derived benefit from their transfusions, and one case of ulcerative colitis in particular, who

had had several transfusions previously with fresh blood, responded to the preserved blood with a very good result. The five cases of leukæmia all derived temporary benefit from their transfusions. In the cases of hæmophilia the transfusion had the same effect in controlling the bleeding as had fresh blood, and the clotting time was also lowered. The three cases of aplastic anæmia derived a temporary benefit from their transfusions. The two cases of microcytic anæmia responded well. In the two cases of pernicious anæmia one did well; while the other, an aged patient in relapse, derived transient benefit. The result in the pre-operative transfusion was good. No ill effects resulted from any of the transfusions, and no rigors occurred. The only reaction encountered was in a hæmophiliac, who developed a mild transient urticaria following the administration of blood which had been stored for twenty-three days. The same patient had, however, had a similar reaction previously following the administration of fresh blood. The transfusion itself was beneficial.

With the exception of one transfusion which was done with placental blood, all of these were done with the blood obtained by venesection. The placental blood was given to a case of leukæmia with temporary benefit, and it is probable that placental blood is quite as satisfactory for transfusions as fresh blood, but it would be uneconomic to use it in most circumstances. The reason for this is that the yield from each placenta is not very great, about 60-80 c.c., and so the blood from more than one case will have to be used for an average transfusion. Also I think it is essential that the blood should be collected by a doctor with the proper experience, and again it should be looked after by a bacteriologist. A great deal of skilled work is therefore entailed with one placental blood, to which has also to be added the preparation of the apparatus and solutions. And as all this requires to be multiplied several times for each transfusion, the method is unsatisfactory where economic factors are taken into account. Regarding the preparation of the apparatus, I consider it as very important in all blood transfusion work that it should be very thoroughly cleaned, ensuring that it is entirely free of blood from any previous transfusions. All the apparatus has been prepared by first washing in tap water, then boiling in a weak alkaline solution; the rubber tubes in weak sodium bicarbonate, and the rest of the apparatus in weak caustic soda. After this it is again thoroughly washed in tap water, and finally with distilled water. Special attention must be paid to the cleaning of the rubber tube used for the venesection, and the mere pouring of water through it is not sufficient to wash out the blood. To ensure proper freeing of the tube of old blood it requires very thorough kneading and the forcing of water through it at high pressure. Attention to these details, and the proper administration of the blood will almost entirely eliminate blood transfusion reactions.

While no essential differences have been noted between fresh blood and preserved blood for transfusions, it is unlikely that the effect of the two is entirely similar. The impression gained is that preserved blood is slightly superior. Its immediate effects would appear to be much the same as those of fresh blood, but

it appears to have a greater stimulating effect on the hæmopœitic system, so that the final effect is rather better. Fresh blood may, however, be superior for cases of infection owing to its higher titre of complement.

SUMMARY.

The advantages of blood storage are stressed. Its greatest advantage is the saving of time, which may be a very important factor in an urgent case.

A satisfactory method of blood preservation is described. While the preservation time of the oldest blood so far administered was thirty-five days, present indications are that this time may be considerably extended. It requires emphasis, as previously stated, that the period during which preserved blood remains in a state suitable for transfusion is not a constant one, but varies with the method of preservation. With many of the methods in use this period is limited to about two weeks; but this time may be considerably extended by the method given here.

The results in the first fifty cases transfused with preserved blood are compared with fresh blood transfusions. No essential differences were noted.

Quacks, Astrologists, and Medicine

By RICHARD H. HUNTER, M.D., M.CH., PH.D., M.R.I.A.

FROM the earliest times all manner of strange substances were used in the treatment of disease, particularly in the seventeenth and the eighteenth centuries. One of the most highly esteemed of these was the so-called bezoar stone, which was said to be found only in the "belly of she-goats." This substance was used in many ways, both internally and externally, and was greatly favoured for curing "the most obstinate Cutaneous Diseases by external application of the Powder to Leprosies, Erisypelas and Pestilential Sores." Its great objection appears to have been the price, for Dr. Slare in 1715 complained that it cost "Three Pound and Ten Shillings per pound weight, and the finest quality no less than Four Pound."

Minced hair was a favourite "drug" at this time for the treatment of worms. This drug was classed as a "dangerous drug," and Dr. Tancrad, in 1715, "a Learned Virtuoso and Experienced Physician," described a case in which death occurred. He wrote: "He was sent for to see a Young Woman, whom he found in such dismal and terrible Convulsions, with such terrible Contorsions of her Body, that made him nicely enquire into the cause of such frightful Symptoms; which he rationally concluded to proceed from a large Quantity of Minced Hair her Mother had given her for several Days together, before the Convulsions attacked her, with the Design to kill the Worms she had been afflicted with."

In country districts in parts of England, it is said even to this day, that a ring made from a piece of silver collected at the communion in church, or from small coins given by five bachelor friends, unknowingly to one another, and worn constantly on one of the patient's fingers, will protect against attacks of epilepsy.

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Warts, contracted sinews, wounds, sores, and skin rashes were treated even to within recent times by the application of saliva, secreted in the morning before breakfast on a fasting stomach.

Practitioners at this period were not expected to be mere specialists, but were on the other hand expected to be, and indeed were, men of wide talents. An old sign-board discovered in a Cornish village, and now in the possession of the Horniman Museum, London, of a surgeon who practised as late as the last century, gives a good idea of the "well read man." It reads as follows:—

ROGER GILES, SURGIN

"Roger Giles, Parish Clerk and Skulmaster, Groser and Hundertaker, Respectably Informs Ladys and Gentlemen That he Drors Teef without waiting a Minute. Applies Laches every hour. Blisters on the Lowest Terms and Visicks for a Penny a Peace. He sells Grandfathers' Kordiales. Kuts Corns and Bunyons. Doctors Hosses, Clips Donkies Wance a Munth and Hundertakes to Luke after every Bodies Nayles and Ears. Joes-Harps. Penny Wissels, Brass Canelsticks, Fryinpans and other Moozikal Hinstruments hat greatly Raydoosed Figers. Young Ladies and Gentlemen Larns Their Garrmur and Langeeudge in the Puritest Manner. Also Grate Care taken of their Morrels and Spellin. Also Zarm-Zinging. Tayching the most Vital and all other Zorts of Fancy Works, Quadrils, Polkers, Weazels and all Country Dances Tort at Home and Abroad at Perfekshun. Perfumery and Snuff in all its Branches." And an almost endless list of articles with little or no connection with medicine, such as "Zinging Burds Keeped sich as Hawks, Donkies, Payrots, Lobsters and Crickets."

In the Middle Ages the recognition of astrology by medical men was very considerable, although it varied from time to time and from place to place in its application. But most authorities were agreed that the stars had a powerful influence on the power of herbs, and favourable stellar arrangements had to be selected or the herb in question would be devoid of virtue.

Culpeper's translation of the London Dispensary (1649) contains many references to "Astrological Pharmacology," as it has been called. For example:—

"Verbascum, Thapsus Barbatus being gathered when the Sun is in Virgo and the Moon in Aries, their mutual antiscious (opposites) helps such of the falling sickness as do carry it about them; worn under the feet it helps such as are troubled with fits of the mother."

By the law of contraries, the regions towards the south where neither sun nor moon rises were regarded by the old astrologers with fear and trembling; and the stars which inhabit this section of the heavens, Orion and Sirius, were associated with deeds of darkness. The Druids are said to have believed this tale, and never gathered their sacred vervain, a herb used for and against witchcraft, except when the dog-star rose from unsunned spots.

The mysteries of astrology were used by many early physicians, and old advertisements openly announce this fact. One such advertisement of a certain Dr.

Sandforth, whose address was given as "by the Watch-house, at the Blew Ball and the Stars hanging out of the Balcony about half a mile beyond White Chapel Church, Middlesex," styled himself an "Astrological Medicus." He claimed "With God's Blessing in his long Studies and Practise in Physick and Astrology hath obtained most proper and experienced Secrets viz: his most excellent, highly approved Soveraign Cordeal, Cathartick, Universal Purging Pills which fortify decaying Nature."

The subject of astrology was frequently associated with advice on love and matrimony. Dr. Selkirk, who "was to be spoken with every day in the week from morning till night," and who gave as his address "The Golden Ball in Gulstone Square, being the next turning beyond Petticoat Lane and the next turning beyond Whitechappel Bars, and the third house in the left-hand side in the square," claimed that he possessed "the Art of Presaging or Foretelling all Remarkable Things that ever shall happen to men and women in the whole course of their lives."

As an example of his powers in this direction he described the following case :—

"A Young Women had a person pretending to love her for many years. I told her she would find him false and deceitful to her, and that he never designed to marry her. She found it True, for shortly after he married another. Soon after she had several sweethearts at a time and came to me for advice: I told her there was one of these she could be happy with, and described him to her. She took my advice and marryed him and they prove a very happy couple."

Dr. Selkirk, in his printed announcement, writes as follows :—"I have Prevented the Ruin of Hundreds of Young Men and Women by advising them to whom to dispose themselves in marriage. Another who had been many years plagued with a Bad Husband, I told her in a few months she'd Bury him and marry again very happily, which she found true."

A further development of the Astrological Medicus was a continental quack in the early seventeenth century, who claimed to purvey a "Secret Arcanum" which he had discovered "after a long course of experiments." This was "the wonderful secret of procreating either sex at the joint option of the parents."

This gentleman wisely declared that "he will pay not attention but to letters post-paid and seigned with real names directed to him at the Antegellican Coffee-house by the Royal Exchange."

"Love-philters"—charms and potions to excite love in backward swains—also were sold by the Astrological Medicus. A practitioner who dispensed these is beautifully described by Thomas Hardy in "Jude."

"Vilbert was an itinerant quack-doctor, well known to the rustic population. Cottagers formed his only patients, and his Wessex-wide repute was among them alone. He was in fact a survival. Jude had one day seen him selling a pot of coloured lard to an old woman as a certain cure for a bad leg, the woman arranging to pay him a guinea in instalments of a shilling a fortnight for the precious salve, which according to the physician could only be obtained from a particular animal

which grazed on Mount Sinai, and was to be captured only with great risk of life and limb."

Dr. Vilbert's love philter activities are described in "Jude" as follows:—"The philter is such as was used by the Ancients with great effect. I found it out by study of their writings and have never known it to fail. A distillation of the juices of doves' hearts is one of the ingredients. It took nearly one hundred hearts to produce this small bottle full. You use the liquid by contriving that the desired man shall take about ten drops of it in his drink," etc.

A development of the activities of sellers of such love philters, was the further side-line of beauty preparations. One practitioner living at "The Surgeon's Sign, just at the corner of Coventry Court in the Haymarket, near Pickadilly," advertised a "Balsamick Essence" at a shilling a bottle. The announcement reads:—

"A super-excellent paste for the shaking and trembling Hands after hard drinking or otherwise. It will also make them smooth, soft and of a delicate white colour, that although you were to Scower Brass and Pewter and to make Coal Fires every day, yet nobody will imagine you to do any such drudgery, as hundreds can testify."

A practitioner of this variety who lived in "Surrey Street in the Strand at the Corner House with a white Balcony and Blue Flower Pots," not only sold a "Wash" which "Beautifies the Face and cures all Reddness, Flushings and Pimples" at five shillings a bottle, and also sold "Night-masks, Forehead-pieces, and red pomatum for the lips, which keeps them all the year plump and smooth and of a delicate colour."

This practitioner also sold "A Plaister and Water which takes off the Hair from any part of the Bodie, so that it will never grow again. Also a most excellent Secret to prevent the Hair from falling, causing it to grow where it is wanting on any part of the head, and colours the Hair grey or red to a lovely brown which never decays, changes or smoots the linnen."

Such were the early practitioners of our art in the sixteenth and seventeenth centuries. And although we have long since ceased to act as advisers of love or to dispense beauty preparations, the general public does not seem to have advanced much further, if we are to judge from the advertisements in the daily press.

REVIEW

ESSENTIALS OF FEVERS. Gerald E. Green, M.D., D.P.H. 7s. 6d. Edinburgh: E. & S. Livingstone.

This little book has many advantages: It has two hundred and seventy-four pages, and is described as being "pocket size." The type is large and the paper good. There is nothing very new about the volume, but the various fevers are described in a manner which indicates that the author has an up-to-date knowledge of his subject. Prophylaxis is dealt with as well as treatment, and this includes a short description, very essential at the present, of the various types of respirator in use. The illustrations, which are not in colour, are not in the main very helpful, while diet might with advantage be considered in more detail. The publication will be acceptable to the student who desires the "essentials" for examination and general practice.

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Carcinoids of the Intestinal Tract

By M. G. NELSON, M.B.

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CARCINOID or argentaffin tumours of the intestine have for a considerable time aroused the interest of pathologists, histologists, and others, and many papers on these peculiar growths have been added to the rapidly growing medical literature. These tumours occur mainly in the small intestine and appendix, which are sites rarely affected by other primary tumours. They are commonly multiple, grow slowly, invade locally, and rarely metastasise.

Interest in carcinoid tumours was reawakened in this department by a series of cases occurring in the appendix, but one case of multiple growths of the ileo-cæcal region which was found at autopsy to have metastasised to the regional lymph-nodes rendered the series sufficiently interesting to warrant publication of the group.

There have been many adequate reviews of this subject up to date, but the paper of Forbus deals admirably with the earlier work. Primary carcinomata of the appendix and small intestine are rare, and the first record of such a case was in 1838 by Merling. Since then some four hundred cases have been described.

Lubarsch in 1888 contributed the first valuable paper on this subject, when he described two cases of new growth in the ileum. These tumours were multiple, whitish in colour, occupied the mucosa and submucosa and infiltrated the muscularis. They were composed microscopically of nests and columns of epithelial cells which, he pointed out, differed from the ordinary epithelial cells of the intestinal mucosa and from the cylindrical cells of the adeno-carcinoma. From these peculiar features—

(1) Multiplicity,
(2) Lack of metastases,
(3) Lack of true glandular structure,
(4) Type of cell present,

it was apparent that, although the tumours were of epithelial origin, they differed from true adeno-carcinoma. Despite the appreciation of these distinctive features, Lubarsch called these tumours "primary carcinomata of the ileum."

Between 1888—1907 numerous new cases of primary tumours of the appendix and small intestine were reported. Of these, two were described which had metastasised, in one case to the regional lymph-nodes and in the other to the liver.

In 1907 Oberndorfer gave a classical description of the morphology and biology of these tumours, and suggested that the name "carcinoid" or little carcinoma be applied to them. Since this date the fact that the growth constitutes a distinct pathological entity has been undisputed, but controversy has raged around the possible histogenesis of the growth, and many theories as to their nature have been put forward.

It was not until Masson, by using a modification of Fontana's silver-impregnation method, demonstrated the presence of silver-reducing or argentaffin granules in the cytoplasm of carcinoid cells, that a sure foundation for their histogenesis was laid. Masson coined the word argentaffinoma as a synonym for these growths which expresses their most marked microchemical characteristic. This work definitely showed the relationship, if not genetically, at least microchemically between the epithelial cells of the carcinoid and certain silver-reducing or argentaffin cells which are normally found along the gastro-intestinal tract. The problem now requiring solution is the derivation, nature, and function of these argentaffin cells.

Their derivation has been variously ascribed to the entoderm, mesoderm, and ectoderm. Masson believes that they arise from the neuroentoderm and that their function is neurocrine, i.e., that their secretion influences nerve-tissue. The nerve-tissue which is acted on by the secretion of these cells is thought to be the periglandular nerve plexus, so that the argentaffin cells eventually control the secretory activity of the normal mucus-secreting cells and also influence the muscularis mucosæ.

Using serial section technique, Masson has demonstrated that in a carcinoid tumour the epithelial argentaffin cells budded off from the base of a crypt of Leiberkuhn and migrated into the nerve-sheaths of the underlying neurinoma. The cells became neoplastic in this situation, and their secretion stimulated the new formation of nerve-fibres and caused hypertrophy of the muscularis mucosæ. Thus nerve-tissue and smooth muscle formed a prominent part of the stroma. This theory since its original proposition has been met by much criticism and opposition.

No.	Sex	Age	Situation	Local Ulceration	Local invasion	Metastases	Associated lesion
1	F	23	Appendix tip	+	+	—	—
2	F	21	Appendix	No	+	—	—
3	F	27	Appendix	+	+	—	—
4	F	30	Ileum	+	+	—	—
5	F	11	Appendix	+	+	—	—
6	F	30	Appendix	+	+	—	—
7	F	40	Appendix	+	+	—	—
8	F	71	Appendix	+	+	—	Mucous cyst ?Mucocele
9	F	47	Cæcum	No	+	—	Mucous cyst Chr. inflamm. reaction
10	M	65	Appendix	+	+	—	—
11	F	40	Appendix	No	+	—	Stenotic appendix
12	F	64	Appendix	No	+	—	Stenotic appendix
13	F	71	Ileo-cæcal	+	+	Yes	Chr. inflamm.
14	M	39	Appendix	+	+	—	—

Despite much work on this field, the physiology and embryology of these argentaffin cells remain to be found.

The object of this paper is to present a series of fourteen cases of carcinoid tumours of the gastro-intestinal tract. It was considered unnecessary to give complete clinical and pathological details of each case, but three cases were chosen which were considered typical and recorded in more detail.

Eleven of these tumours occurred in the appendix. Of these, ten had been removed at operation for some symptoms of an ill-defined nature referable to the right side of the abdomen. In one case it was an accidental finding at post-mortem in an elderly female dying of cardiac failure. Of the remaining three, one occurred in the ileum, one in the cæcum, and the other in the terminal ileum and around the ileo-cæcal valve.

CASE 5—Female, aged 30; *occupation:* cloth examiner.

Clinical History: No previous history of scarlet fever or tonsillitis. In 1932 she had pleurisy, type not recorded. In 1935 patient was curetted. From this until the onset of the present complaint all her bodily habits were regular and sleep good.

One month before admission patient took a sudden severe pain in the epigastrium, which lasted four days. This pain eventually localised in the right iliac fossa. Patient was then seen by her own doctor, who put her to bed for five days, but the pain, though diminishing in severity, did not disappear entirely and was present at the time of examination. On examination there were no physical signs beyond a little tenderness in the right iliac fossa. A clinical diagnosis of subacute appendicitis or appendicitis in the quiescent phase was made.

Operation—The patient was operated on and the appendix removed. The appendix was long, measuring four inches from base to tip, but was not kinked or mechanically obstructed in any way. About one and a half inches from the tip there was situated a small whitish-grey tumour which occupied the submucosa.

Histological Examination—This appendix was fixed in formol and cytological details are thereby destroyed.

The tumour occupies the region of the submucosa, has not infiltrated the muscle, and the mucous membrane over the tumour is intact. The muscularis mucosæ has been broken up, and lies in fragments in the stroma of the growth. Through these gaps in the muscularis mucosæ groups of tumour cells have wandered into the mucous membrane, and are found lying between the bases of the glands of Lieberkuhn, which themselves do not show any histological changes.

The main tumour is composed of sheets and columns of exceedingly regular epithelial cells, which lie in spaces formed by the stroma. The cells have a regular oval nucleus, with a wide-meshed chromatin net which shows nodal condensation. The nuclear membrane is clear cut, and none of the cells show evidence of mitotic division, although some of the nuclei are more hyperchromatic than others.

The cytoplasm of the cells is finely granular, and these granules are characterised by being—

(a) acidophilic staining red with acid fuschin.
(b) siderophilic—black with iron hæmatoxylin.
(c) argentaffin—or silver reducing.

Their chromaffin nature was not demonstrated. The cell outlines were indistinct, and one cell fused into the next.

Attempts at palisading, i.e., acquisition of a definite polarity by the cells lying in contact with stroma, and even pseudo-acinar formation was noted.

The stroma is composed mainly of dense bands of collagen which interlace and separate the epithelial elements. Elastic tissue was present also in the stroma, and the reticulum stained by Foot's modification of Bielchowsky's method has a definite carcinomatous arrangement—the argyrophilic fibrils lying between the masses of cells, but no fibrils were demonstrable among the cells of the epithelial columns themselves. Muscle-tissue and nerve-fibres were not prominent in the stroma of this growth.

There is no cellular infiltration in the stroma, and the growth is not associated with any of the lymphoid follicles.

The blood-vessels in the tumour have well-formed walls, and no tumour cells can be seen inside endothelial-lined spaces.

Case 4—Female, aged 30 years.

Clinical History—Patient has suffered off and on with "indigestion," which has occasionally wakened her at night. The symptoms were of considerable duration. A few days before examination she got a severe pain in the abdomen, which was followed twenty-four hours later by pain and tenderness in the right iliac fossa. She was then seen by her own doctor, who made a diagnosis of chronic appendicitis, the temperature and pulse being normal. X-ray after a through-going barium meal was suggestive of chronic appendicitis.

23/1/35—Patient was operated on through a right paramedian incision. An appendix which was much kinked but not inflamed was removed. It still contained barium six days after ingestion of the meal. On palpating the ileum, a small nodule was felt about two inches from the ileo-cæcal valve, which appeared to move freely with the mucous membrane. The bowel was incised and the nodule removed. There was a well-marked Lane's band at the level of the tumour, which was divided. No enlarged glands were palpable and the other intra-abdominal viscera appeared normal.

Microscopical Description—The tumour is composed of masses of epithelial cells lying mainly in the submucosa. These masses are mostly compact, but in the groups of cells lying in relation to the glands of Lieberkuhn, acinar and rosette formation occurs. The cells are regular in type and in the larger columns are polyhedral, although the peripheral cells show attempts at palisading. The cells which enclose a central cavity are columnar in shape, but mucous cells do not occur. The cells are regular in type, and the nuclear pattern is distinct and differs from the pattern of the normal columnar cell. The nucleus has a well-marked

nuclear membrane and a wide-meshed chromatin net with condensation at nodal points.

The cytoplasm is finely granular, and the intra-cytoplasmic granules give the usual reactions.

The growth is more cellular than most, and the stroma which separated the epithelial columns is composed of bands of fibrous tissue interlaced with muscle. Elastic tissue is not prominent in the stroma of this growth, and no nerve-fibres were seen.

The mucosa over the growth has been infiltrated and ulceration has occurred, so that the masses of tumour cells are in contact with the lumen of the gut. Inflammatory reaction at this ulcer site is of very mild degree. The muscle-coat has also been invaded, but further extension could not be made out.

Follow-up.—Patient alive and well five years after her operation.

CASE 13—Female, aged 71, old-age pensioner.

Clinical History—Patient gave a vague history of an operation for a "bone abscess" in the region of the right ilium seventeen years ago.

She enjoyed good health until about one year before admission, when she commenced to have attacks of crampy pain which were just vaguely above the umbilicus. These pains were intermittent, did not radiate or localise in any spot.

Associated with the pain, patient noticed that the abdomen became swollen, but this swelling disappeared with a rumbling noise, and then the pain abated. These attacks of pain were often associated with bouts of vomiting.

For the past few months patient had to indulge in a daily purgative in order to keep the bowels open.

Loss of weight was considerable, and the patient claimed she had lost two stone since the onset of the present complaint.

On Examination—The patient was an elderly, frail, somewhat anæmic female subject. Jaundice and cyanosis were absent, and the superficial lymph-glands were not palpable. There was a large scar present on the right side anterior to the sacro-iliac joint associated with a small scar below the anterior superior spine.

The tongue was coated and dry. On examining the abdomen, the skin and muscles were dry and lax. Loss of weight was obvious. No visible peristalsis or "laddering" of the gut were present. The liver and spleen were not palpable. A small tumour was palpable to the right of the umbilicus which did not move either with or apart from respiration. This growth was slightly tender on pressure. On massaging the abdominal wall the small intestine could readily be felt. P.R.—Nothing abnormal could be made out, and the rectum was empty of fæces.

Further examination only revealed signs of chronic bronchitis and a hypertension of 140/100, with slightly enlarged heart and normal rhythm.

Operation—At operation the small gut was distended and its wall hypertrophied. The cæcum showed a tumour mass which was fixed to the posterior abdominal

wall. The appendix was hard, distended and kinked, and was removed for biopsy. A side-to-side anastomosis was performed between ileum and transverse colon.

Post-operative Course was stormy and the abdominal wound became infected, but was drained satisfactorily. Patient began to vomit altered blood on the eleventh post-operative day, but this was treated by rest, morphia, and diet, and the patient recovered. On the nineteenth day patient had a sudden attack of epigastric pain and vomited. Abdomen became rigid and pulse rose to 160. Death occurred in two hours.

Autopsy—The relevant features were :—

(1) The peritoneal sac contained a large amount of brownish-black fluid with floccules of black granules of altered blood (coffee-grounds).

(2) The stomach showed the presence of numerous subacute peptic ulcers varying in size from 1 mm. to 10 mm. The edge was clean and the floor covered with altered blood. Many of these ulcers had perforated and were the source of the terminal general peritonitis.

(3) There was present in the terminal half-inch of ileum just before it entered the cæcum a tight annular constriction which looked as if a piece of string had been tightly tied round the gut. The ileum at this site was firmly united to the posterior abdominal wall by fibrous tissue, and into this fibrous focus were drawn the cæcum and related mesentery and glands. The lumen of the gut was so reduced that it only admitted a probe, and the gut proximal to the obstruction was dilated and hypertrophied. On section, the wall was infiltrated by a whitish growth with well-marked fibrous tissue formation, which had completely surrounded the lumen and was ulcerated on its mucosal surface. The related glands, although readily palpable, did not show any naked-eye infiltrations. On opening the cæcum, the mucous membrane was found to be studded over with numerous whitish-yellow nodular sessile growths varying in size from 1 mm. to 5 mm. These growths were found especially in relationship to the ileo-cæcal valve, and many had ulcerated slightly at their tip. Gross ulceration and excavation did not occur. The appendix had been removed.

(4) A short-circuit operation between ileum and transverse colon (side-to-side ileo-colostomy) had been performed, and was functioning normally.

(5) The right psoas muscle had been replaced by a hard fibrotic mass which involved the posterior wall of cæcum and terminal ileum. This was either

(a) Result of old "bone abscess," or

(b) Reaction to the growth.

(6) The appendix removed at biopsy was the seat of multiple growths in its wall with which were associated a mucocele.

Microscopically the tumour is characterised by the presence of sheets and masses of epithelial cells. Some of the columns appear to branch and unite with nearby groups of cells. The masses are for the most part compact, but in relationship to the mucous membrane many pseudo-glandular arrangements exist. The cells are

remarkably uniform in type. In the larger group these cells are polygonal from mutual pressure, while nearer the mucosa and in the pseudo-glandular arrangements the cells tend to be more columnar in shape, although they can be readily distinguished even with routine stains from the ordinary columnar cells lining the glands of Lieberkuhn. The nuclei are round or oval and the chromatin net coarse. Some nuclei show chromatin condensation, but no mitoses were noted. The cytoplasm was faintly granular and the cell outlines could be distinguished. Vacuolation of the cells was not in evidence. The intra-cytoplasm granules gave the usual reactions. The stroma was made up of dense bands of collagen with a reticulum network and varying amounts of elastic tissue. The blood-vessels were well formed, and many showed evidence of endarteritis obliterans.

The ileal growth had infiltrated extensively through the muscle coats and into the root of the mesentery, where it was found among the nerve-trunks at this site. Evidence of extension by the perineural lymphatics was well marked.

The related lymph-nodes showed the presence of multiple metastases, microscopic in size and situated in the central sinusoids. The metastases were similar to the primary growth, but the stroma was little in evidence.

Commentary.

A group of fourteen cases of argentaffin or carcinoid tumours has been reviewed. Three cases—

(1) Single submucous tumour in the appendix,
(2) Single tumour of the ileum,
(3) Multiple tumours of the ileo-cæcal region with metastases to the regional lymph-glands,

were chosen to illustrate in detail the morphology and nature of the group, and also to indicate ascending grades of malignancy.

Of these fourteen tumours, twelve occurred in females and the remaining two in males.

This predominant incidence in the female sex has not been found in other groups of cases recorded, where the sex incidence has been found to be about equal. The age of the group varied from 11 to 74, but on the whole tended to be rather older than usual, especially in the appendix group, where the average age was 39. The whole series occurred in the ileo-cæcal angle, thus confirming the predominant incidence already noted in this site.

There was no lesion invariably associated with the growths, but well-marked signs of a pre-existing chronic inflammatory lesion were present in four cases. The occurrence of a carcinoid growth in the wall of a mucocele in two cases was interesting, but it could not be determined which lesion had antedated the other.

The clinical history was in no way typical, and Ariel has stated that these tumours rarely produce signs and symptoms per se. However, a number of the appendicular cases gave histories which suggested an acute or subacute appendicitis. Case 10 was admitted to hospital with a three-day history of a sudden acute

abdominal pain which settled in the right iliac fossa, and was accompanied by tenderness and some rigidity. He was opened as an acute appendicitis, and at operation a small tumour was found in the appendix tip, with no signs of inflammation. The ileal and ileo-cæcal growths produce subacute intestinal obstruction of an ill-defined nature, and it has been stated that on X-ray, following a barium meal, the multiplicity of the growths can be determined. However, the diagnosis is rarely made clinically, but it is important to recognise those tumours at operation, because removal of these growths with their metastases (if any) offers a good prognosis.

Pathology.

The pathological features are distinctive. Although these tumours can occur (theoretically) in any situation in the gastro-intestinal tract below the œsophagus, i.e., in any site where the argentaffin cells normally occur, their commonest situation is in the region of the appendix and ileo-cæcal angle. Of all the growths described, some ninety per cent. have occurred in this situation. The tumours may occur singly, but are more commonly thought to be multiple. In this series all the tumours were single except No. 13, which was both multiple and had also metastasised to the regional lymph-glands. This association is probably entirely fortuitous.

The most commonly associated lesion is said to be a chronic inflammatory one, and Masson has postulated that the presence of an old chronic stenosis with its associated neurinoma is a necessary prerequisite for the growth. In many old chronic appendices with fibrous stenotic lesions a great increase in nerve-fibres and occasionally nerve-cells can be readily demonstrated in the submucous fibrous tissue. These nerves Masson considers to be derived from the peri-glandular nerve plexus, and that argentaffin cells migrate into the sheaths of these nerves before neoplasia occurs. A chronic inflammatory lesion did not occur frequently in this group, and Case 3 is interesting, as there was a history of an ileal abscess with fibrosis of the right psoas, i.e., a chronic inflammatory lesion outside the gut altogether, so that the neurinomatous theory could not apply. In two of the cases the carcinoid occurred in the wall of a mucocele, which is itself a somewhat rare pathological finding.

These tumours occur as small, firm, white or yellow nodules, which are usually sessile, but may be pedunculated and occupy the region of the submucosa and infiltrate the muscle-coats. The overlying mucosa is usually intact, but may be ulcerated. This ulceration is produced more by pressure of the underlying growth than by infiltration and necrosis. On section they have an opaque appearance and are a yellowish or yellow-grey colour. Microscopically they are composed of two clearly defined elements, the epithelial, argentaffin or carcinoid cells, and the stroma. In their gross arrangement they resemble carcinomata in that they are composed of columns and masses of cells which infiltrate. This apparent histological similarity is, however, only superficial. The cells comprising the carcinoid are remarkably uniform in type; they rarely form acini, and their intra-cytoplasmic granules have

peculiar reactions. The great difference, however, is in their biological behaviour, because the carcinoid tumour, although locally malignant, grows slowly, never necroses, and rarely metastasises. The epithelial cells are arranged in columns and masses of varying size which may branch and unite in an irregular manner. Sometimes small nests of carcinoid cells are found lying in stromal spaces. This apparent space between cells and stroma is an artefact produced by shrinkage during fixation, and during life epithelial cells and stroma were in contact. Polygonal cells are the commonest type, and no doubt this shape is determined by mutual pressure. There is a tendency for the cells resting on the connective tissue stroma to form peripheral palisades, i.e., in contact with the stroma they acquire a definite polarity. In this respect they resemble the peripheral palisading found in rodent ulcers (baselomata) of the skin.

Columnar cells do occur, especially grouped round a cavity or vesicle which may contain a granular colloidal material. These columnar cells differ from the normal mucus-secreting columnar cells of the intestine, while the contents of the vesicle are never mucus. These pseudo-acinar formations are found most commonly in the more superficial parts of the growth.

The nuclei are oval in shape and usually central in position. The nuclear membrane is clear, and the network coarsely reticular with chromatin condensation at nodal points. Many of the nuclei are more hyperchromatic than others, but mitotic figures were not seen in any of the tumours examined in this group. On the whole the cells are exceedingly uniform in type and the pleomorphism found in adeno-carcinomata is never seen.

The cytoplasm of the argentaffin and carcinoid cells shows the presence of fine granules which have distinct microchemical reactions, while occasionally they contain vacuoles containing fatty material stainable with sudan.

The stroma of these growths is exceedingly complex and composed of many diverse elements, which, however, cannot be demonstrated in all the growths.

Fibrous tissue is very abundant and interlacing bands of collagen form the most prominent part of the stroma. Fibres of smooth muscle can be demonstrated in the primary growth, but not in the metastases. The tumour evidently either stimulates the new formation of smooth muscle in the sites where it normally occurs, or it may be strands of smooth muscle already present at the site of the neoplasm which have been incorporated in the stroma during growth. Elastic tissue was found to be extremely variable in amount, but this may have been due to differences in staining technique. In the mesenteric extensions the elastic tissue was most abundant, especially in relation to blood-vessels in this site. The elastic tissue of the adventitia was markedly hyperplastic, and sent prolongations into the stroma of the argentaffinoma.

Argyrophilic reticulum was present in all the tumours and in the metastases—in both sites showing the characteristic carcinomatous arrangement.

Nerve-fibres could not be demonstrated in many of these growths. They probably do not occur as frequently as is stated.

Two other points serve to differentiate these growths histologically from adenocarcinomata. Firstly, all the blood-vessels have good muscular walls, while secondly, infiltration of the stroma is minimal in degree.

Biology.

The biological behaviour of the argentaffinomas is entirely different from the adenocarcinomata. Argentaffinomas are relatively benign. They are usually confined to the wall of the intestine which they invade locally, infiltrating the muscle coats, and may extend into the root of the mesentery.

Lymphatic invasion is rarely seen, although secondaries in lymph-nodes do occur. The total number of metastasising carcinoids reported to date is about thirty-eight. Of these, the commonest site for the metastasis is the regional lymph-glands, and in this series one tumour had a small microscopic secondary in the related glands.

Dissemination by the blood-stream with metastases in remote parts is very rare indeed. Because of this, the prognosis after operative removal of the primary growth and the related lymph-glands is exceedingly good.

Histogenesis.

The following is a summary of the various theories advanced to explain the histogenesis of the carcinoid tumours :—

1. True carcinoma arising from the intestinal epithelium.
2. Analogous to the basal cell carcinoma of the skin.
3. Derived from embryonic rests.
4. Derived from the sympathetic nervous system.
5. Nævi of mucous membrane.
6. Derived from the cells of Paneth.
7. Derived from argentaffin cells.

1. *True carcinoma arising from the intestinal epithelium.*—If this conception were true, then these tumours would be adenocarcinomata. It is because they differ morphologically and biologically that they have been separated from the carcinomata.

2. *Analogous to the basal cell carcinoma of the skin.*—This theory received the ardent support of Krompecher, who was interested in the separation of baselomata (rodent ulcers) from the squamous epitheliomata of the skin. The basis for this theory rested mainly on morphological grounds, and the analogy in structure between the two growths is extremely close. Both consist of sheets of cells with a tendency to peripheral palisading, and both are only locally malignant.

3. *Derived from embryonic rests.*—The postulation of any theory of embryonic rests to explain neoplastic formation is to neglect the modern trends in carcinogenesis and is of historical interest only.

(a) Islets of Langerhans.—Heterotopic foci of islets of Langerhans have been found along the intestinal tract. Saltkow postulated the origin of carcinoids from such aberrant islets. He pointed out that the intracytoplasmic granules of

carcinoid tumour cells were acidophilic and that their arrangement in the basal part of the cell is typically endocrine in nature. However, the presence of a positive chrome reaction and the fact that the granules were silver-reducing, definitely precluded their origin from pancreatic islet tissue, the cells of which gave neither reaction.

(b) PANCREATIC RESTS.—The basis for this theory has little foundation, and need not be discussed.

(c) ADRENAL RESTS.—Because the carcinoid cells contained fatty droplets stainable with sudan, gave a positive chrome reaction, and their intracytoplasmic granules were siderophilic, they therefore resembled the cells of the adrenal. However, the carcinoid cells partook of the characters of the cells of both cortex and medulla. Anatomically, embryologically, and functionally the cortex and medulla are distinct, and a tumour cannot be composed of both.

4. *Derived from the sympathetic nervous system.*—Ehrlich believed that these tumours arose from Auerbach's plexus, and called them immature sympathetic neurocytomata.

5. *Nævi of mucous membrane.*—The origin of skin nævi or melanomata has occasioned much speculation and more theory. The nervous theory of origin has much to commend it, and probably owes its origin to Soldan, who traced nerve fibrils among groups of nævi cells. Masson then brought forward evidence in favour of the origin of nævi from the cutaneous sensory nerve endings, and showed their relationship to the neurofibromatosis of von Recklinghausen. Although the relationship of nerve fibres and nævi cells is beyond dispute, the actual origin of these cells is unknown. Theoretically they should be mesodermal in origin, while histologically they partake more of the morphological type of epidermal cells. Aschoff considered carcinoids to represent nævi of mucous membranes. Certainly this resemblance is more than superficial, but it does not explain the peculiar biochemical characters of the granules or their site of occurrence.

6. *Derived from the cells of Paneth.*—There are exocrine cells found along the gastro-intestinal tract lying among the mucus-secreting cells, and contain zymogenic granules stainable by special stains. These granules are not silver-reducing when stained by the methods of Masson and Hasegawa. They do reduce the silver in Popoff's stain, and have been found to discharge their contents into the lumen of the gut. They are not concerned in the formation of carcinoids, but do form a distinctive growth of their own.

7. *Derived from argentaffin cells.*—Masson was the first to shed light on the histogenesis of carcinoids. By using a special histological method he showed that the intracytoplasmic granules in the carcinoid cells possessed the power to reduce silver salts to silver and become readily visible as black granules. He suggested that the term argentaffinoma be applied to these growths.

The cells composing the carcinoid therefore resembled certain cells normally found along the gastro-intestinal tract. These cells were first noted by Heidenhain, and later were more fully described by Schmidt and Kultschitzky and have been

variously called Schmidt cells, Kultschitzky cells, and argentaffin cells. They occur all along the intestinal tract, but especially in the colon, where five or six occur in each crypt of Lieberkuhn, where they are parietal in position and rarely abut on the lumen of the crypt. The nucleus is regular, oval in shape, but is never basal in position, while the cell is plump and of the "comma" type. The supranuclear protoplasm is clear, but occasionally contains a vacuole stainable by sudan. The basal protoplasm is granular, and these granules are acidophilic, chromaffin, siderophilic, and argentaffin. There is usually a cytoplasmic projection from the apex of these cells which passes between the columnar or mucus-secreting cells, but rarely reaches the lumen of the gut. The embryological derivation of these cells is disputed, while their function is unknown. Masson has attributed an endocrine function to these cells, and has suggested that their secretion stimulates the mucosal plexuses and influences the muscularis mucosæ.

Recently Popoff in a long and closely reasoned paper has brought histological and experimental evidence to prove that the argentaffin cell is merely a phase in the rejuvenation of the ordinary mucus-secreting cell. He shows that the mucus-secreting cell passes through a phase of secretory activity with discharge of mucus into the lumen of the gut, but the cell may exhaust its store of potential energy by succeeding waves of secretory activity. It then sinks to the basement membrane, becomes squat in shape, and peculiar changes occur in the cytoplasm. Granules appear which are stainable by metallic stains, including silver. These granules have never been shown to be discharged from the cell as an exocrine secretory product, nor is there any well-substantiated evidence to show that they are endocrine. This cytomorphosis is a chemical change resulting in functional rejuvenation. The cell then grows in length, loses the argentaffin granules, and again becomes a mucus-secreting cell capable of further functional activity. Contrary to the work of Masson, Popoff has shown that argentaffin cells form an integral part of the mucous membrane of the gut, and do not wander from this site into the submucosa. Cells with silver-reducing granules in the submucosa are in reality macrophages.

If the work of Popoff is correct, then this is a tumour the cells of which do not show evidence of active proliferation, but instead are always undergoing functional rejuvenation as a preliminary to mucus-secretory activity. In all the tumours examined the cells were uniform in type, and no attempt at differentiation to mucus-secreting cells could be made out, nor were there any variants of this tumour which showed any tendency to produce cells of the mucus-secreting type. One would have thought it possible to have found tumours showing various intermediate stages between the adenocarcinoma and the carcinoid. In spite of the relative frequency of these neoplasms, such intermediate types have not been recognised.

Through this mass of conflicting theory a few facts arise. Firstly, that the carcinoid tumour or argentaffinoma is a distinct entity with a peculiar morphology, and differs from the adeno-carcinoma of the intestinal tract. Secondly, that although the relationship between the carcinoid cell and the argentaffin cell of the gastro-intestinal tract has been established (whether this cell be a distinct entity or a

columnar cell undergoing functional rejuvenation), yet little further light can be shed on their genetic relationship.

Prognosis.

The prognosis in carcinoid tumour of the appendix and small intestine is considered to be good. Removal of the tumour is rarely followed by local recurrence or death from metastatic spread.

Ariel points out that the number of carcinoid tumours with metastasis is on the increase in recent years. This he attributes to better diagnosis and more full investigation of the cases. If this is so, then the vaunted benignity of these tumours has been over-stressed.

Although this series of tumours has not been followed up to determine the prognosis clinically, the morphological features do not suggest a high degree of malignancy. Despite the fact that the tumour is locally invasive, lymph-spread occurred only in one of the cases, and blood-spread not at all.

Summary.

1. Fourteen cases of carcinoid or argentaffin tumours of the gastro-intestinal tract are reported, one of which has metastasised to the regional lymph-nodes.
2. Three of the cases are recorded in some detail.
3. The characters of these growths are described and the various thories as to their histogenesis discussed.
4. The prognosis after removal of these growths is good.

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I am indebted to Prof. Biggart for his advice and kindly criticism, and to Mr. S. T. Irwin for access to the clinical records of his cases. To the technicians and others who helped in their various ways I wish to express my sincere appreciation.

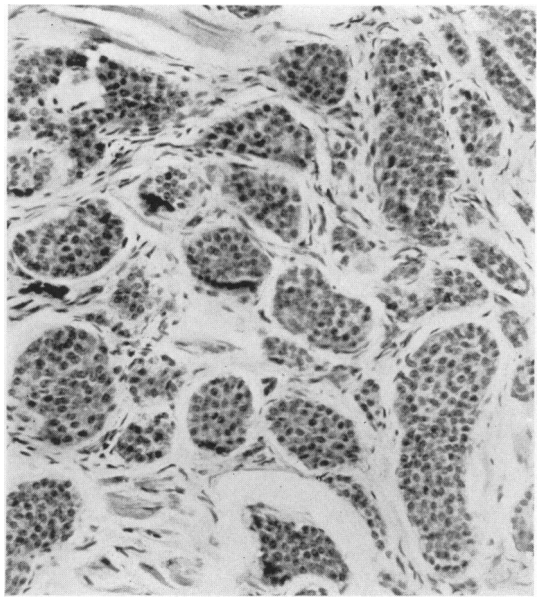

Fig. 1.—General low-power view of the tumour, showing the masses of epithelium and the fibrous stroma.

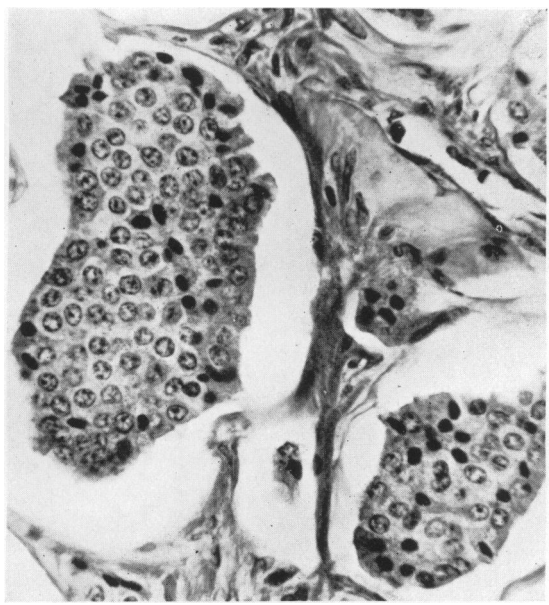

Fig. 2.—Under high power the cytological details can be readily made out. The nuclear pattern of the cells is distinct, and some hyperchomatic nuclei are present although there are no mitotic figures. Some attempt at peripheral palisading is present.

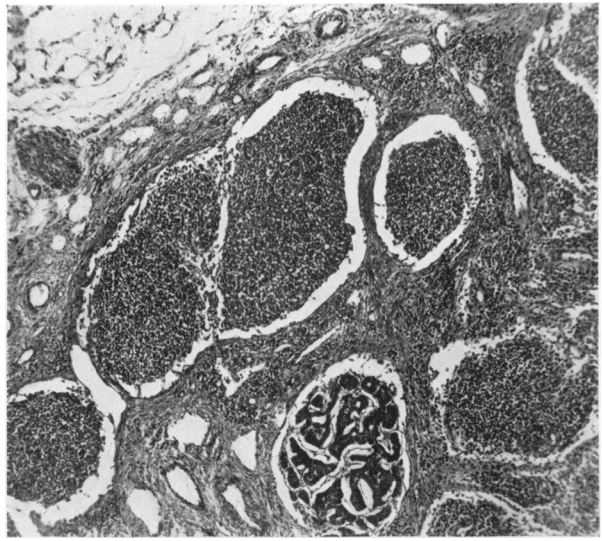

Fig. 3.—The secondary nodule can be seen lying in the central sinuses of the related lymph-gland.

Fig. 4.—This is a gland of Lieberkuhn stained by Masson's silver method. Most of the cells are ordinary mucus-secreting cells, but there is one argentaffin cell present containing black dots in the infranuclear cytoplasm.

The photographs are the work of Mr. D. McA. Mehaffey.

Studies from the Institute of Pathology

CASE VI—A2256.

A Patient with Coronary Occlusion.

Clinical History.

The patient was a male aged sixty-two years. He had suffered from no previous illnesses of note, and was temperate in his habits. For two weeks before admission he had been feeling tired, complained of breathlessness, and was unable to work. He had never noted any swelling of his feet or ankles. Three days before admission he began to suffer from pain in his chest. This began over his heart and seemed to radiate out over his chest, and through to his back.

On admission he was seen to be a fairly healthy-looking man. There was no œdema, but there appeared to be a slight cyanotic discolouration of his lips and ears. His pulse-rate was 92, and was regular. The radial artery was palpable. The apex beat was in the fifth intercostal space five inches from the mid-line. There was a slight pericardial friction rub noted on admission, which gradually disappeared. The chest was everywhere resonant, but on auscultation a few rales and crepitations were heard over both lungs, especially marked at the base.

Examination of the alimentary and nervous systems revealed no abnormality.

Electrocardiographic readings showed a flat T wave in lead i, with rounded and inverted T wave in leads ii and iii.

The patient showed a gradually rising pulse-rate with increasing general weakness, and finally died three weeks following his admission.

Clinical diagnosis: Coronary thrombosis.

Post-mortem.

The body is that of a well developed male subject. There is no discharge from nose or ears. Rigor mortis is present. There is no œdema of the legs. The body distribution of hair is normal.

Body cavities.—The pleural cavities contain neither free fluid nor gas. The pericardial sac is completely obliterated, and the parietal pericardium is everywhere adherent to the underlying heart. There are no extra-pericardial adhesions. The peritoneal cavity is normal.

Heart.—The heart appears rather globular in shape. It weighs 1 lb. 2 oz. with the attached pericardium. The tricuspid valve admits four fingers, and the right auricle and ventricle appear dilated. The right auricular appendage is distended by ante-mortem blood-clot, which is firmly adherent to its wall. Elsewhere the endocardium of this side of the heart is thin and smooth. The muscle of the right ventricle is thin and appears to be grossly infiltrated by adipose tissue. There is a thin yellow line of exudate with red hyperæmic margins demarcating the fusion of the parietal and visceral layers of the pericardium. The left auricle appears

normal. Its appendage does not contain any clot. The mitral valve is of normal size, and its cusps are not thickened. There is slight thickening of the left ventricular wall. In the upper half of the wall of the obtuse margin of the ventricle, the myocardium is replaced by a yellowish structureless necrotic mass. The surrounding myocardium appears congested. There is a thrombus adherent to the endocardium at the posterior margin of the altered muscle. The left coronary artery, about half an inch from its origin, can be felt to be much harder than usual, and on cross-section at this point is seen to present a curious appearance. There is a large atheromatous plaque into the substance of which there has been a recent extravasation of blood. This lesion presses upon the intima of the vessel, so that its lumen is almost completely occluded. The remainder of the artery shows atheromatous changes, but there are no other sites of occlusion.

Lungs.—The pleura is smooth. The bronchial glands are not enlarged and are anthracotic. The larger bronchi are filled with mucous secretion. On section the lung tissue is everywhere œdematous. In the left lung, at the anterior margin of the diaphragmatic surface, is a hæmorrhagic area which feels firm and suggests an infarct.

Liver.—This is of normal size. The cystic and common bile-ducts are patent. The capsule is smooth. On section the liver lobules are distinct. The centre of each lobule appears red, whilst the peripheral zone is a bright yellow. The radicles of the portal vein and bile-ducts are patent. The gall-bladder presents no lesions.

Spleen weighs 6 oz. The capsule is smooth and the viscus feels tense. On section the cut surface is firm and has a smooth edge. The Malpighian corpuscles are indistinct. The pulp is deep red. The trabeculæ are prominent.

Pancreas.—This is of normal size. Its ducts are patent. On section the acinar tissue appears normal.

Adrenals.—There is no autolysis of the medulla. The amount of cortical lipoid appears diminished.

Kidneys.—These are of normal size. The capsule strips easily, leaving a smooth surface, on which some irregular areas are seen. Some of these are coloured red, others yellow with a red margin. They appear to be areas of infarction. On section the infarcts are seen to be confined to the cortex. The remaining cortex is of normal width, with regular striæ.

Neck organs.—There are large numbers of petechial hæmorrhages in the fascia over the thyroid and œsophagus. The œsphagus is normal. The trachea appears congested and contains some mucoid secretion. The cricoid and thyroid cartilages are calcified.

The thyroid is not enlarged, and on section appears to be a normal colloid-containing gland. The parathyroids are normal.

The aorta shows calcified plaques of atheroma throughout its length. There is no arterio-sclerosis of the mesenteric or renal vessels.

Brain.—The meninges are thin and translucent. The basal vessels show no atheroma. On section of the fixed brain no lesions were found.

Heart.—The two layers of the pericardium are adherent by reason of the formation of a vascular granulation tissue. Islands of structureless fibrin are found incorporated in this granulation tissue, and represent the histological basis for the yellow exudate seen on microscopical examination. The myocardium in the upper part of the left ventricle shows infarction. There is necrosis of the muscle with complete loss of nuclear-staining. At the margins of the area of necrosis there is a proliferation of capillaries and the formation of cellular fibrous tissue. This granulation tissue seems to originate in the stroma around the blood-vessels. The necrosis of the myocardium extends out to the epicardium, and also to the endocardium. There are a few polymorphonuclears scattered around the margins of the infarct, and large mononuclear phagocytes containing iron pigment.

Section of the occluded coronary artery shows an extensive plaque of atheroma. This contains numerous large sinusoidal blood-filled spaces, and from some of these hæmorrhage has occurred into the soft detritus of the plaque. The hæmorrhage is present not only in the deeper layers of the plaque, but also extends to the intima, and has elevated the vascular endothelium from its wall. The lumen is thus reduced to a narrow slit, but there is no evidence of thrombosis.

Lungs.—One lung section shows œdema and congestion of the capillary walls. There is no fibrous thickening of the capillaries. Other areas show necrosis of alveolar walls and hæmorrhage. Several of the branches of the pulmonary arteries contain hyaline thrombi.

Spleen.—This shows a marked degree of congestion, which, however, is not associated with the thickening of the sinusoidal walls that is to be found in chronic venous congestion.

Liver.—The central zone of each lobule shows atrophy of the liver cells with dilatation of the sinusoids. A few cells are necrotic. In the more peripheral cells there is some vacuolisation, representing fatty change. The veins and bile-ducts show no lesion.

Adrenals.—These appear normal.

Pancreas.—The islets and acinar tissue appear normal. A few arterioles show hyalinisation, but this is not marked.

Kidneys.—Large areas of the cortex show necrosis. These infarcts have been present for some time. There is thickening and vascularisation of the overlying capsule. At the apex of one of the infarcts a branch of the renal artery shows a thrombus which is almost completely organised. In the centre, however, a small fragment of hyaline fibrin still remains.

The other organs show nothing of note.

Anatomical diagnosis.—

Coronary atheroma :
Hæmorrhage into atheromatous plaque :
Coronary occlusion :

Infarct of heart :
Thrombi on endocardium of left ventricle and right auricle :
Infarcts of lung and kidneys :
Venous congestion of viscera :
Terminal œdema of lungs.

COMMENTARY.

This patient is an interesting example of coronary occlusion—interesting not only in the effects of this lesion, but also by reason of the mechanism whereby the occlusion was produced. Other specimens in the museum show occlusion as the result of—

(1) Thrombosis.
(2) Severe arterio-sclerosis with stenosis.
(3) Syphilitic aortitis and coronary arteritis with narrowing of the ostia.
(4) Endarteritis.
(5) Embolism.

The present case, however, presents a method of occlusion which appears less common.

From the clinical history it is obvious that the function of the cardio-vascular system was sufficient for this man's needs until within a few weeks of death. Then the onset of breathlessness on exertion is the first symptom of a relative cardiac insufficiency. The pathological examination reveals no valvular disease, and no old myocardial lesions, so that this breathlessness must be put down as due to the coronary arterial disease. These coronary arteries, thickened and stenosed as they appear, were evidently quite competent for the supply of sufficient nourishment to the cardiac muscle so long as no excessive demands for nutriment were made. Exercise, however, rendered clinically obvious their relative insufficiency.

The appearance of præcordial pain in this patient probably denotes the ischæmia of the myocardium consequent upon the gradually increasing stenosis of the left coronary artery. Here this stenosis has been produced by an extravasation of blood into the atheromatous plaque, and this has progressed until the lumen is reduced to a mere slit and a large mass of the left ventricular wall is completely deprived of nutrition, and infarction results.

The histological examination of the heart suggests that the infarct has been present for some weeks. Organisation of its margins is well advanced, and the fibrinous exudate in the pericardial sac, which resulted from the irritation of the necrotic muscle upon the vessels of the epicardium, is also now almost completely replaced by vascular fibrous tissue. Such an aseptic pericarditis has only been seen in those cases of myocardial infarction in which the infarcted area involves the muscle immediately in contact with the epicardium.

The present infarct has also extended to involve the muscle in contact with a portion of the endocardium. This has resulted in alterations in the endocardium, which in turn have stimulated the production of a thrombus. Such an occurrence

is by no means uncommon. This thrombus has served as a source of emboli which have lodged in the renal vessels, and probably produced a slight hæmaturia which clinically passed unnoticed. The several renal infarcts show much the same histological changes and therefore appear to be of similar age. The degree of organisation of the embolus in the renal vessels suggests also an age of two or more weeks, and supports the suggestion that the period of embolism occurred soon after the appearance of the cardiac infarct whilst the endocardial thrombus was in the process of formation.

Following the damage to the left ventricular wall, the findings indicate some degree of cardiac insufficiency, which in effect was of obstructive character. The appearance of wet sounds in the chest—crepitations—denotes the beginning of cardiac failure. Venous congestion and slight œdema of the lungs are followed by some change in the right heart—dilatation and relative stasis. In this way an opportunity arises for thrombosis to occur in the right auricular appendage, which in turn was the source of the emboli responsible for the production of the pulmonary infarcts. The dilatation of the heart must be the cause of the cardiac murmurs, and is probably related to the dilatation and consequent insufficiency of the valve-rings, since no endocardial lesion was found on any of the valve-cusps.

The mechanism of coronary occlusion shown in this patient has recently attracted much attention. Paterson (1936), Wartman (1938), and more especially Winternitz, Thomas, and Le Compte (1938) have studied similar cases. Whilst the number of cases in which this mechanism of coronary occlusion has been verified is still small, it is probable that with more careful study it will be found that intramural lesions are frequently the cause of the final occlusion. The demonstration by injection methods of a rich vascular plexus in the walls of these vessels, especially in relationship to the plaques of atheromatous degeneration, renders obvious the source of these intramural hæmorrhages. These vessels are often thin-walled sinusoidal structures, and the detritus of the atheromatous plaque can offer but little support to their poorly developed walls. The presence of such a vascular network in the vessel-wall also must mean that there is a free access for blood-borne toxins, and that the endothelium of these sinusoids will suffer in the course of any infection. In this way it may eventually be possible to present a pathological basis for the clinical association of intercurrent infections and surgical operations as predisposing factors in the evolution of coronary occlusion.

The frequent association of coronary occlusion with hypertension will also be more easily understood if it is demonstrated that lesions similar to those in the present case are more frequent than we have hitherto believed.

In summary, therefore, a patient with coronary occlusion has been studied. Following the coronary occlusion there has appeared the clinical signs of cardiac failure. Various embolic lesions have developed as the result of the cardiac infarction and the subsequent cardiac defeat. The mechanism of the coronary occlusion is briefly discussed.

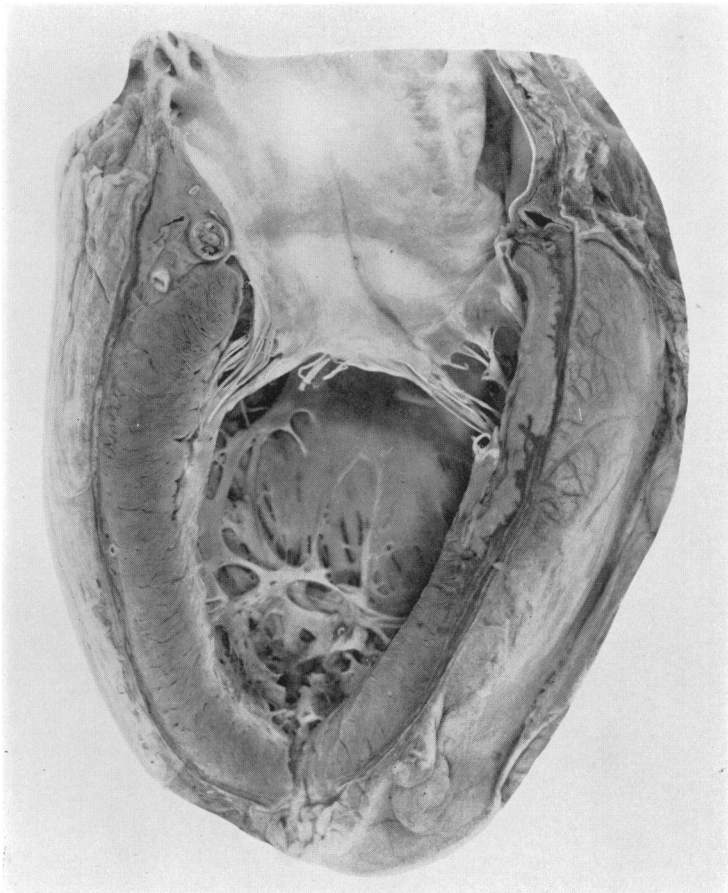

Fig. 1—Photograph of heart, showing the infarct in the left ventricular wall, and the occluded coronary artery.

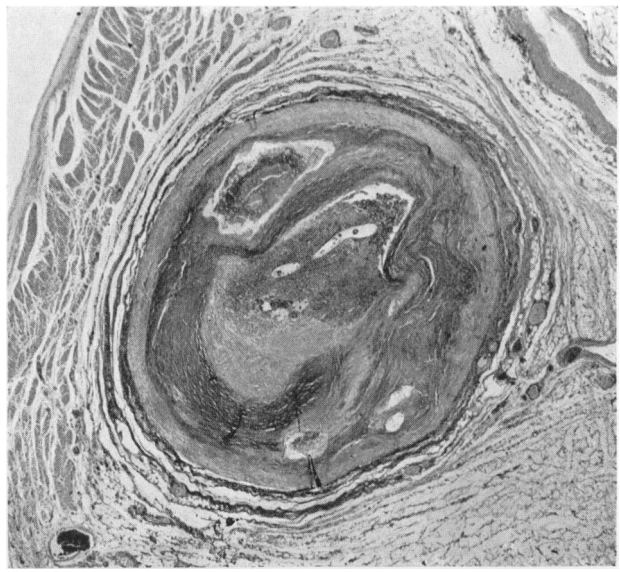

Fig. 2.—To show the occluded coronary artery. The lumen is reduced to a mere slit by the hæmorrhage into the atheromatous plaque.

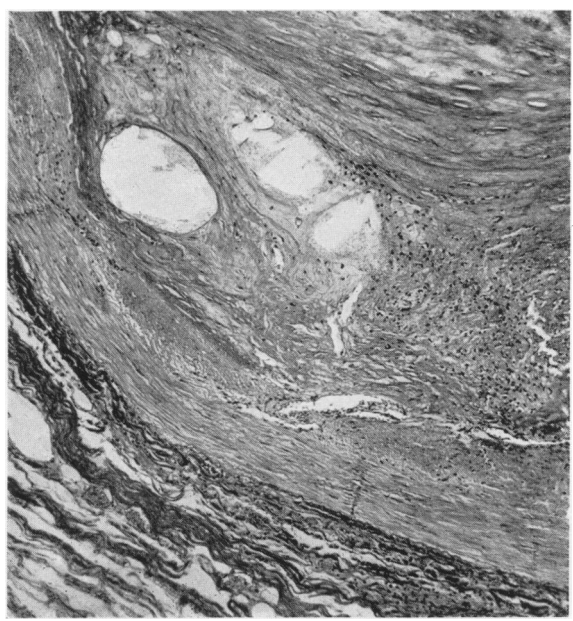

Fig. 3.—Section shows a few of the large sinusoidal vascular spaces in the wall of the coronary artery.

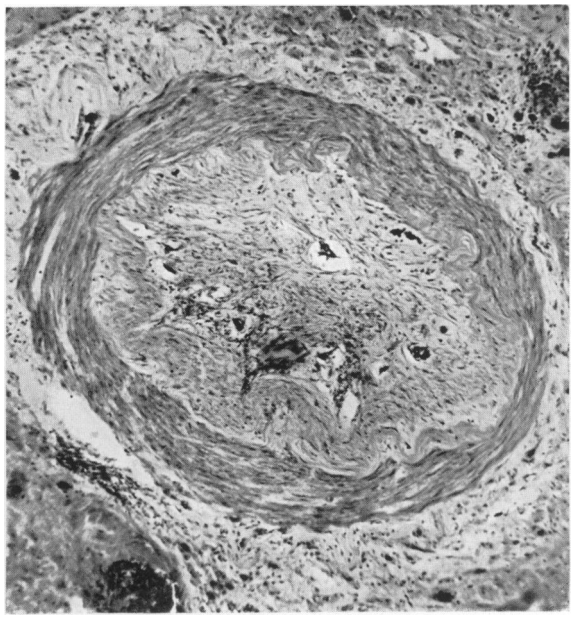

Fig. 4.—Section showing the organising thrombus in a cortical branch of the renal artery.

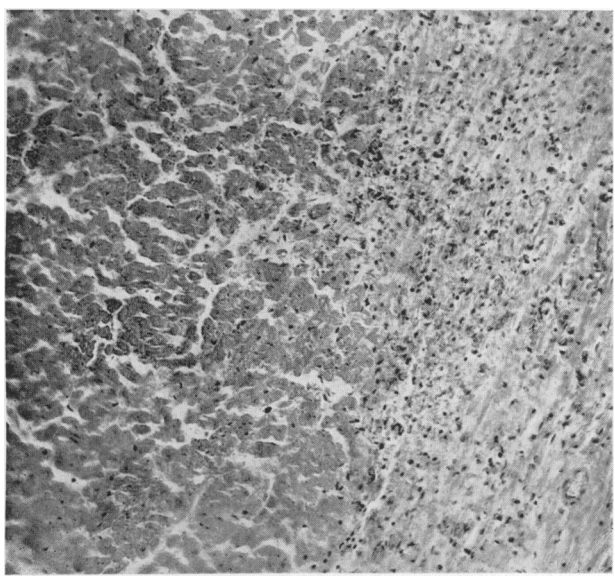

Fig. 5.—Section showing the fibrous tissue reaction at the edge of the cardiac infarct.

Photographs by Mr. D. McA. Mehaffey.

Manchurian Memories

By W. R. Sloan, M.D., F.R.C.S.ED.
formerly Irish Presbyterian Mission Hospital, Kirin, Manchuria

Blue-gowned Chinese, Koreans in voluminous white, bearded and booted exiles from Russia, Japanese in kimono and geita, or swaggering in khaki with outsize two-handed sabres, all parade confusedly in the composite picture that is Manchuria—or to its Japanese masters, Manchukuo.

The 30,000,000 first-named have an overwhelming preponderance in numbers over all others together, and work amongst them provides these random reminiscences.

The first word of Chinese I learned to speak was "k'ai shui," meaning boiled water, and this because none other was safe to drink and I had to ask my hostess's houseboy for it frequently. This too, before I knew any other word, came in useful as a prescription.

Immediately upon my arrival, a Chinese, trained in Western medicine and anxious to acquire prestige by having the foreigner out in consultation on one of his patients, took me to see an infant obviously febrile and diarrhœic. He had a dozen words or so of English which he used with considerable fluency and effect on the assembled relatives (or were they just neighbours?) but little or no enlightenment for me, confused by the babble around me, assailed by the strange odours that perplex the newcomer to China, and feeling altogether at a loss linguistically, I had an inspiration and thought of "k'ai shui." Repeating this magic formula in a voice meant to exclude all other articles of diet, I folded my hands and laid my head on them in an attitude of sleep. My doctor friend quickly jumped to the idea and set about putting it across in Chinese—"boiled water only for twenty-four hours." All were greatly impressed, whether by my diagnostic acumen, my sparing use of words, or the colour of my eyes does not matter, for I learned afterwards the child recovered.

One is continually impressed by the striking contrast between ancient and modern seen in China. The wheelbarrow and mule-cart are being succeeded directly by the motor-car and aeroplane, with no stage coach and but little of a steam locomotive period. Candles and flickering bean-oil lamps are being replaced by electric light. There has been no gas age.

Similarly in medicine, modern science competes with mediæval prescribing popular before Confucius, and I have had the privilege of friendship with several practitioners of the native art, who readily admit the superiority of the new methods in matters surgical, though not converted to the less dramatic ways of modern medicine. They believe on the whole in more drastic remedies than we do, as evidenced by the following story :

A weakly child with broncho-pneumonia following measles was brought to us when at death's door. Just as hope began to revive the patient developed scarlatina, and was quite properly given serum by my female assistant. Shortly afterwards

the child died. The opium-smoking ingrate of a father, who was in a strong position as a legal official, brought an action against the doctor. I went to court with her merely as a moral support, since I as a foreigner enjoying extra-territorial status was not wanted there. I was not admitted, and so spent the time in the filthy little waiting-room, where miserable manacled criminals from the prison and civil litigants alike awaited their turn.

The entertainment was tremendous, particularly so long as it was assumed that I could not speak Chinese, and I was able to listen-in to an interesting discussion on my personal appearance, mingled with amusing conjecture as to who or what I might be. Finally one enterprising merchant decided to try me, and as I was not averse to a chat to while away the hours, I responded, much to the general amazement. This friendly soul then proceeded to tell me he was there in an action he had taken against a doctor (native style).

His child, a boy in his early teens, as I recall, had been ill for some time. After trying numerous doctors and remedies, on a friend's recommendation he had called in a certain practitioner. This "son of a turtle" had ordered a draught containing five powdered scorpions. Shortly after ingestion his boy had taken a violent fit, and after much foaming at the mouth had died.

This dramatic story was followed by a dissertation on the appalling stupidity and wickedness of doctors in general. His remarks were most diverting, but I was just beginning to feel definitely apprehensive when the speaker paused and asked me what I was doing there. I replied that I had "come on a little business with a friend," and immediately made myself scarce.

Before I learned to know trachoma when I saw it, I was called to see a wealthy and most irascible official whom I found pacing excitedly up and down his house rubbing his inflamed eye and bemoaning his fate. When we had calmed him sufficiently to get a coherent story, he told us that he had been away to the capital for a few days. Whilst there he had been entertained to a drunken carouse in a sing-song house. His story finished with a wail of woe as he himself diagnosed his trouble as gonorrhœal ophthalmia—a condition well known to the Chinese lay public. He was brought to hospital, where it soon became evident that his condition was nothing but a particularly acute attack of trachoma. Appropriate treatment finally sent him home with his previous sight unimpared.

Shortly afterwards this gentleman paid me a state visit, and out of his gratitude presented me with a precious sample of what had hitherto proved his unfailing remedy for eye trouble—a bear's gall! The bladder was shrunken and dried, but still full of bile. This latter, being from a "cold"-blooded animal, is suppsed to have particularly cooling effects when, in accordance with the prevalent humoral theory, it is poured into an eye afflicted with "fire"—the humoral equivalent of inflammation.

The most surprising prescription I heard of was probably a "home" remedy. I found a mouse's nest in which were five naked little day-old mice. Before disposing of them I showed them to an old coolie who was working in our garden. He immediately expressed his regret that there had not been seven, as that number

of new-born mice was said to be "a very good medicine"—just for what I could not find out.

A few years ago I had the good fortune to be appointed a delegate to the Biennial Conference of the China Medical Association. For this I had to travel to Canton, at the other extreme of China, a journey of between two and three thousand miles. I had the privilege en route of seeing modern medicine at work in places like Peking, Tsinan, Nanking, Shanghai, and Hangchow, and finally of seeing the vigorous young profession in force at Canton. The great majority, of course, were Chinese. There was a goodish number of British and Americans, mostly medical missionaries, and a few of other nationalities present.

This meeting provided a splendid example of Chinese generosity and breadth of mind, for we were all permitted to join in debate and vote on matters affecting the Association, and indeed to hold office. The Association has even done the foreigner the compliment of creating a special medical missionary division, where the peculiar problems of mission hospitals can be thrashed out by those interested. The scientific papers read were of a high standard, and it seemed incredible that in the narrow streets nearby, the ancient order of physicians should still be dispensing their empirical, sometimes dramatic, usually nauseating, and by no means always ineffective remedies.

Many of these remedies are the same as those found in our own pharmacopeia, but usually in cruder form. They not infrequently are put to the same therapeutic use. Opium, of course, is the too much used pain-killer and a favourite means of suicide. Mercury, both internally and externally in the form of crude vapour baths, is a known cure for syphilis that not infrequently results in poisoning. I have seen extensive necrosis of the jaw in more than one case. The ephedra herb, of course, has been known and used by the Chinese for centuries, though in my experience always internally. Cersline rhubarb, liquorice, myrrh, aloes, peppermint, and many other remedies familiar to us are to be found in Chinese prescribing.

In some instances the native medicine would appear to have anticipated modern western methods. One example is in the very popular use of adhesive plaster. Indeed, a native practitioner's place of business is universally recognised by the presence outside of the guild sign, a pair of plasters imitated in brass or wood. These, though often apparantly illogically applied, are frequently an excellent dressing for boils and other septic sores, a fact only recently recognised by our modern school.

It seems not improbable too that the Chinese physician's empirical use of many animal substances, such for example as bear's gall, tiger bones, tortoise shell, and donkey's urine, may in some cases prove to have hitherto unsuspected merits. It has recently been shown that the highly valued tonic made of the velvet from deerhorn has at any rate a high vitamin content. Similarly with donkey's skin, in which there is a huge trade in Shanghai. Our own pharmacopeia in an age of chemistry and scepticism was stripped of almost all animal substances. Now, with the recognition of internal secretions and other principles, we find them coming back in the form of thyroid, parathyroid, stomach, liver, suprarenal, and other extracts.

War Gases in a Nutshell

By THE KERNEL

HISTORY records numerous abortive attempts to utilize chemical substances as war weapons, but it is not within the scope of this article to go into such occurrences prior to the Great War, except to mention that with the exception of "Greek Fire," none of them produced important results nor challenged the supremacy of existing weapons. The first toxic gases used in the Great War were the lachrymators—substances having a specific action on the eyes and producing a copious flow of tears and temporary blindness. It is difficult to attach the blame for the first use of toxic gases during the Great War, for the effects of the lachrymators were so transitory that no one at the time regarded them as coming within the meaning of the agreement of the Hague Conventions, 1899 and 1907.

In the low concentrations met with in the open, lachrymation was the only effect produced. However, when used against enclosed places, such as field fortifications, deep trenches, and dug-outs, toxic concentrations could accumulate and serious casualties result.

The first gas used in the War was "ethylbromacetate," and was used by the French in August, 1914. The success attained by the French police in suppressing lawless gangs with this gas undoubtedly led to its adoption by the French Army as a filling for 26 mm. rifle grenades.

The great advantage of the lachrymators is the extremely low concentration required to necessitate wearing of the respirator, they are also useful for masking the presence of other toxic gases.

It was noted early in the War that concentrations of the lachrymators which caused profuse lachrymation in men produced no visible effect upon horses or mules. The reason has never been explained, although the fact is well established by tests and war experience.

The three principal tear gases are :—

1. Chloracetophenone—C.A.P. solid and non-persistent.
2. Ethyliodoacetate—K.S.K. liquid and persistent.
3. Bromo-benzyl-cyanide—B.B.C. liquid and persistent.

All produce their effects on the eyes only, and in low concentrations likely to be met with in the open.

The symptoms disappear on removing the victim from the gas area, and they can be relieved by irrigation of the nose and conjunctivæ with warm saline solution or even warm water. The respirator gives complete protection against these gases.

Nose-Irritants or Sternutators.

By the summer of 1917 the respirators of all the belligerents had improved to a stage where they furnished adequate protection against the lung irritants. Also the lung-irritant gases were slow-acting and did not incapacitate until several hours after exposure.

The problem was to find a quick-acting non-persistent gas that would penetrate the respirator then in use, and the nose-irritants were the solution of the German chemists to this problem. When used in the last War, the enemy's object was to penetrate the respirator then in use and cause it to be discarded, thereby exposing the victim to a deadly gas such as phosgene, which was released simultaneously. All the modern respirators will give adequate protection against these gases.

Lung Irritants.

The lung irritants were the next group of gases to make their appearance in the War, in the famous chlorine cloud attack by the Germans on the French and British Colonial troops in the trenches around Ypres, April 22nd—24th, 1915. The casualties amounted to fifteen thousand, of which five thousand were fatal. The master-mind behind this new method of warfare was Professor Haber—a civilian and a Jew. These two disabilities so prejudiced the minds of the German General Staff against his project that it was only after great opposition it was given a trial. German Headquarters distrusted poisonous gas so much that no measures were taken to follow up its possible success.

The most important members of the lung irritant group are :—Chlorine, phosgene, diphosgene, and chloropicrin.

Their principal action is injury to the trachea, bronchi, and lungs, and the result of this injury is to cause fluid to pass from the blood into the air-cells of the lungs and thus obstruct the oxygen supply to the blood.

Their action may be compared to death by drowning, the fluid in which the victim drowns being drawn into his lungs from his blood-vessels.

All the lung irritants cause the same type of pathological effect, the great danger being the onset of acute pulmonary œdema.

In chlorine and chloropicrin poisoning the trachea and bronchi show serious damage. A marked feature in chlorine and chloropicrin poisoning is painful dyspnœa, paroxysmal cough accompanied by vomiting, which occurs during exposure and persists for a long time afterwards.

Phosgene exerts its physiological and toxic effects through its hydrolisis products — viz., H.C.L. and CO_2. Unlike chlorine, phosgene causes slight irritation of the nerves in the upper air-passages, owing to the amount of moisture there being small. With prolonged breathing, sufficient phosgene is decomposed in the trachea and bronchi to produce marked inflammation and erosion.

These effects reach their maximum in the alveoli of the lungs, where the air is saturated with moisture.

Phosgene is very insidious in its action, and victims gassed with it often have no warning symptoms until too late to avoid serious poisoning.

Generally the victim first experiences a temporary weak spell, but otherwise feels well and has a good appetite; suddenly he grows worse, and death frequently follows in a few days from pulmonary œdema, etc.

Phosgene is about ten times more toxic than chlorine, and since it has the odour of musty hay is not so easily detected.

The symptoms of poisoning by phosgene only are mentioned, as the use of the

other gases of the lung irritant group in warfare is considered unlikely. Depending on the concentration and length of exposure, symptoms may be—acute with violent onset, or acute with insidious onset. In the latter case the victim may be able to carry on his work, etc., for some hours with only trivial discomfort, and then suddenly collapse. Apart from cases in which death occurs within two to three hours after exposure, lung casualties may be divided into three types :—

1. The *mild case* with flushed face, rapid respiration, and painful cough.
2. *Severe case* with marked cyanosis, distended neck veins and rapid breathing, full strong pulse, cough and expectoration of large quantities of frothy sputum. This is known as the "blue type."
3. The collapsed type with ashen pallor, leaden coloured lips, and general collapse. Pulse rapid, weak, and irregular, pointing to cardiac dilatation. This is known as the "grey type" with marked circulatory collapse. These cases are even more asphyxiated than those with the plum-coloured cyanosis and in greater need of oxygen treatment.

In the early acute stage the physical signs give little indication of the gravity of the case or the extent of damage to the lungs.

The colour, pulse, character of the respirations, and the mental condition of the victim are the chief guide to prognosis.

Treatment in the acute stage comprises :—Rest, warmth, venesection, and oxygen.

The respirator gives complete protection against any concentration of lung irritants likely to be encountered.

Blister Gases or Vesicants.

Mustard-gas was first used by the Germans on the night of 12th July, 1917, at Ypres in Flanders, in an artillery bombardment against the British troops.

The vapours arising from the bursting shells had no immediate irritating action on the eyes or lungs, and the troops at first suffered no immediate discomfort from gas except irritation of the nose, which caused sneezing, etc. In the course of a couple of hours the signs of mustard-gas poisoning began to appear in the form of inflammation of the eyes and vomiting, followed by erythema of the skin and blistering.

Altogether about 12,000 tons of mustard-gas were used in the War and caused a total of 400,000 casualties.

Mustard-gas proved to be not only the best defensive gas, but the best all-round casualty producer used in the Great War.

In its pure state mustard is a transparent amber oily liquid, but in the crude form in which it is usually used it resembles dirty oil from a motor engine. It is almost odourless in ordinary field concentration, and in strong concentrations resembles horse-radish or garlic. The sense of smell becomes quickly dulled to the vapour, and the gas is consequently very insidious and dangerous in weak concentrations. It is one of the most persistent gases known and is very difficult to destroy.

The respirator only protects the eyes and respiratory passages from the vapour, leaving the other parts of the body vulnerable.

Mustard-gas will produce casualties from the vapour and from the liquid.

The main features of casualties from mustard vapour are :—

1. Insidious onset with delay of obvious effects varying from two to forty-eight hours.
2. Phinitis resembling a severe "cold" in the head.
3. Conjunctivitis of varying degree.
4. Brassy cough, laryngitis, hoarseness and ophonia, appearing about the same time as the conjunctivitis.
5. Nausea, vomiting, and epigastric pain, due to swallowing of the saliva or nasal secretions impregnated with the gas.
6. Inflammation of the trachea or bronchi with subsequent bronchitis or broncho-pneumonia.
7. Erythema of exposed surfaces and of moist protected skin areas followed by blistering.

From the point of view of mortality and lasting after-effects, it is injury to the trachea and lungs that is the most important feature of mustard-gas poisoning.

The effects are the result, not of the actual gas, but of the secondary bacterial invasion which follows.

The effects of the liquid are observed on the skin and in the eye.

On the skin redness appears at the site of contact in a couple of hours and is accompanied by itching.

Later the skin becomes congested and œdematous, and within twelve to twenty-four hours a blister filled with clear yellow serum which contains no actual mustard-gas forms.

Injury may result to the eye from splash or spray, and permanent damage will result. This is the only occasion on which mustard advertises its presence by immediate irritation, as stinging of the eye results on contact. This passes off and symptoms will return in half an hour and progress rapidly.

Damage may vary from a simple burn to complete destruction of the eye.

Treatment.

Blisters should be opened and the condition treated as an ordinary thermal burn. The eyes should be frequently irrigated as soon as possible. In liquid contamination immediate action is essential, and even then the best that can be hoped for is mitigation of the damage.

The most important treatment is preventive measures, and in case of vapour contamination consists in rapid removal of clothing and thorough washing of the body with soap and water. The eyes should be irrigated in all cases with warm water or saline.

For liquid contamination three forms of treatment are available, viz :—

1. *Bleach treatment*—by ointment or paste which neutralises the mustard-gas.
2. *Treatment by a solvent*—such as petrol or kerosene. By this method the

mustard-gas is not destroyed but only dissolved, and care must be taken not to spread the contamination by allowing the solvent to run. Thorough washing with soap and water will complete the treatment.

3. *Thorough washing with soap and water.*—If some time has elapsed after contamination, the washing treatment should still be carried out at the first opportunity with the hopes of mitigating the degree of burning.

Bleach ointment or paste should never be applied to a skin already showing signs of irritation, as it aggravates the condition.

Speed is the essence of all preventive treatment, and a delay of *three minutes* with liquid contamination or twenty minutes following exposure to vapour before cleansing the skin is carried out will result in definite burns.

The other important blister gas—Lewisite—is a vesicant compound containing arsenic, and is America's principal contribution to the war gases. It was not used during the Great War, but twenty thousand tons of it were on the way to Europe when the Armistice was signed, and it was destroyed at sea.

It is an oily liquid, colourless in the pure state, but darkening on standing. Pure Lewisite is odourless, but on contact with moisture or in the impure form it smells strongly of geraniums.

Lewisite is more rapid than mustard in its action, producing more discomfort when breathed and more irritation when placed on the skin.

It lacks the insidious character of mustard-gas, and its extreme pungency and penetrative odour renders it early of detection when similar concentraitons of mustard-gas would not be noticed.

Broadly speaking, its effects on the body are similar to mustard.

Lewisite can be neutralised by water, especially if it is hot and contains an alkali. So that preventive treatment consists essentially in rapid removal of clothing followed by washing in soap and water.

Lewisite can also be neutralised by a five per cent. aqueous solution of sodium hydroxide or removed by solvents or destroyed by bleach.

REVIEWS

THE DYSENTERIC DISORDERS. By Philip Manson-Bahr, C.M.G., D.S.O., M.D., F.R.C.P. 1939. London. Cassell & Co., Ltd. Pp. xiv + 613. Figs. 106. Plates 25. 25s. net.

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The use of the term "epithelium" for the cells of the capillary walls in figure 11 is incorrect, and few will accept the derivation of macrophages from such cells. It is doubtful if any useful information is to be gained from a microscopical examination of the exudate in carcinoma of the rectum, or if the pain of carcinoma of the pancreas is exceptionally severe. The technical appendix by Mr. Muggleton contains much condensed information, but it is difficult to see what class of reader is intended to consult it.

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