

required to contribute 5% of annual stipend and to which the Society will make a contribution of 10%.

Applications should be made on forms to be obtained from the Assistant Secretary, The Royal Society, Burlington House, London, W.1, and should be received as early as possible and not later than April 30, 1954.

Notice.

NATIONAL ASSOCIATION FOR THE PREVENTION OF TUBERCULOSIS IN AUSTRALIA (NEW SOUTH WALES DIVISION).

Laennec Society.

A CLINICAL MEETING of the Laennec Society will be held at the Anti-Tuberculosis Association Chest Clinic, at Crown Street, Sydney, on Monday, March 22, 1954, at 8 p.m. Members are invited to bring any guests who may be interested.

SECTION OF PREVENTIVE MEDICINE, VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION.

The first meeting for 1954 of the Section of Preventive Medicine of the Victorian Branch of the British Medical Association will be held in the Medical Society Hall, 426 Albert Street, East Melbourne, at 4.30 p.m. on Thursday, March 11. Dr. N. H. Andrews, Deputy Director of Child Health (Dental), Department of Health, will give an address entitled "Fluoridation of Water and its Place in the Prevention of Dental Caries". The discussion will be opened by Dr. E. J. Crowe. All members of the Branch are invited to be present.

Medical Practice.

NATIONAL HEALTH (PENSIONERS' MEDICAL SERVICES COMMITTEE OF INQUIRY) REGULATIONS.

The following notice appeared in the *Commonwealth of Australia Gazette*, Number 83, of December 23, 1953.

REPRIMAND OF MEDICAL PRACTITIONER.

I, Earle Page, the Minister of State for Health, hereby give notice, in pursuance of sub-regulation (3.) of Regulation 26 of the National Health (Pensioners' Medical Services Committees of Inquiry) Regulations that I have this day reprimanded Oscar Rychter, of 761 Darling Street, Rozelle, in the State of New South Wales, medical practitioner, following receipt of a report and recommendation concerning his conduct in relation to the provision of medical services to pensioners and their dependants under an arrangement made by the Director-General of Health under section 7 of the *National Health Service Act 1948-49* and the National Health (Medical Services to Pensioners) Regulations.

Dated this eleventh day of December, 1953.

EARLE PAGE,
Minister of State for Health.

Deaths.

THE following deaths have been announced:

STEPHEN.—Edgar Horatio Milner Stephen, on February 10, 1954, at Sydney.

MATTHEWS.—Walter Frederick Matthews, on February 14, 1954, at Orange, New South Wales.

NIALL.—John Henry Niall, on February 15, 1954, at Toorak, Victoria.

WATSON.—Arthur Harrison Edward Watson, on February 12, 1954, at Adelaide.

FOY.—Donovan Sylvester Foy, on February 19, 1954, at Sydney.

LEARY.—Thomas Garnet Stirling Leary, on February 20, 1954, at Sandringham, Victoria.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Hoyle, Mary Beatrice, M.B., B.S., 1953 (Univ. Adelaide), Queenbeyan District Hospital, Queenbeyan, New South Wales.

Diary for the Month.

MARCH 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

MARCH 12.—Queensland Branch, B.M.A.: Council Meeting.

MARCH 15.—Victorian Branch, B.M.A.: Finance Subcommittee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Tasmania: Part-time specialist appointments for the north-west coast of Tasmania.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and book-sellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 per annum within Australia and the British Commonwealth of Nations, and £6 10s. per annum within America and foreign countries, payable in advance.

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OBSERVATIONS UPON THE EARLY DAYS OF ANÆSTHESIA IN AUSTRALIA.¹

By ERIC GANDEVIA,
Retiring President, Australian Society of Anæsthetists,
Melbourne.

If men will tend to observe, they shall find much worthy to observe.
—FRANCIS BACON, "The Advancement of Learning".

VERY little has been published on the history of anæsthesia in this country, and none of it, to my knowledge, has been written by an anæsthetist. I feel that the Australian Society of Anæsthetists should encourage members to interest themselves in this important subject, and with that object in view the State sections might with advantage devote one meeting each year to a paper on the historical aspect of anæsthesia. Three articles provided me with most of the material for this survey: "The Introduction of Surgical Anæsthesia in Van Diemen's Land", by W. E. L. H. Crowther, read at the Centenary of the Introduction of Surgical Anæsthesia to Australia; "An Essay Relating Chiefly to Anæsthetics and their Introduction into Australia", by N. J. Dunlop (1927); and an excellent article

¹ Read at a meeting of the Australian Society of Anæsthetists on April 20, 1953, at Adelaide.

by W. L. Potter (1938), "Anæsthetics in Australia in the Early Days".

It is not inappropriate that this address should be delivered in Adelaide, for some of the most notable contributions to the early Australian literature came from J. D. Thomas, W. E. Jay, and others of the Adelaide Hospital, who established a tradition so worthily carried on by Gilbert Brown.

On June 7, 1847, ether was administered to two patients at Launceston by Dr. W. R. Pugh. The first patient was suffering from a painful disease of the lower jaw; the second from a cataract. This was the first occasion that general anæsthesia was employed in Australia. It is worthy of note that these two administrations took place only eight months after the first use of ether by Morton in Boston, Massachusetts.

The lay Press at that time was the chief means of disseminating medical information, not only to the general public, but also to members of the medical profession—a practice which perhaps is tending to recur. The *Launceston Examiner* had, on June 2, reported the use of ether in London five and a half months before, and on June 9 its issue contained a detailed and accurate report of the first two administrations by Dr. Pugh, together with a description of the apparatus employed. This Pugh had constructed on the same lines as Nouth's carbon dioxide apparatus, which was described in the *Illustrated London News*. How would one of us fare if asked to induce anæsthesia with this machine?

It consisted of two glass vessels, one placed on the other and both containing pieces of sponge saturated with ether. Connected with the lower vessel is a flexible tube provided with a stopcock, etc., terminating in a pipe which is placed in the patient's mouth. The upper vessel is fitted with a glass stopper which is removed when the patient inhales, so that the air he breathes passes through the saturated sponges and thus becomes saturated with the ether they contain. The nostrils being compressed, the process of breathing is precisely as if a person inhaled and expressed the atmosphere through a tobacco pipe.

No attempt was made to maintain anaesthesia for any length of time, for it was in fact a "single-dose" method suitable only for short operations.

If we bear in mind the difficulty all of us have experienced in anaesthetizing robust patients with ether alone, even with the help of premedication and modern apparatus, it is not surprising that early enthusiasm gave way to doubt. Ten days later the *Examiner* published the following letter from Dr. Pugh.

Sir,—In a recent number of your journal, you noticed two surgical operations performed by me at St. John's Hospital, in which the recently-discovered agent, Sulphuric Ether, was employed to render the parties unconscious and insensible to pain. The result of this trial was so far satisfactory as to lead me to hope that in future surgery would cease to be looked on with that dread which had been from the earliest times associated with its proceedings. I regret that my further acquaintance with this much lauded agent has tended materially to lessen its value in my estimation. I have found that its effects on individuals are as variable as the constitutions of those by whom it is inhaled. Persons weakened by previous disease are quickly brought within its influence and those of feeble frame offer but little resistance to its action. Not so, however, with the hearty and robust; the stage of depression in such is deferred and all the excitement common to excessive drunkenness is presented, the features become bloated and livid, the eyes protruded and suffused, and the disposition of the party when inebriated is fully developed, and these effects are not of the transitory character they are reputed to possess. The brain remains confused and the stupor of the drunkard is experienced for long subsequent to the application which occasioned it. I have seen sufficient to create alarm in my mind and therefore would caution the profession against the applying of the inhalation of Ether without special reference to the individual case. The remedy, like its twin brother, nitrous oxide gas, is, I feel assured, destined to enjoy a short lived notoriety. Their objectionable qualities are of a similar character, having alike a similar tendency to produce congestion of the brain, and therefore those circumstances which occasioned the removal of nitrous oxide from the list of remedial agents, in which for a short time it held a high position, will in all probability deprive the sulphuric ether of portion of the credit it has recently received.

I have the honour to be,
Yours most obediently,
W. R. PUGH, M.D.

In June, 1847, in an editorial in the short-lived *Australian Medical Journal*, the following statement was made:

The plan now proposed and which has been imported to Great Britain from America is to intoxicate the patient by causing him to inhale the vapour of Sulphuric Ether. Now, although the inebriation produced is evanescent, it is still inebriation and it does not appear to us of much consequence if the operatee must be drunk what the intoxicating medium may be. We have no hesitation in predicting for this process a transient popularity, it will have its day, ultimately to be abandoned as useless or injurious.

Finally, about this time, a medical practitioner wrote to a London paper to the effect that inhalation of ether seriously affected the blood and tended to produce pulmonary tuberculosis.

The critical attitude of those early pioneers seems to be in contrast to the enthusiasm shown for new anaesthetic drugs by the profession today, and so well illustrated by the history of cyclopropane. However, one member of the profession did not share these pessimistic views. He was Dr. D. J. Thomas, who on August 2, 1847, performed the first surgical operation under ether at Port Phillip. He

also had the distinction of reading the first scientific paper before a medical society in Victoria, the title being "On the Inhalation of the Vapour of Æther, with Cases". This paper was rediscovered by Dr. G. T. Howard. The *Australian Medical Journal* became extinct before the paper was published, but the manuscript is in the library of the British Medical Association in Melbourne and was reprinted in full in the *Royal Melbourne Hospital Clinical Reports* in 1933. Dr. Howard describes Dr. Thomas as "a genial Welshman, a Member of the Royal College of Physicians and a Licentiate of the Society of Apothecaries (1838), a delightful combination of Puck, Peter Pan, Fluelen and shrewd alert efficient leader of the profession". Thomas disagreed with the remarks of the editor of the *Australian Medical Journal* and others that ether would be short-lived. He said:

Who would give ether vapour to a patient in whose lungs there existed a deposit of tuberculous material? I would be sorry to etherize such a patient. Neither would I recommend a long walk or a shower every day. From all I have seen and from cases I have read in which it has proved injurious, I am convinced they are the result of improper administration.

Following the use of general anaesthesia one would have expected surgical operations to show a progressive increase in numbers; but, as was pointed out by Potter, the reverse was the case. Potter stated that after early cases had been reported there were 21 operations under ether in ten months, 13 during the first five months and eight during the next five months. A similar but more pronounced falling-off in the use of chloroform occurred after its introduction. There were 24 operations in ten months, 20 during the first five months and four during the next five months. These figures are derived from a survey of newspaper reports (1847 to 1849) made by Dr. Potter. However, it is doubtful whether they reflect the position accurately, as newspaper interest in the innovation may have subsided. It would be of value to examine some hospital statistics of the period. The falling-off in the case of ether was ascribed to (i) Dr. Pugh's letter to the *Examiner*, (ii) the editorial in the *Australian Medical Journal*, and (iii) the letter by a medical practitioner to a London paper. The decrease in the use of chloroform may have been due to the high mortality. Later still, there was a temporary abandonment of ether because of many supposed advantages of chloroform.

Chloroform was first used in Australia on April 11, 1848, by Dr. McEwan, of Sydney, who was also the first New South Welshman to use ether. The nature of the operation was not specified, but it was said to be "most tedious, difficult and hitherto excruciating". This operation took place only five months after the introduction of chloroform by Simpson. I have been unable to find a record of the first administration of chloroform in Melbourne, but the Melbourne *Argus* of May 26, 1848—that is, about six weeks after McEwan used chloroform in Sydney—contained the following paragraph:

Chloroform. We have much satisfaction in drawing attention to a notice in another column intimating that Mr. Hood, the druggist, has succeeded in the preparation of chloroform, the invaluable agent now used by the medical profession for doing away with all sense of pain in submitting to surgical operations.

In another column appeared the following:

Mr. Hood begs to intimate that he has succeeded in preparing chloroform in a pure state and that he is enabled to supply it at a moderate price. Collins Street, opposite Commercial Inn.

It is interesting to note that in 1852 the famous J. G. Beane was working as an assistant in Thomas Hood's shop. In Beane's "Original Contributions to Conservative Surgery" (1859), the first book on surgery produced in Victoria, a chapter is devoted to anaesthesia, while a monograph entitled "The Necessity for Anaesthetics to Alleviate Human Suffering" appeared under his name in the *Medical and Surgical Review of Australasia* in 1873. Despite his apparently authoritative position, we find that Beane, when confronted with an anaesthetic emergency, favoured brandy given by mouth as a vital resuscitative measure (B. Gandevia, 1952).

From 1852, and for some years thereafter, chloroform figured prominently in the journals and ether scarcely at all. There were two reasons for this: (i) chloroform had largely superseded ether; (ii) deaths from chloroform were frequently reported. This was borne out by Dr. J. Davies Thomas (not to be confused with Dr. D. J. Thomas, mentioned earlier), formerly chloroformist at University College Hospital, London, who in May, 1875, when resident surgeon at Clunes Hospital, read a paper entitled "A Consideration of Respective Merits of Chloroform and Ether". In November, 1875, when senior house surgeon at Adelaide Hospital, he contributed an article on ether and chloroform as anaesthetics. Thomas explained that, in the former paper, he had endeavoured to show the reasons which had led him, as they had many others, to question the validity of the general preference of British surgeons for chloroform. He was able to collect reports of 177 deaths from chloroform, but only 45 from ether. The estimated deaths from ether were 1 in 23,000 and from chloroform 1 in 2500. The account of the first death under ether was obtained by Thomas from Dr. Snow's book on anaesthetics. This occurred on July 10, 1847, and Thomas makes the following statement:

The patient was simply asphyxiated and no proper attempt at resuscitation made . . . but nowadays I cannot conceive a qualified man allowing a patient to die in this way.

Could Thomas review a series of notifiable deaths today he would doubtless be disappointed to note that asphyxial deaths are still occurring. Detailed accounts of death during ether anaesthesia indicate that they were nearly all asphyxial, even as they are today. Thomas stressed the fact that not all deaths during anaesthesia were due to the action of the anaesthetic, but that some were caused by "accidental epi-phenomena". He mentioned four: (i) Terror or mental anxiety may cause fatal syncope. (ii) It may happen that the predestined "supreme moment" (that is, death) may coincide with the time of administration of the anaesthetic. (iii) The physical state of the patient is sometimes such that the most trifling additional injury may cause fatal syncope. (iv) Certain operative procedures tend to cause syncope and, although anaesthesia diminishes shock, it does not altogether abolish it—for example, when the spermatic cord is being cut.

This is of interest, as it seems to foreshadow Crile's work of about thirty years later.

In 1876 Thomas again wrote on chloroform *versus* ether and quoted twenty rules for the administration of the latter from the work of Dr. Bigelow, of Boston. All of them, with slight modification, are applicable to the administration of ether today. Of special interest are the following:

1. If you can devote more time to the process [of induction] the resistance will be less.
2. If the patient is rigid or livid give him air.
3. If his glottis contracts (i.e., laryngeal stridor) give him air.
4. If he breathes badly put the finger inside the cheek to admit air over the base of the tongue.
5. In an operation about the nose and throat, if such an operation promises much blood, have a tracheotomy tube ready, or insert the tube before operation and put a sponge in the pharynx.
6. Although there is less nausea with an empty stomach, it is not well to starve a patient about to encounter a protracted operation.

As was mentioned previously, the high mortality under chloroform gave occasion for frequent discussion in the journals. The conclusions arrived at during the first ten years, although the knowledge was empirical, were amazingly accurate. In 1856 the following statements were made: (i) In nearly every case of death during chloroform anaesthesia the patient died during induction. (ii) Autopsy disclosed nothing to account for death. (This still holds good for deaths during the administration of other toxic agents—for example, "Pentothal", spinal analgesics.) (iii) Dr. Snow, who wrote a book on anaesthesia in 1847, observed that deaths during chloroform anaesthesia were occasioned by sudden arrest of the heart, but that if the vapour was

inhaled in a regular and gradual manner it would be impossible to paralyse the heart by its direct influence.

If every anaesthetic agent was administered in the "regular and gradual manner" which Snow advised nearly a century ago, fewer accidents would occur with the potent drugs available today.

With the high mortality of chloroform, methods of resuscitation were frequently debated. In the main, the basic principles adopted during the first fifteen years of general anaesthesia persisted until only a few years ago. Some were tried and found wanting. For example, on one occasion 20 ounces of blood were removed from a distended jugular vein, doubtless distended because of respiratory obstruction. Dr. Maloney, during a discussion on chloroform, said that vigorous bumping of the head against the table was practised by Mr. T. N. Fitzgerald and alarming symptoms were quickly banished in this way. Ammonia had been used orally as a stimulant in cases of poisoning; but Professor Halford, professor of anatomy and pathology at the University of Melbourne, to use his own words, "determined to follow up the poison as quickly as possible by injecting directly into the blood, thus avoiding rejection and decomposition by the stomach and intestine and in the case of ammonia reaching the heart without obstruction by or danger to the respiratory passages". Professor Halford was reported to have resuscitated dogs from a state of anaesthesia in which the heart's action had actually ceased, by means of the intravenous injection of ammonia. Hence for some years this was used as a routine resuscitatory measure. One issue of the *Australian Medical Journal* was devoted to the cure of snake-bite by this means. Forty-two cases were reported in full, with only one death. The preparation used was *Liquor Ammonii* (British Pharmacopoeia), and about 1.5 drachms, diluted with water, were injected. Probably this method was just as effective for cardiac arrest as the intravenous injection of "Coramine" of recent years.

Details of the usual methods of resuscitation at that time are well described by Dr. W. E. Jay, senior house surgeon of the Adelaide Hospital. In February, 1875, Dr. Jay described a death due to the administration of chloroform, "to which hitherto we have had immunity". The patient's death seemed to be instantaneous and Dr. Jay then described the measures employed to resuscitate him:

Every door and window was opened, the tongue pulled forward, cold water dashed on face and abdomen. Artificial respiration resorted to, galvanism too, along course of phrenic nerve and over heart—Nélaton's method based on supposed anaemia of brain was followed, namely:—head and body inverted, legs thrown over shoulders of one of the house surgeons while others continued artificial respiration. This was persevered with for three-quarters of an hour without getting symptoms of returning consciousness.

He concludes:

My object in sending above case is not merely that all such should be known to the profession, but, when such a lamentable occurrence as death from chloroform takes place, it may be published and quoted to serve as a guide to juries and to inform the public how impossible it is to prevent such accidents notwithstanding the greatest caution that can be used.

The use of galvanism is of special interest. Sansom in 1866 described the use of galvanism over the phrenic nerve as a means of resuscitating patients who had collapsed under anaesthesia. Sarnoff in America recently developed it as a means of artificial respiration. Recently, in the *Royal Melbourne Hospital Clinical Reports*, there was the report of an investigation undertaken to confirm the claim that adequate ventilation was produced by unilateral phrenic nerve stimulation (B. Gandevia, Ross and Bolton, 1952). The Director of Anaesthesia, having offered himself as a guinea-pig, is said to have been impressed with the possibilities of this method for resuscitating patients who have collapsed during anaesthesia.

It would be invidious to compare the results of the first generation of anaesthetists with the results of our own generation, in view of the vast advances in physiological and pharmacological knowledge and the development of

new techniques. Nevertheless, it would be most unwise to underrate the skill of the early exponents of the anæsthetic art (for it is no less an art with a "rag and bottle" than it is with a closed circuit and controlled respiration), who, as we have seen, were able to formulate the essential principles of safe anæsthetic administration on a basis of empirical observation. Although isolated by a voyage of perhaps months from the chief medical centres of the world, they were unafraid to put a new idea to the test as soon as reports appeared of its use overseas. Thrust upon their own resources to a considerable extent, they were able to appreciate the difficulties and dangers of, and the indications and contraindications for, each of the available agents.

The accuracy of their conclusions is evidenced by the fact that, although ignorant of "ventricular fibrillation", they realized the direct action of chloroform on the heart and the risk of sudden death, especially during the induction stage. They also realized that toxic agents were safer if given diluted and in gradually increasing doses; that most deaths during ether were asphyxial; perhaps, too, they anticipated an application of electricity to medicine. Other examples could be quoted. If we have lessons to learn from the anæsthetists of yesteryear, then I suggest that they are the following: (i) the value of careful, accurate clinical observation; (ii) the value of independence of thought and practice without recourse to reliance on the reports of others; (iii) the value of a critical approach to a new method, drug or appliance.

I would suggest that the future of our specialty lies ultimately more in the application of these lessons than in the specialized researches of the biochemist, the pharmacologist and the physiologist. While we are dependent upon these for our technical advances, the responsibility for their application rests with us. In this regard the approach of our predecessors may be commended. They followed another of Bacon's precepts:

If a man will begin with certainties, he shall end in doubts; but if he will be content to begin with doubts, he shall end in certainties.

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FUNDAMENTAL ASPECTS OF ALLERGY.¹

By E. R. TRETHERWIE,
 Department of Physiology, University of Melbourne.

I AM honoured that you have invited me to address you on the subject of allergy. I have been asked to speak largely on work with which I have been associated personally, and that I consider "fundamental aspects". This, within limits, I shall endeavour to do.

¹Read at a meeting of the Section for the Study of Allergic Diseases of the Victorian Branch of the British Medical Association on November 5, 1953.

There are two major problems concerned: (i) the pharmacology of the process involved; (ii) the reason for the development of the sensitized state.

Rather loosely we group the state of allergy with that of anaphylaxis, though there are fundamental differences. In anaphylaxis following the exhibition of a pharmacologically moderate (though actually very tiny) dose of antigen, desensitization is then complete. In allergy the sensitized state remains or readily recurs, apparently *de novo*. It may be in the latter instance that the nuclei of the cells have "learned" to develop certain biochemical phenomena. This process may then recur in the absence of the sensitizing agent.

The first clear-cut evidence that histamine was indeed responsible for many of the phenomena of anaphylaxis was presented by Bartosch, Feldberg and Nagel in 1932. At the same time, and independently in America, Dragstedt and Gebauer-Fuelnegg (1932) showed that histamine being derived from the liver appeared in thoracic duct lymph in the dog in anaphylaxis. This was the continuation of the work of Dale on the subject, who many years previously had produced indirect evidence that histamine was probably liberated. It was then believed that the combination of antigen with antibody in the cell (though probably on the surface) caused profound alteration of permeability of the cell membrane and the release of preformed histamine. This was released largely into the tissue spaces. That other substances were released was shown by Dr. C. H. Kellaway and myself in 1940, when we demonstrated the release of S.R.S., a slow-reacting muscle-stimulating substance, whose release was a little more prolonged than that of histamine. In Canada, Jaques and Waters (1941) showed that heparin was released in the anaphylactic reaction. Probably many other substances are liberated too.

That the substance histamine was indeed released was disputed from time to time, although the evidence was practically conclusive. More recently with the aid of anti-histamines I have been able to show (Trethewie, 1951a) that in addition to multiple assay indicating its nature there is a strictly parallel differential inhibition by anti-histamine for both histamine and the histamine-like substance released in anaphylaxis. No one has doubted seriously in the past ten years that histamine itself is the substance released.

Now during this period one aspect has been overlooked. The significance of the formation of a compound of the nature of anaphylotoxin—that is, a substance formed between say peptone and plasma, acting as a damaging agent like that of anaphylaxis, has been relegated to the background. Much literature had been written on this subject in the past. Rocha e Silva has renewed interest in this phenomenon. Ungar and Mist (1949) have shown that fibrinolysin is formed this way. Feldberg and O'Connor (1937) showed that peptone caused the release of histamine from the Tyrode solution perfused (blood free) lung of the guinea-pig, and I attempted to show (Trethewie, 1938) in the same laboratory the following year that histamine was released by peptone from the Tyrode solution perfused liver of the dog. The experiments, eight in all, completely failed to show the release of histamine. This puzzled us greatly. Again, at about that time, Dr. Kellaway and I (Kellaway and Trethewie, 1939) attempted to show the release of histamine in anaphylaxis from the Tyrode solution perfused liver of the dog, and again the experiments were completely unsuccessful. The explanation of this was forthcoming from the work of Rocha e Silva and Grana, who showed in 1946 that peptone did not cause the release of histamine from the blood-free perfused liver, but that when the organ was perfused with blood (Rocha e Silva *et alii*, 1947) histamine was indeed liberated. This, then, explains why Dragstedt and Gebauer-Fuelnegg were able to demonstrate the release of histamine from the liver of the intact dog, while Dr. Kellaway and I were unsuccessful with the isolated organ perfused with Tyrode solution. The significance of this was pointed out by Dr. Kellaway in a recent lecture (Kellaway, 1947) in Edinburgh. It would appear that, as was maintained by Rocha e Silva, the formed elements of the blood and

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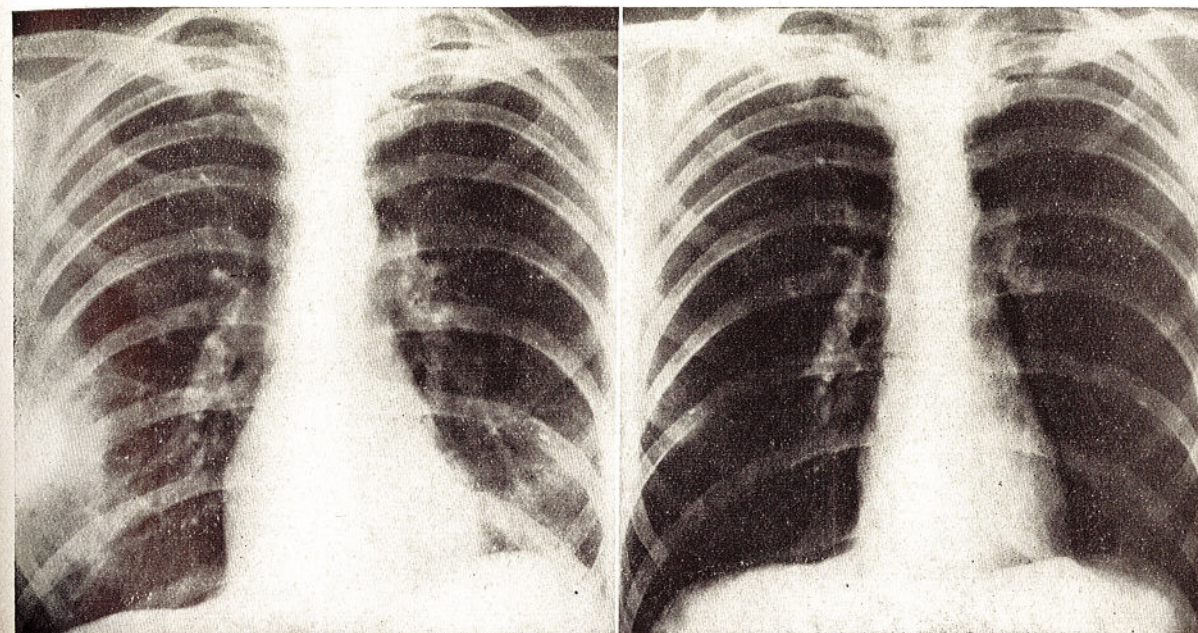


FIGURE II.

Radiograph of the chest in a case of psittacosis (Case IV) before commencement of therapy. There are hazy "ground-glass" opacities in the right mid-zone and at the base of the left lung.

FIGURE III.

Radiograph of the chest in the same case (Case IV) after treatment with aureomycin. Some faint opacity persists in the right mid-zone and at the base of the left lung, although clinical examination revealed no abnormality and the patient had returned to work.

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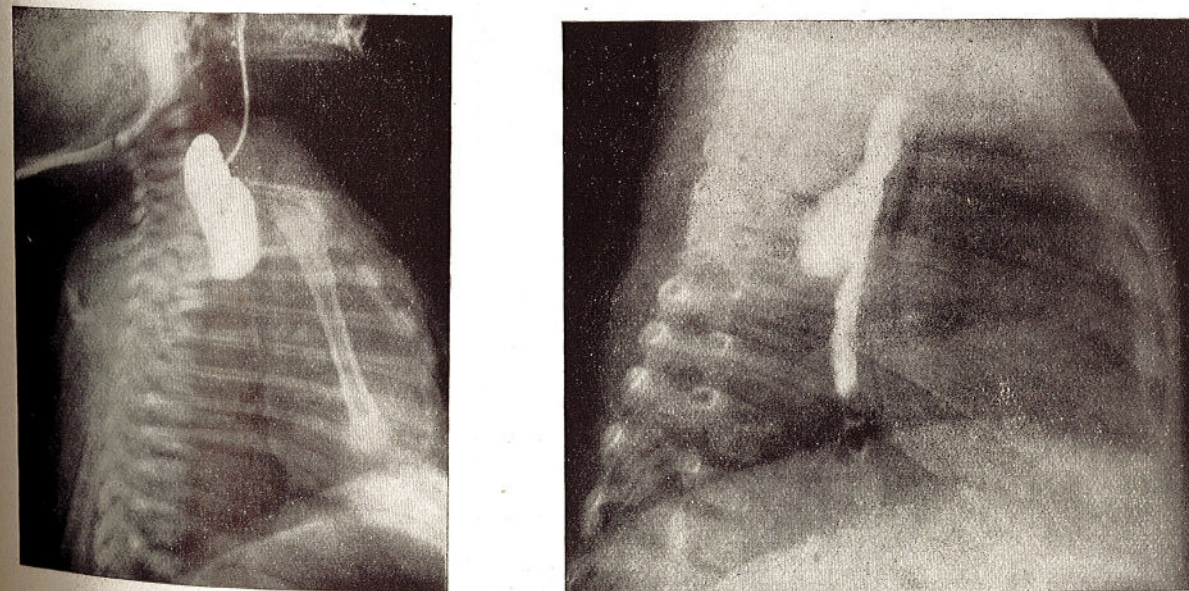


FIGURE I.

FIGURE II.