TWENTY YEARS *

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X.

The litle of this paper was chosen for two reasons. Firstly, it is written at the mid-point of the century, after two decades of very rapid progress in anaesthesia. Secondly, it happens to be just twenty years since the writer received his appointment as honorary anaesthetist to a teaching hospital. It seemed profitable, therefore, to look backwards over the past twenty years and to contrast the attitude of the anaesthetist to his work in 1930 with that which prevails today.

1. The Background

The anaesthetist of 1930 was regarded, in almost all countries except Britain and North America, as a junior member of the sur gical team and an unavoidable nuisance. He had seldom received any formal training in his speciality. In consequence, the difference between himself and the general practitioner anaesthetist was merely one of experience, not of range of technique. The writer can remember the calling-in of the Physician for Children's Diaseases at his hospital to anaesthetize a child suffering from empyaema: it was felt, presumably, that he, of all the staff, would be most likely to understand the handling of a sick child!

It was then usual for the anaesthetist to be also a physician or a general practitioner. The specialist anaesthetist was, in fact, often a man debarred from general practice by ill-health: it was not supposed that anyone would wish to take up anaesthesia deliberately, because he liked the speciality or thought it capable of reaching equality with other specialities. Few people dreamed that

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anaesthesia would prove capable of opening new fields to the surgeon or of contributing to the post-operative welfare of his patients. The older surgeons were loud in praise of the orderlies whom they had trained as anaesthetists in the field-hospitals of the First World War. One such surgeon maintained that any intelligent bricklayer could be made into an excellent anaesthetist within a few weeks. Another, in the year 1929, asked the present writer what he proposed to become. When told "an anaesthetist", the surgeon exclaimed: "Ridiculous! You should not waste your opportunities!"

Since formal training hardly existed in most countries, the novice was compelled to watch older anaesthetists at work and to copy their methods by rule-of-thumb. Few indeed were the people who realized that the administration of an anaesthetic is a demonstration in applied physiology, or that chemistry, physics and pharmacalogy have direct and practical bearing upon the anaesthetist's daily work. Any suggestion upon these lines was deribed as introducing academic considerations into a subject essentially "practical". Only in North America, and to some degree in Britain, was any attempt made to use the basic sciences as a foundation in the teaching of anaesthesia. In 1930, moreover, it was most uncommon for men to travel over seas for the exclusive study of anaesthesia.

2. Pre-Operative Care of the Patient

It was not then customary for pre-operative visits to be paid; anaesthetist and patient usually met for the first time in the operating theatre. A time honoured ritual, of purgation and starvation before anaesthesia, was in force. Post-anaethetic vomiting was accepted almost as a matter of course. In the early 1930's, it was found possible to mitigate it by the giving of carbohydrate pre-operatively, so as augment the glycogenic reserve of the liver and "spare" the breakdown of proteins. It is only recently that, with the recognition of the rôle played by the deaminating enzyme, any systematic attack upon the problem has become possible.

The task of bringing the patient into the best possible condition for operation devolved, in 1930, upon the surgeon or the physician. The anaesthetist, being regarded as a mere technician, was rarely asked to share in it. The importance of correcting any imbalance of fluid, chloride or protein was not recognised. Vitamin-K, the anti-coagulants, the sulphonamides and the antibiotics were as yet unknown. Pre-operative transfusion of blood was performed, but comparatively seldom. It usually had to be done by the surgeon, because blood-banks did not yet exist, haematologists were few and anaesthetists lacked the necessary training. Transfusions were therefore, by modern standards, inadequate in amount and far too long delayed. One of the major differences between 1930 and 1950

lies in the ease and speed with which blood, accurately grouped and unlimited in quantity, may now be procured in institutional practice. One could wish that it were obtainable equally rapidly in private hospitals.

The use of sedatives before anaesthesia had been known for many years, but had not yet become a routine. Morphine, hyoscine, atropine and the longer acting barbiturates were all employed. Shorter-acting barbiturates, such as pentobarbital, had just been evolved in the United States. Bromethol, then comparatively new, was popular as a rectal narcotic, but the use of colonic oil-ether was still to be seen. Intravenous inductions were rare, the available barbiturates ("Somnifène", "Sodium Amytal" and "Pernocton") being unsatisfactory. Much debate existed as to the depth to which sedation ought to be carried. The consequent respiratory depression was more feared than it is today, when the maintenance of an effective tidal exchange by "aided" respiration is a familiar procedure. The anaesthetist of 1930 was more culpable in his failure to realize that heavy premedication, by reducing pulmonary ventilation and delaying the return of the defensive reflexes, contributes to post-anaesthetic respiratory infection. The necessity of transporting patients to the operating-theatre was imperfectly recognised in 1930; it was not unusual to see heavily-premedicated patients' attempting to walk there and suffering from respiratory depression in consequence.

3. Anaesthesia with Volatile Agents

The volatile anaesthetics of 1930 were ether, chloroform and ethyl chloride: vinyl ether and thichlorethylene had yet to be introduced. In Melbourne, at least, the influence of Embley had made chloroform suspect. It was still used, however, for small children, in respiratory disease, in cautery cases and as a prelude to ether. The older surgeons hankered after it, even for abdominal operations, because it was potent and minimized bleeding. They did not realize that this ischaemia was, in fact, due to depression of the blood pressure and decline in the cardiac output.

Ether was the dominating agent: indeed, it is still used more in Australia than in many countries over seas. One hesitates to say that this preference is mistaken. Ether is admittedly irritating and productive of after-sickness. It is, however, easily given, is comparatively safe and is possessed of a marked curariform action. When given by modern methods, with abundance of oxygen and due care for pulmonary ventilation, its results in routine practice compare well with those of its later rivals.

In 1930, ether was most often given by the "open" method, although the mask was draped with towels more than would be

now approved. The intake of oxygen and elimination of carbon dioxide must, therefore, have been imperfect. The advantages of a trickle of oxygen beneath the "open" mask were appreciated even then by individual workers: they have recently been established by oximetric studies made in the Mayo Clinic. The endopharyngeal administration of ether-vapour was being superseded in 1930 by the endotracheal. The latter was uniformly insufflational, Magill's work being almost unknown outside of Britain. Since the insufflational method precluded effective packing of the pharynx, contamination of the bronchial tree was not rare. Too much faith was put in the ability of the return-flow of air to blow foreign matter way from the glottis. This return-flow required a minute-volume of delivery of 12 litres or more, so that acapnic apnoea, now a rarity, was then a frequent phenomenon. Surgical emphysema was occasionally reported, in consequence of the use of too large a tube or of too high a pressure of delivery. It did not then occur to anaesthetists to intubate the trachea for the sole purpose of aspirating secretions. Indeed, the aspirator reserved for the anaesthetist's use, now a commonplace of the operating-theatre, was then unknown.

4. The Gaseous Anaesthetics

The gaseous anaesthetics of 1930 were nitrous oxide and ethylene. Acetylene was almost entirely confined to Germany: cyclopropane had yet to be introduced. Apart from asphyxial "single-dose" administrations in dentistry, the gases were not widely used before the 1920's. They then acquired great vogue, especially in North America and Britain: their use became, indeed, the hallmark of the professional anaesthetist. A pathetic faith existed in their safety, especially for handicapped patients. It is now realized that ether-and-oxygen, capably given, is safer than gas anaesthesia conducted with deficiency of oxygen. The method of administration in 1930 was grossly and unreasoningly hypoxic.

The apparatus of the time was mostly of the water-flowmeter type and the method of administration the "semi-closed". Valves were, and until very recently remained, of such narrow bore as to produce definite respiratory resistance. The introduction of the McKesson intermittent-flow apparatus, which attracted worldwide interest in the early 1930's, was not an unmixed blessing. It certainly enabled the anaesthetist to exploit to the full the limited potency of nitrous oxide and ethylene. On the other hand, it armed him with a weapon potentially dangerous. The danger lay, of course, in the mistaken concept of gas anaesthesia which prevailed at the time. It is now realized that nitrous oxide and ethylene are but weak anaesthetics, lacking in curariforme action and incapable of producing muscular relaxation in robust subjects, unless reinforced by volatile supplement or by hypoxia. In the early 1930's,

many anaesthetists accepted McKesson's view that percentages of oxygen below the atmospheric were permissible. Clinical results were certainly achieved: it became a matter of pride to administer nitrous oxide for cholecystectomy without resort to volatile supplement. In so doing, too much stress was placed upon the freedom of nitrous oxide from histotoxie effect; too little upon the danger of the intercurrent hypoxia. Secondary depression of the circulation, post-anaesthetic headache and nausea, even encephalopathy, were amongst the occasional sequelae. The modern view is that nitrous oxide possesses a weak anaesthetic action of its own, quite apart from any element of hypoxic hypoxia. This can be readily demonstrated by causing a patient to inhale a mixture cantaining 21 per cent. of oxygen. The tension of oxygen in the pulmonary alveoli is identical with that recorded when the suject breathes ordinary air, which also contains 21 per cent. of oxygen. None the less, the patitnt breathing nitrous oxide becomes unconscious. The inference is that the gas possesses some degree of histotoxic action. The further inference is that mixtures containing less than an atmospheric percentage of oxygen are permissible, if at all, for very brief periods only. In other cases, percentages equal to or greater than the atmospheric should be maintained, any deficiency in potericy being met by volatile or intravenous supplement.

The gas anaesthesia of 1930 seldom employed absorption methods. The latter had been introduced by Waters in 1923, but had not extended widely beyond the United States. In Melbourne, D. G. Renton had begun to practice absorption in 1930, but his example was not followed by his colleagues until several years afterwards. The "semi-closed" administration of the day differed from its modern counterpart in the emphasis then placed upon rebreathing. For this, a desire to economise gases was not the only motive. It was felt obscurely, and probably because of Yandall Henderson's teaching, that some accumulation of carbon dioxide was helpful to respiration.

Rebreathing was therefore employed to an extent which would not be tolerated today, when the anaesthetist tries to get rid of earbon dioxide rather than to accumulate it. The patient of 1930 was exposed to more-or-less continuous stimulation of this respiratory centre and it is surprising that the latter did not fail more often than was the case. So much confidence was placed in the stimulating effect of carbon dioxide that it was recommended for the treatment of narcotic or anaesthetic overdosage or of surgical "shock". No one would now employ it in these conditions, for fear of burdening the already labouring respiratory centre.

The endotracheal administration of the gases was comparatively rare in 1930. Attempts were made to achieve it by the insufflational method of that day, the small catheter being retained and a gas-anaesthesia apparatus being substituted for the more usual va-

porizer. Such attempts were not particularly successful. The McKesson apparatus, with its ability to deliver under positive pressure, would have made this form of anaesthesia practicable. In 1928, however, Magill published his inhalational technique and the practice of insufflation was discarded.

5. Spinal Analgesia

Spinal analgesia has always been subject to fashion and, in the early 1930's, it was much in vogue. The usual agent was procaine in five or eight per cent. solution. Stovaine had been abandoned owing to its high incidence of neurological sequelae; nupercaine, and the hypobaric technique in general, lay in the near future. The possibility of limiting analgesia to the sacral or lumbar segments was just beginning to be recognised. Unilateral block was not practiced.

Since blocks were then bilateral and for rather uncontrolled extent, circulatory depression was frequent. It was currently attributed to dilatation of the splanchnic vascular pool. Exceptionally, a surgeon would protest that he did not, in fact, find the splanchnic vessels to be dilated when the abdomen was opened, so that not much was to be hoped from the usual treatment with vasopressor drugs. The rôle played by the intercostal muscular paresis, and consequent declive in pulmonary ventilation, went unrecognised. It seems to have been first put forward by the Wisconsin group of workers in the late 1930's. Until then, the usual treatment for circulatory depression during spinal analgesia was the intravenous infusion of a saline solution containing adrenalin. Later, came improved vasopressor drugs, such as neosynephrin. The Wisconsin workers emphasized the need for oxygen therapy and manual ventilation of the lungs. Recent studies made by workers at the Mayo Clinic suggest that the intercostal paresis does not ordinarily produce unsaturation of the arterial haemoglobin. It would therefore seem that the diaphragm can, if unembarrassed, manage to compensate for the loss of intercostal activity. It may be that this compensation is precarious, so that, if the diaphragm should become embarrassed by operation or otherwise, the hypoxia postulated by the Wisconsin workers will supervene.

6. Some Problems of Operation

The major advances of the past twenty years are to be found in the fields of abdominal, thoracic and oral surgery. It is doubtful, indeed, whether the younger anaethetists of today appreciate the difficulties of the quite recent past.

The anaesthetists who, in 1930, proposed to give "open" ether for an abdominal operation faced a dilemma. He was expected to

carry anaesthesia to a plane which would paralyse the whole group of muscles, abdominal as well as thoracic, which find attachment to the ribs. Since these are muscles of respiration, their paralysis throws the entire burden upon the diaphragm. In consequence, the respiratory exchange becomes dangerously reduced. For this, the giving of oxygen was soon found to be an inadequate remedy. The possibility of aiding the tidal exchange, by those manual manocuvres now called "aided respiration", was not then appreciated. Further, the jerky diaphragmatic breathing was likely to draw protests from the surgeon. The anaesthetists was tempted, therefore, to remain in the second plane of anaesthesia, at which the respiratory exchange is adequate, but at which muscular relaxation is still incomplete.

To overcome this difficulty, three courses were proposed. The first was endotracheal insufflation of ether vapour, which certainly maintained the respiratory exchange. It still demanded, however, a plane of anaesthesia sufficient to produce muscular paresis and therefore a relatively great histotoxic effect. The second course was to employ nitrous oxide or ethylene, in the hope of reducing the histotoxic factor. This, however, failed to solve the real problem, that of declining tidal exchange as muscular paresis was achieved. Further, the prevailing concept of gas anaesthesia permitted of hypoxia as an aid to anaesthetic potency. Many workers hence turned to the third course, viz., spinal analgesia. The enthusiasm for this method at the time was based upon two assumptions now recognized as erroneous. The first was that spinal analgesia was safer than general anaesthesia for the handicapped patient. Whilst sacral or lumbar block is now held to be relatively safe, "high" thoracic block is recognized as having definite hazards. The second assumption was that spinal analgesia reduced the likelibood of post-operative respiratory sequelae. This belief was explosed by Sise in 1932. It is now realized that these sequelae are of atelectatic origin and are common to all forms of analgesia and anaesthesia. In 1930, however, atelectasis and its prevention were only just beginning to be recognized.

The modern approach to abdominal surgery is to accept the inevitability of widespread muscular paresis. It can be produced by either the muscular relaxants or an agent such as ether, carried to a plane at which its curariform action is evident. The resulting decline in tidal excursion is met by the giving of oxygen and by the manoeuvres of "aided" or "controlled" respiration. The purpose of these manoeuvres is to reproduce a tidal exchange normal for that individual patient. Without such an exchange, the removal of carbon dioxide from the body will not be accomplished and circulatory depression or emergence-delirium will ensue, as described by Dripps.

The thoracic surgery of 1930 was a grim business. It was realized that thoracotomy introduced problems which the "open" method of anaesthesia could not solve. "Clean" operations, such as those for pulmonary hydatidosis, were performed under endotracheal insufflation of ether vapour. Very progressive anaesthetists passed a second, small-bored catheter into the trachea for the aspiration of blood or secretions. In infective cases, for which ether was held to be inapplicable, resort was made to nitrous oxide or ethylene. The oxygen supply was necessarily low and was made lower by the hypoxic concept of gas anaesthesia which ruled at that time. Many surgeons therefore turned to spinal analgesia, although this did nothing to compensate for the acute hypoxia developed as soon as one side of the thorax was opened.

The position was slyghtly improved by the combination of Magill's endotracheal technique with the McKesson gas-anaesthesia apparatus, which admitted of delivery under positive pressure. The improvement was attributed to better diffuison of gases through the alveolar endothelium. Actually, it was due rather to some degree of stabilization of the mediastinum, but the problems of "flap" and "paradoxical respiration" were not appreciated at that time. In consequence, the introduction of cyclopropane, which eliminated the factor of hypoxic hypoxia, did not produce revolutionary effects. These had to await the development of "controlled" respiration, of the cuffed tube, of endobronchial technique and of curare. Anaesthesia for thoracic surgery now exhibits such control over the respiratory functions that it is difficult to picture the conditions which existed before Waters and Guedel, Nosworthy and Craaford, Griffith and Orton made their contribution to the subject.

An unsatisfactory position existed in 1930 in regard to operations upon the nose, throat and teeth. Professional anaesthetists were fully aware of the necessity for endotracheal anaesthesia. Others, however, were content to share in operations conducted on the lines of a "smash-and-grab" raid. Pulmonary abscess was therefore a not uncommon sequel. When a case of it presented at a teaching hospital, the Admitting Officer was apt to ask: "When did you have your teeth out... or was it your tonsils?":

7. Care at Operation

The anaesthetists of 1930 was less well trained than his modern confrère. He therefore held a junior position in the surgical team. Surgeons were grateful for progress-reports upon the patient's condition, but they rarely welcomed suggestions as to the scope of the operation, feeling them to trespass upon their own province. The modern surgeon, by contrast, is always ready to discuss his

plans with the anaesthetists and to accept comment upon their physiological practicability.

The big problems of 1930 seem, in retrospect, to have been those of inadequate pulmonary ventilation and tardy treatment of shock. By ventilation is meant, of course, the maintenance of an effective tidal exchange appropriate to the individual. Oxygen is thus brought to the alveoli, but is not by itself enough; the respiratory exchange must also suffice to maintain a normally low tension of alveolar carbon dioxide. In the treatment of "shock", too much confidence was placed in analeptics: the time spent in giving them could have been better employed in giving intravenous therapy and in ventilating the lungs with oxygen.

The anaesthetist was prone to rely upon clinical impressions in the evaluation of his patient's condition: he did not usually take blood pressure readings or keep a chart. McKesson had published his first 6,000 charted cases in 1915: in the Australia of 1930, the only anaesthetist to follow his example was Brown of Adelaide. The signs and treatment of haemorrhagie "shock" were, of course, familiar to a generation of surgeons who had gained their experience in the carnage of Passchendaele, to which the Second World War happily offered few parallels. The syndrome of secondary "shock" was not appreciated. Treatment was in any case tardy, as was perhaps inevitable before blood-banks existed. It was sometimes possible to stave off a crisis for twenty minutes or so by the intravenous infusion of saline solution. In this interval, a donor could be secured and citrated blood be collected. The introduction of unmodified blood, of serum, plasma, dextran and the rotary pump lay, of course, in the future.

8. Post-Operative Care

In 1930, post-operative care was undertaken by the surgeon or physician. The anaesthetists was not expected to pay routine post-operative visits. The care of the "shocked" patient was complicated by the difficulty of obtaining blood speedily and in sufficient quantity. The value of oxygen therapy to the "shocked" or thyreotoxic patient was insufficiently recognised: indeed, the very administration of oxygen was inefficient. A mere funnel, which enriched the inhaled atmosphere by two or three per cent., was often used. An alternative was a pair of small catheters, inserted an inch or two inside the nostrils, through which a minute-volume of about three litres of oxygen was delivered. This apparatus was entrusted to a nurse, with instructions to run the oxygen at such a rate that she could still count the individual bubbles. The alveolar tension of oxygen was, therefore, probably less than it would have been had no oxygen been given and the nostrils left

unimpeded for ordinary respiration. Progressive anaesthetists were using small tents, in which water-vapour and carbon dioxide accumulated so rapidly that treatment could be given for only half-an-hour at a time. To compensate for inefficient oxygen therapy, much emphasis was put upon vasopressor drugs and heat. The patient in "shock" was often baked in an electric-light bath until the compensatory constriction of his peripheral vessels broke down and his last state was worse than his first.

Respiratory sequelae were still regarded very much as "Acts of God". Their atelectasis bas's was only just beginning to be recognised from the work of Mathes, Holman and others. Undue attention was being paid to the selection of a non-irritating anaesthetic and not enough to post-operative movement, coughing and deep breathing. The value of post-operative alveolar expansion by inhalation of carbon dioxide was over-rated. Bronchoscopy was already established as the treatment for missive collapse of the lungs, but the measures taken against lobular collapse were insufficiently active. It is only within the last decade that the "stir-up" regime and tracheobronchial toilet of Waters have become standard practice.

The present writer found in the 1930's that, with reasonable care in the selection of agents and the protection of the bronchial tree, his incidence of major respiratory infection was 0.6 per 100 unselected operations. This figure would be thought high today. Its worst feature was the mortality, 27 per cent. of those who developed respiratory infection dying of it. This position has been revolutionized in recent years by better understanding of "stir-up" treatment, tracheobronchial toilet and bronchoscopy, as well as by the introduction of antibiotics and sulphonamides.

9. Conclusion

It is probable that the mortality "on the table" is not greatly different today from what it was in 1930, viz., one death in approximately 1200 unselected operations. Improvement in this respect is unlikely until we learn to control the circulation as effectively as we can now control the respiration. Post-operative mortality is, however, in a different category. The writer's personal records for the 1930's show an appaling post-operative mortality, in combating which he took no active part, was not invited to take any, and indeed could have taken none of much value. Both the responsibility of the anaesthetist and his ability to help are much greater today.

It is remarkable how much more slowly knowledge was diffused twenty years ago than today. As an example, Magill's endotracheal technique was published in London in 1928, but was not adopted in Australia until early in 1931. By contrast, the various muscular relaxants became available in Australia within a few weeks of their introduction in the United States or in Britain. This speedier diffusion of knowledge is not due merely to improved means of communication or to a greater number of technical journals. It reflects the growth, in all civilized countries, of a new standard of education for anaesthetists. Technically, the speciality is practised in much the same way from Stockholm to São Paulo and from Edinburgh to Sidney. There exists in every country a body of informed opinion which is quick to seize upon and to evaluate any development introduced elsewhere. Francis Hoeffer McMechan of Cleveland dreamed, years ago, of an effective International Society of Anaesthetists. Te died, sadly disappointed, in the era of intense nationalism which preceded the Second World War. His dream may be closer to fulfilment than he imagined, although our present international link is not so much community of culture as community of technique.

Anaesthesia, for so long an art, has become a science. Research in it has passed beyond the capacity of the talented amateur. It now demands the team, in which physiologist, pharmacologist, chemist, physicist, engineer and practising anaesthetist may work in concert. Instruments of precision are being developed, of which the oximeter, the paramagnetic oxygen analyser, the acoustic ether analyser and the heart-lung apparatus may stand as examples. The development of anaesthesia is falling more and more upon the laboratory worker. It must not be left to him entirely: anaesthesia is, and will remain, a science of the living human body, a science based upon clinical realities.

The major difference between the anaesthetist of today and of twenty years ago is the former's wider medical education. He now recognises his responsibility for bringing the patient into optimal condition for operation. He knows, therefore, how to deal with such pre-operative conditions as respiratory disease, anaemia, cardiac decompensation or deficient hepatic function. At operation, he knows how to ensure an effective respiratory exchange and to protect his patient against anaemic, stagnant and hypoxic hypoxia. In the post-operative period, he can play his part in the control of respiratory infection and the maintenance of the respiratory, circulatory and metabolic functions. His outlook is so different from that of the technician anaesthetist of 1930 that he views the latter's methods with astonishment, wondering how they

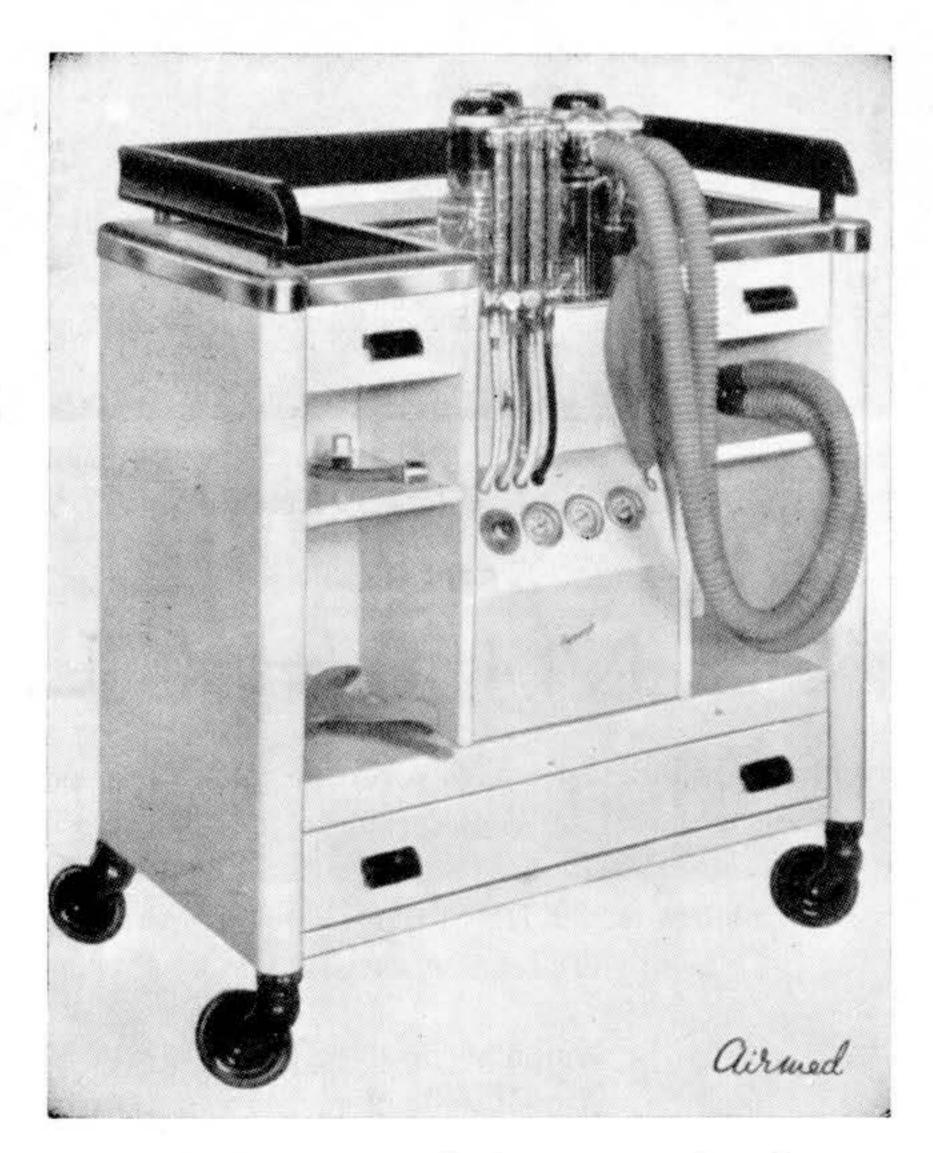
ever came to be tolerated. He can rest assured that, twenty years hence, he will look back with no less astonishment upon the methods of today. The future development of anaesthesia can only be conjectured. The first objective, obviously, is to find means of controlling the circulatory function. The second may be, perhaps, the development of some form of intravenous anaesthesia free from the present drawbacks. The third objective is, conceivably, the development of electro-narcosis of a clinically useful type. Whatever be the lines of future progress of our speciality, it is probable that the watchword of the anaesthetist, in the future as at present, will be "Ventilation".

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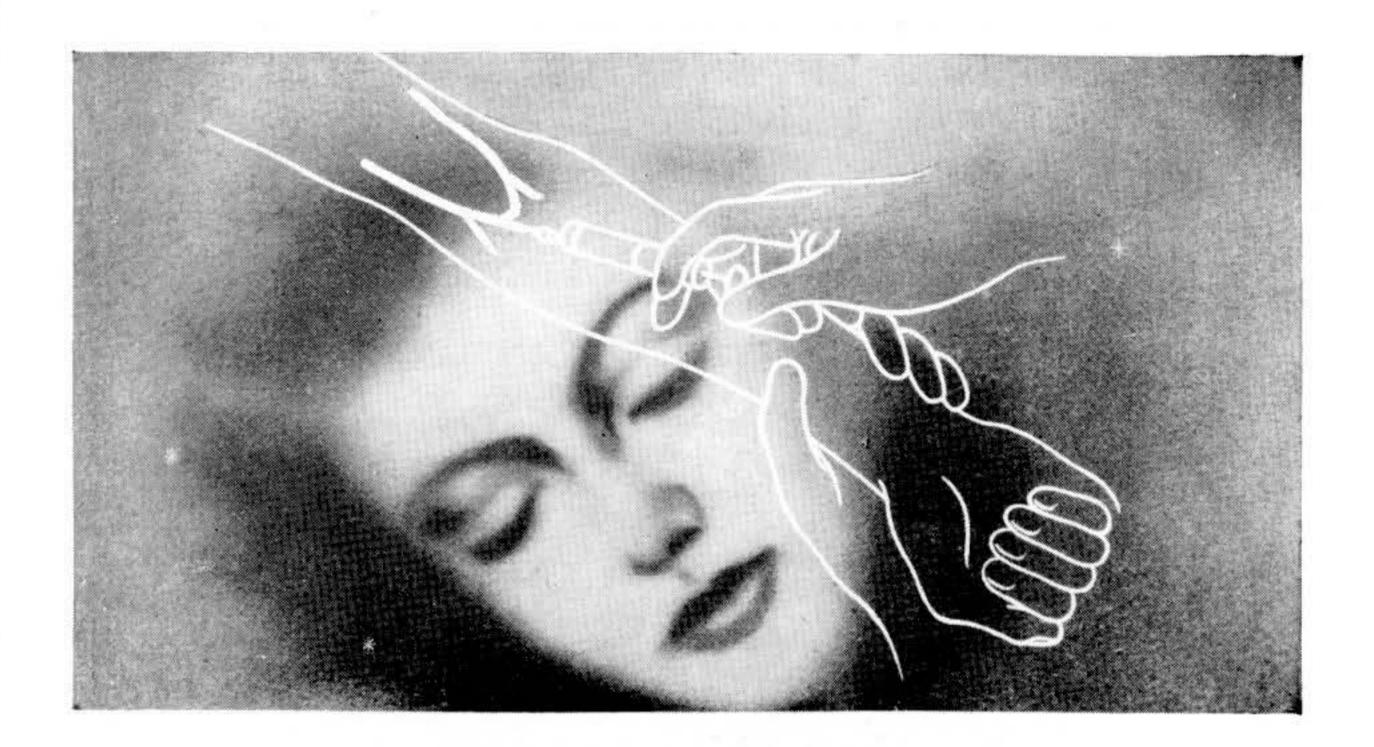
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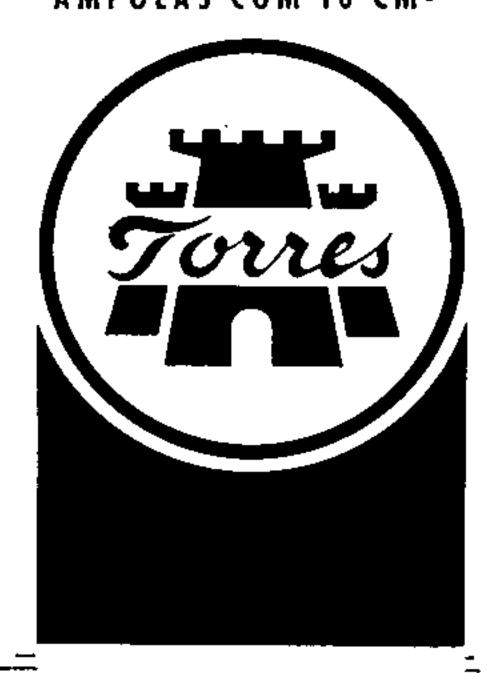
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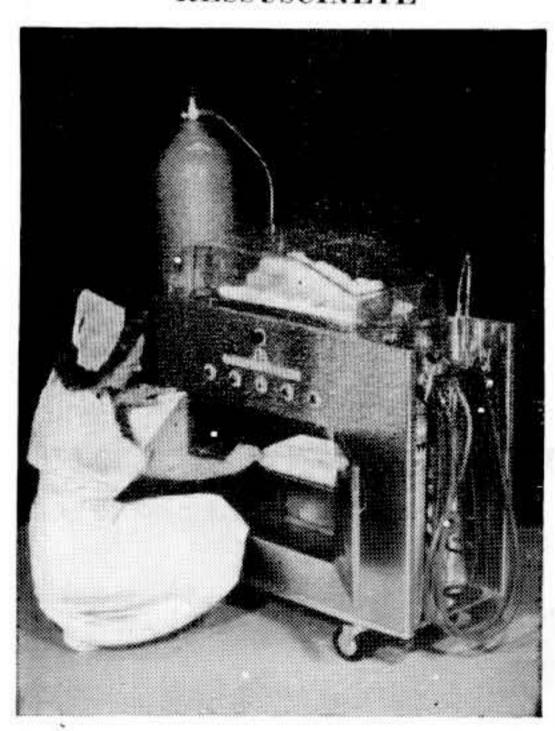
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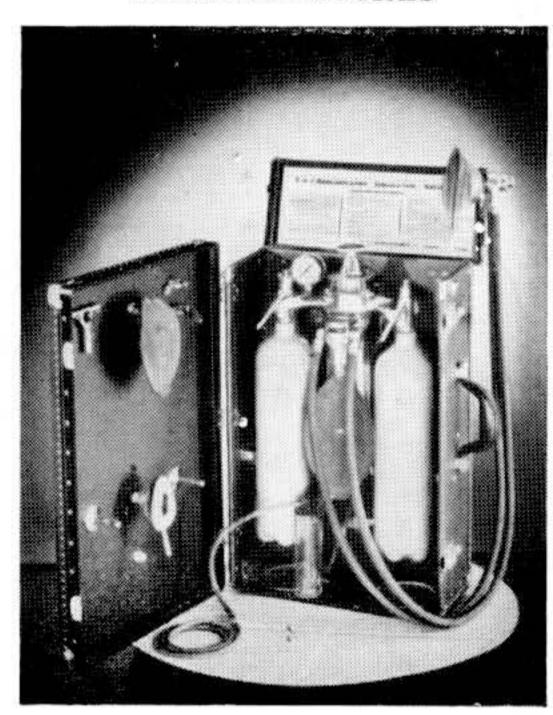


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- Franca portalidade.
- Incubadora de urgência.

INDÚSTRIAS QUÍMICAS MANGUAL S. A.

MATRIZ: Rio de Janeiro — Rua Paulino Fernandes, 53-55 — Tel. 46-1818 C. Postal 3.705 — End. Telegr. "PICOT" LABORATÓRIOS: Duque de Caxias — Estado do Rio — Rua Campos, 543 FILIAL: São Paulo — Rua Manoel Dutra, 218 — Tel. 32-9626 End. Telegr. "BAXTER"

CURARIZANTE

DE

SINTESE

FLAXEDIL

2559 F - 3697 RP

CAIXA DE 10 AMPOLAS DE 2 cm³ DOSADAS A 0,04 g INJEÇÕES INTRAVENOSAS



CIRURGIA

ABDOMINOPELVIANA, TORÁCICA, PULMONAR
ANESTESIA ENDOTRAQUEAL
CONVULSOTERAPIA



ATIVIDADE DO CURARE NATURAL LARGA MARGEM DE SEGURANÇA SEM EFEITOS HISTAMINICOS



AMOSTRAS E LITERATURAS À DISPOSIÇÃO DA CLASSE MÉDICA



RHODIA

CAIXA POSTAL 8095 — SÃO PAULO, SP



A marca de confiança