NEWS LETTER

The SCOTTISH SOCIETY of ANAESTHETISTS

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THE SCOTTISH SOCIETY OF ANÆSTHETISTS

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Vice-President	Dr. D. W. SHANNON, Edinburgh
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Editor of Newsletter

Dr. WALTER NORRIS

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"The objects of the Society will be to further the study of the science and practice of anæsthetics and the proper teaching thereof, and to conserve and advance the interests of anæsthetists."

"Ordinary membership will be restricted to members of the medical profession practising the specialty of anæsthetics."

—Extracts from the Constitution.

Subscriptions

£1 per annum.

10/- per annum for Senior House Officers and Registrars.

Presidents of the Society since 1950

1950—Dr. John Gillies.
1951—Dr. H. H. Pinkerton.
1952—Dr. T. J. C. MacDonald.
1953—Dr. W. M. Shearer.
1954—Dr. I. M. C. Dewar.
1955—Dr. F. G. Gibb.
1956—Dr. H. Bruce Wilson.
1957—Dr. R. Lawrie.
1958—Dr. R. N. Sinclair.
1959—Dr. Alison Ritchie.
1960—Dr. A. Tindal.
1961—Dr. J. W. L. Bain.
1962—Dr. Margaret Muir.
1963—Dr. Alex. C. Forrester.
1964—Dr. J. D. Robertson.
1965—Dr. A. G. Miller.
1966—Dr. J. A. Bolster.
1967—Dr. A. W. Raffan.
1968—Dr. J. R. Kyles.
1969—Dr. Malcolm Shaw.
1970—Dr. K. C. Grigor.

Guest Speakers at Annual General Meeting

1951—Dr. W. W. Mushin.
1952—Dr. M. H. Armstrong Davison.
1953—Dr. Ivan Magill.
1954—Prof. R. R. Macintosh.
1955—Dr. T. Cecil Gray.
1956—Dr. M. D. Nosworthy.
1957—Dr. J. Alfred Lee.
1958—Dr. L. B. Wevill.
1959—Dr. Margaret Hawksley.
1960—Sir Dugald Baird.
1961—Dr. G. S. W. Organe.
1962—Prof. W. D. M. Paton.
1963—Prof. E. A. Pask.
1964—Dr. Martin Holmdahl.
1965—Prof. J. G. Robson.
1966—Prof. A. Crampton Smith.
1967—Dr. Sheila Kenny.
1968—Dr. R. B. Goudie.
1969—Dr. R. P. W. Shackleton.
1970—Prof. J. W. Dundee.

Honorary Secretaries of the Society since 1950

1950-53—Dr. R. N. Sinclair, Glasgow.
1953-57—Dr. A. G. Miller, Glasgow
1957-63—Dr. M. Shaw, Glasgow.
1963-67—Dr. A. H. B. Masson, Edinburgh.
1967 —Dr. D. Campbell, Glasgow.

Honorary Members

Dr. D. Keir Fisher, Glasgow.
Dr. John Gillies, Edinburgh.
Dr. D. S. Middleton, Edinburgh.
Dr. Margaret C. Muir, Dundee.
Dr. W. B. Primrose, Glasgow.
Dr. Winifred Wood, Coll.
Dr. H. H. Pinkerton, Glasgow.
Dr. Alison Ritchie, Edinburgh.
Dr. J. W. L. Bain, Aberdeen.
Dr. I. M. C. Dewar, Glasgow.

Senior Members

Dr. Ellen B. Cowan, Glasgow.
Dr. Margot W. Goldsmith, Edinburgh.
Dr. A. McCallum Millar, Edinburgh.
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Dr. Sheina Watters, Edinburgh.
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Dr. Mary Brown, Glasgow.
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Dr. R. G. Grieve, Glasgow.
Dr. Lillie S. Dummer, Edinburgh.
Dr. Frances Redhead, Pencaitland.
Dr. Mary Richmond, Mauchline.
Dr. W. M. Christie, Arbroath.

The Scottish Society of Anæsthetists

. . . Founded 20th FEBRUARY, 1914

A. CONSTITUTION

(1) The name of the Society will be "THE SCOTTISH SOCIETY OF ANÆSTHETISTS."

(2) The objects of the Society will be to further the study of the science and practice of Anæsthetics, and the proper teaching thereof, and to conserve and advance the interests of Anæsthetists.

(3) The Society will consist of Honorary Members, Senior Members, Ordinary Members, a President, a Vice-President, a Secretary, a Treasurer, and an Executive Council formed by the above Office-bearers, together with seven Ordinary Members, two from each of the regions centred on Edinburgh and Glasgow, and one from each of the regions centred on Aberdeen, Dundee and Inverness.

(4) Ordinary Membership will be restricted to Members of the Medical Profession practising the specialty of Anæsthetics.

(5) Senior Members may be elected from Ordinary Members who have retired from active practice.

(6) Honorary Members may be elected on the recommendation of the Council and with the approval of the Society. Such Honorary Members would be elected from those who, either as Anæsthetists or in other spheres, have contributed in some special way to the advancement of Anæsthesia.

(7) A meeting will be held every year, at a time and place to be appointed by the Executive Council.

B. ELECTION

(1) Ordinary Members may be elected by a two-thirds majority of those present, at any regular meeting, nominations by an existing Member to be sent to the Secretary one calendar month before the day of election.

(2) Nominations for Vice-President, Secretary and Treasurer will be made annually by the Executive Council, and will be circulated to Members along with the notice of the Annual General Meeting. Any further nominations for these Offices may be submitted to the Secretary 14 days before the date of the Annual General Meeting.

(3) Regional Representatives will serve on the Executive Council for a period not exceeding three years, and on retiring from office will not be eligible for re-election to the Council within a period of one year.

(4) Nominations for vacancies in the Executive Council created by retirement will be called for at the Annual General Meeting, and a ballot held if necessary.

(5) The President who retires at the Annual Meeting will automatically become an additional member of the Executive Council for the ensuing year.

C. DUTIES OF OFFICE-BEARERS AND MEMBERS OF EXECUTIVE

(1) The President will preside at the Meetings both of the Society and Executive Council, and will have a casting as well as a deliberative vote. He will hold office for one year.

(2) The Vice-President will act for the President when required to do so. He will automatically become President for the following year.

(3) The Secretary will keep all the records of the Society, will notify all Members of the business of the Society, and send accounts of the Meeting to the Journals. The Treasurer will collect subscriptions, pay accounts and render a financial statement to the Annual Meeting.

(4) The Executive Council will be consulted by the President upon all matters concerning the conduct and interests of the Society, and will be permitted to record their vote by post upon any question in dispute.

D. SUBSCRIPTION

(1) Ordinary Members will pay an annual subscription of £1 ; Registrars and House Officers will pay 10/-.

(2) Any Member who has not paid his subscription for the current year may, at the discretion of the Executive Council, cease to be a Member of the Society.

E. GENERAL

(1) No alteration of, or addition to, the rules may be made save at an Ordinary Meeting after one month's notice given to the Secretary, who will place the suggestion upon the Agenda.

(2) Personal as well as official guests may be invited to the Meetings and Dinners of the Society.

Activities of the Year 1969-70

Registrars' Meeting

Edinburgh, 31st October, 1969

The meeting this year was again well attended by junior staff from all parts of the country. In the morning the programme included:—

Visits to the E.N.T. Theatre Suite, the Respiratory Laboratory, a General Surgical Theatre, the Dental Hospital and the Assisted Ventilatory Unit.

A Videotape film and panel discussion on Local Anæsthetic Techniques.

After lunch the programme took the form of a Symposium on the future of Intensive Care.

The Annual General Meeting was this year held in the Marine Hotel, Elie, and is fully reported later.

The Scientific Meeting was held in Aberdeen on 30th May when an excellent programme was sustained by local and guest speakers. Summaries of the papers kindly provided by the speakers are included later in the Newsletter.

Lunch and afternoon tea in the delightful surroundings of Foresterhill completed a most enjoyable day for the many members attending this meeting.

Neurosurgical Anæsthetists' Travel Group

This Group met on 9th May, 1970, at the Western General Hospital, Edinburgh. Anæsthetists attended from Aberdeen, Dundee, Edinburgh, Newcastle and Glasgow. Also attending were Neurosurgeons, Accident Surgeons, Pathologists and a Biochemist.

Papers were read during the morning on "Long-term monitoring of intraventricular and intra-arterial pressures in head injuries" (I. Johnston, Institute, Glasgow), "Neuropathology of head injuries" (A. F. Maloney, Edinburgh), and "I.P.P.V. for management of respiratory defects in severe head injuries" (A. S. Brown, Edinburgh). After lunch papers were read on "Problems of neurosurgical anæsthesia in the tropics" (J. M. Horton, Edinburgh) and "The critical period" (A. S. Brown, Edinburgh).

Each paper provoked considerable discussion on these important developments.

Payment of Annual Subscription by Banker's Order

FROM time to time, members have requested that they be allowed to pay the annual subscription to the Society by Banker's Order. It was realised that this would be of benefit to the member and to the Society alike, but with successive secretaries operating through different banking accounts it was not considered workable to inaugurate such a scheme.

Arrangements have now been made whereby those members who prefer to pay the annual subscription by Banker's Order may do so through the Head Office of the Bank of Scotland, The Mound, Edinburgh. The Society's financial year ends 31st March, and payment by Banker's Order may therefore begin with the subscription for the ensuing year, payable 1st April. The scheme is commended to members for their own convenience, for the Society's financial situation, and for the facilitation of the Hon. Treasurer's duties.

A form suitable for use is available on application to the Hon. Treasurer.

Annual General Meeting — Elie

THE choice of a suitable site for the Annual General Meeting presents many problems. In addition to providing suitable accommodation for the meeting it should ideally cater for Friday evening entertainment, Saturday morning diversion for the ladies and those members who do not even profess to play golf, and, of course, a GOLF COURSE.

Such a place is ELIE.

Friday evening entertainment comprised a visit to the Byre Theatre in St. Andrews to see Stevenson's "Weir of Hermiston."

On Saturday morning the golfers played in glorious weather, while the non-golfers repaired to Haig's Distillery at Markinch — to see the raw material for the 19th hole being produced.

At the Business Meeting, Dr. Grigor was installed as President. The Society was shown to be in a sound financial state and improving year by year—a condition envied by many individual members!

Professor Robertson reported on the activities of the Scottish Joint Consultants' Committee on which he represents the Faculty of Anæsthetists.

The scientific part of the afternoon consisted of Dr. Grigor's Presidential Address, the Guest Lecture by Professor Dundee, and the Registrar's Prize Paper read by Dr. Robinson. All are reported separately elsewhere.

In the evening the Reception and Dinner were attended by some 115 members and guests.

An excellent trade exhibition and golf on Sunday morning for the enthusiasts completed a successful week-end. The winners of the golf competition on Saturday were—

Stableford Competition

Gentlemen — 1st, Dr. A. W. Raffan, Aberdeen, 35 points; 2nd (yet again), Dr. W. L. M. Baird, Glasgow, 33 points; 3rd, Dr. Wm. Bargh, Glasgow, 32 points; 4th, Dr. J. G. Mone, Glasgow, 32 points.

Medal, Nett Score

Ladies—1st, Mrs. K. B. Holloway, 57; 2nd, Dr. Lillie Dummer, 75; 3rd, Mrs. A. G. Miller, 76; 4th, Mrs. K. C. Grigor, 85.

The Scottish Society of Anæsthetists

Programme for 1970-71

1. Registrars' Meeting — Victoria Infirmary, Glasgow. 23rd October, 1970.
2. Neurosurgical Anæsthetists' Travel Group—The next meeting will take place at the Institute of Neurological Sciences, Southern General Hospital, Glasgow, S.W.1, during May 1971. Information from Dr. A. H. Granat, Killearn Hospital, and Dr. S. W. McGowan, Dundee.
3. Registrars' Prize—Entries to be in by the end of February 1971.
4. Annual General Meeting—Dunblane Hydro Hotel, 23rd-25th April, 1971. Guest speaker —Dr. A. R. Hunter.
5. Scientific Meeting—Edinburgh, May 1971.

Presidential Address . . . Dr. KENNETH C. GRIGOR

"ALONG MY WAY"

I HAVE borrowed the title of my Presidential Address from the autobiography of the late Gilbert Harding, and indeed my talk takes the form of an abridged and bawdlerized clinical autobiography — a whistle stop tour extending over 32 years. The only justification for such an egotistical presentation is that anæsthetists of my vintage form perhaps the last true link connecting the old with the new. We are old enough to have spent a significant part of our professional life when, at least in the West of Scotland, standard techniques were open chloroform, ethyl chloride and ether, gas - oxygen and ether and spinal analgesia. We intubated with rather crude equipment, we made limited use of intravenous infusions and even set up an occasional blood transfusion. It is perhaps true to say, however, that it was largely his skill and experience that separated the professional anæsthetist from the enthusiastic amateur.

When the breakthrough came, fortunately for us, we were not too old or too set in our ways to adapt to new concepts, new techniques and new skills, or to make the essential radical readjustments necessary to keep abreast of the amazing progress which has overtaken our speciality and enabled it to grow in stature to become at its highest level one of the most skilled and essential services in the field of medicine to-day.

If you will bear with me, I will take you on a sentimental journey which, if it does nothing else, will at least mean that I have fulfilled my obligation to address the Society.

We pushed anæsthesia with gas, oxygen and ether to the very limits of its potential and used our ingenuity to extract the last ml. of tidal volume with spontaneous respiration. This perhaps explains why old-timers like me seem to take such pains to secure maximal tidal exchange when using mask and harness. The anæsthetic chin support (1) proved a satisfactory device for controlling the type of airway obstruction which results from lower jaw sag during general anæsthesia with spontaneous respiration. It has an added advantage in that the single-handed anæsthetist is freed to discharge his other duties to his patient. The elastic side straps are sufficiently long to permit of use with the lithotomy position.

"Ether pneumonia" was a frequent complication of major surgery and there was much confusion regarding the true nature of this condition. As often as not, it was none other than our old college friend, post-operative atelectasis. This, however, was not generally recognized and it was not until portable chest radiography became readily available that the sceptics were convinced and treatment of post-operative pulmonary complications was placed on a rational basis.

The nature of the pulmonary stresses resulting from the elastic hypertension developed in atelectasis and capable of producing such distortion within the thorax fascinated me. (2)

Andrus (3) explained the distribution of such stresses in atelectasis of the lower lobe of the right lung. The dimensions of the atelectatic right lower lobe suffer reduction in all three planes. Compensatory replacement must be effected therefore in three planes, i.e. in vertical, lateral and antero-posterior directions. Shortening in the vertical dimension of the lung is in large part compensated by elevation of the homo-lateral diaphragm and by emphysema of the remaining aerated lung. Loss of lung volume in the lateral dimension is partly compensated by dislocation of the related mediastinal structures to the affected side and by over-stretching of the opposite lung. In the antero-posterior plane, however, but little relief is afforded by crowding of ribs and narrowing of intercostal spaces. It is in this plane, and to a lesser degree in the lateral plane, that the maximum abnormal stress occurs. Vertically disposed bronchi are thus submitted to a considerable dilating force and it is in these bronchi that the bronchiectasis of unrelieved atelectasis is most frequently encountered.

Our standard techniques of anæsthesia could cope with the operation of paravertebral thoracoplasty performed to effect cavity closure in pulmonary tuberculosis. This was

my introduction to thoracic surgery. Post-operative atelectasis was a frequent complication. This is not surprising when one considers the predisposing causes associated with both the disease and the operation, viz.: copious sputum, endobronchial granulations, bronchial stenosis, pre-operative phrenic crush and pneumoperitoneum, disruption of the integrity of the hemi-thorax, paradoxical respiration, ineffective cough, wound pain, etc. Strenuous efforts were made to effect early re-aeration of the atelectasis and one remembers the fortitude of many of the patients.

Late, partial or non-reversal of atelectasis was associated with gross bronchiectatic changes and persistent cavitation. Although most of these patients had a dismal prognosis, the picture was not one of unmitigated gloom. Occasionally massive atelectasis was so complete that the airless lung created an environment which was totally hostile to the tubercle bacillus. In regard to the unfavourable cases, some of those who lived to see the advent of streptomycin therapy were treated with pleuro-pneumonectomy and given a further lease of life.

Post-operative pulmonary complications still plague us so it is perhaps not such a far cry to those days of yester year. At the Victoria Infirmary in Glasgow we have an Out Patients' Clinic for pre-operative assessment and preparation of patients considered unfavourable risks for surgery on account of obesity, cardiac and respiratory distress, bronchitis and other disability. The protocol for this enterprise was drawn up in 1956 and is still relevant to present day conditions. I apologise for the rather pedantic style but I was even more insufferable in those days.

Pre-Anæsthetic Clinic — Desiderata

1. Liaison with other Departments viz.—
   (a) Surgical.
   (b) Dietary.
   (c) Physiotherapy.
   (d) Radiological.
   (e) Cardiological.
   (f) Bacteriological.
2. Availability of—
   (a) Drugs.
   (b) Beds for pre-operative preparation.
   (c) Timeous admission to hospital.
   (d) Secretarial help.

During the period 1957-59, 86 patients were dealt with (Table I); 19 of those patients were admitted to Mearnskirk Hospital for pre-operative preparation and, when considered fit for operation, were later transferred to the Victoria Infirmary.

TABLE I

Pre-Anæsthetic Clinic (1957-59)

	No. of Cases
Obesity	40
Bronchitis and allied conditions	33
Assessment	10
Miscellaneous	3
Total	86

(Prepared at Mearnskirk Hospital—19)

We have gained a considerable reputation for persuading, with the help of our dietitians, obese patients to reduce weight. Table II shows the results of our combined efforts with the six obese patients of Table I who were prepared for repair of umbilical hernia.

TABLE II

Weight Reductions in Six Cases of Unbilical Hernia

	Initial Weight	Final Weight	Reduction	Time Taken
	15st. 7½lbs.	14st. 0lbs.	1st. 7½lbs.	2 months
	15st. 8lbs.	13st. 10lbs.	1st. 12lbs.	4 months
	16st. 1¾lbs.	13st. 3½lbs.	2st. 12¼lbs.	6 months
	15st. 1½lbs.	13st. 8lbs.	1st. 7½lbs.	3 months
	16st. 1½lbs.	14st. 3½lbs.	1st. 12lbs.	3 months
	11st. 4½lbs.	10st. 3½lbs.	1st. 1lb.	1 month
Average:	14st. 13⅓lbs.	13st. 2⅔lbs.	1st. 11lbs.	3⅓ months

Since its inception, Dr. Douglas Simpson and I have dealt with more than 600 patients at our so-called "Pre-Anæsthetic Clinic." I would suggest to you this afternoon that this is a field of endeavour that merits more attention from surgeons and anæsthetists.

If the pace of the first stage of my journey was rather pedestrian, the latter part developed into a strenuous effort to keep up with the demands of the cardio-thoracic surgeons. On one occasion Dr. Shaw and I (4) had to exercise considerable ingenuity to maintain anæsthesia during local resection of a tumour in the region of the carina. With the patient in the face-down position, access was gained to the chest by means of a right thoracotomy incision. A Magill tube was inserted into the left main bronchus through an incision into the lower end of the trachea and a one-lung anæsthesia was conducted through the thoracotomy wound during the period of tumour resection.

Flushed with success, our surgeons presented us with a further two cases in which they wished to resect the lower end of the trachea, together with the origins of both main bronchi (i.e. trunk and trouser legs). Again we used a right thoracotomy in the face-down position. The left main bronchus was severed and intubated as before. Following resection of the tumour bearing area, the cut end of the trachea was anastomosed to the right main bronchus. Thereafter anæsthesia was conducted by the orthodox route while an end-to-side anastomisis of the left main bronchus to the right intermediate bronchus was carried out to complete the final tracheo-bronchial reconstruction.

In spite of such triumphs of technique over judgment the surgeons were only marking time. It was obvious that they were itching to embark on open-heart surgery. Within days of our guest of honour, Professor Dundee, publishing his first results with hypothermia, I was whisked off to Liverpool to study his methods. I believe that hypothermia for cardiac surgery represents a genuine milestone in our developing speciality. It led into a specialised territory which the anæsthetist was best equipped to explore. It provided an impetus to our growing interest in blood-gas analysis and acid-base balance. The jump from orthodox techniques to hypothermia for limited open-heart surgery was, in my opinion, greater than the subsequent step to cardio-pulmonary bypass and the more complicated surgery of the heart and great vessels. With hypothermia the anæsthetist became an equal partner with the surgeon.

The various stages of development of surface cooling hypothermia at the Cardio-Thoracic Centre at Mearnskirk Hospital, Glasgow were—

1. Direct application of ice and electric blanket rewarming—average time 8 hours.
2. Cooling and rewarming in a domestic bath—average time 5½ hours.
3. Continuous Water Immersion in the Mearnskirk Bath (5) — average time 1½ hours.

Controlled Water Immersion Hypothermia with the Mearnskirk Bath was developed by one of our surgeons, Mr. T. Welsh. It has proved an effective and safe method for direct suture of secundum type atrial septal defect. Compared with cardio-pulmonary bypass it is less traumatic, less complicated and less time consuming. One feels that more cardiac surgical centres should use this technique.

Cardio-pulmonary bypass! At first a seven-day wonder but now a routine procedure. In this setting the anæsthetist not only has his traditional technical role, but in the vital post-operative stage finds himself with the responsibilities and status of a clinician.

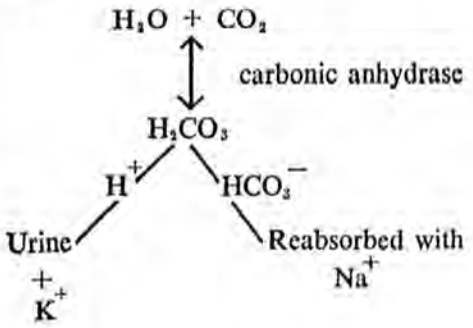
As routine blood gas analysis is carried out from induction of anæsthesia until the second post-operative day, a mass of biochemical data has accumulated. This has afforded an opportunity of studying the fascinating paradox of post-perfusion metabolic alkalosis associated with acid urine (6). Some of the facts which have emerged from this investigation have relevance to anæsthesia generally and I hope will be of interest to my audience to-day.

Several sources of exogenous bicarbonate are readily identified—when the citrate content of one litre of acid-citrate-dextrose (ACD) blood is metabolized, 30 meq. of NaHCO is added to the patients' plasma. Similarly, one litre of ringer lactate solution adds 22 meq. of bicarbonate. As several litres of ACD blood and ringer lactate may be used during a bypass procedure, a considerable addition of potential bicarbonate occurs. In addition, 40-50 meq. of NaHCO are added to the priming volume of the heart-lung machine and further bicarbonate may be necessary to treat an incident of hypoxic acidosis. We thus have a decided loading with bicarbonate.

An unexpected finding of this investigation concerned the degree of post-operative urinary acidity which was associated with established post-perfusion metabolic alkalosis, the urine pH being repeatedly below 5.6 units. Normally the renal response to loading with alkali is a massive excretion of bicarbonate along with sodium. Gamble's (7) classical histogram "carbonic acid and bicarbonate in urine" indicates that the urine contains more than 90 meq./litre of bicarbonate when its pH is 7.8. Thereafter bicarbonate content decreases progressively with fall in urine pH until no bicarbonate is contained in urine whose pH measures 5.6 or below. Thus a loading of bicarbonate sufficiently in excess of the total buffering capacity of the blood and a pH of urine consistently below 5.6 makes metabolic alkalosis inevitable. We thus have a logical explanation of our paradox. (The hypothesis, of course, assumes that there is no counter-vailing cause of metabolic acidosis such as hypoxia).

In renal tubular acid secretion, the enzyme carbonic anhydrase catalizes the hydration of carbon dioxide to form carbonic acid in the tubular cells. An ionic exchange follows the dissociation of H_2CO_3 resulting in the secretion of cellular H^+ and HCO_3^- reabsorption. This process may be represented as follows:—

Renal Tubular Acid Secretion



In the traumatic setting of open-heart surgery with cardio-pulmonary bypass, one can expect increased secretion of aldosterone. This promotes retention of Na^+ by the renal tubules. In the proximal tubules Na^+ is reabsorbed with HCO^-. In consequence, the ionic exchange already mentioned will operate and H^+ will be added to the urine. In other words, a normal adjustment to trauma is conservation of base and secretion of acid urine irrespective of the acid-base status of the plasma.

As carbonic anhydrase seemed to play a key role in the apparent failure of the kidney to restore acid-base equilibrium, the effect of inhibition of this enzyme with acetazolamide was studied in a group of 10 unselected patients undergoing mitral valve replacement. The protocol of the investigation provided for a similar number of unselected controls. Following acetazolamide therapy metabolic alkalosis was significantly reduced, the urine was significantly less acid and the sodium content of the urine was significantly increased. These findings add weight to the argument adduced to account for post-perfusion metabolic alkalosis associated with acid urine.

The second stage of my journey ends here. Gilbert Harding was a pessimist—he concluded his autobiography by stating that he wished the future was over. I am the eternal optimist —I hope the best has yet to come.

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Guest Lecture . . .

25th APRIL, 1969

PITFALLS IN CLINICAL TRIALS

Professor JOHN W. DUNDEE

"THERE are many paths which lead to the acquisition of clinical knowledge that might profitably be explored . . . but there is only one high road to an increase in therapeutic knowledge and that is the controlled clinical trial."

Few would disagree with the above quotation made by Sir Hedley Atkins, past President of the Royal College of Surgeons of England, and it aptly summarises the importance of clinical trials. With the introduction of so many new drugs in recent years, it is obvious that one can no longer rely solely on "clinical impressions" as to their merits and demerits. New drugs are generally much more powerful (with respect to both their efficacy and toxicity) than their predecessors—as well as being more expensive—and it is important to get a reliable opinion of their value as soon after their introduction as possible. The pharmaceutical industry is well aware of the bottleneck produced by the lack of adequate clinical trials. While most agree that there is no such a thing as the ideal clinical trial, it is important to realise that badly executed trials, or the production of wrong conclusions from the available data, can have disastrous sequelae.

Evolution of New Drugs

The following scheme represents the course followed by most new preparations. This is nothing new, but it has become more formalised, with greater emphasis on early investigations, since the inception of the Committee on Safety of Drugs:

(1) Laboratory and animal studies.

(2) Human pharmacological studies (volunteers or paid subjects).

(3) Clinical trials investigating
  (a) therapeutic activity.
  (b) side effects, contraindications and necessary precautions.

(4) Release
  (a) Limited.
  (b) General.

(5) Reports on efficacy and side effects and re-assessment of its value by many workers.

Limited release differs from the clinical trial in that it may include patients of differing ages, sex, physical status, pathology, etc., whereas the clinical trial is more "controlled." It may be organised by the same person as the initial clinical trial and can be considered to be an extension of it.

Role of the Anæsthetist

By training, the anæsthetist is well fitted to be a "clinical pharmacologist" since anæsthesia is essentially applied clinical pharmacology/physiology. In no branch of medicine does one so frequently see the onset, peak effect, regression and termination of drug action, and this is coupled with the discipline of detailed data recording.

Even in our specialty, researches in applied physiology and pharmacology have far outstripped work on the evaluation of new drugs. But our work need not be simply limited to anæsthetic drugs for we can also study analgesics, hypnotics, anti-emetics, vasopressors, anti-arrhythmia compounds and various ganglion or receptor blockers.

Clinical Trials

Cecil Gray has defined the purpose of these as follows:

". . . to obtain the MAXIMUM amount of UNBIASED information concerning the principal action and side effects of a drug or procedure from the MINIMUM number of patients in the SHORTEST time with the LEAST potential hazard or inconvenience to them."

Control or Standardisation

This is the hall-mark of a good clinical trial and uncontrolled trials often give misleading results and are probably of no more value than clinical trials—they may even be dangerous, as readers may assume that extensive statistical analysis, or colourful presentation of the data, guarantee their validity. This can only be avoided if the

design of the trial allows for adequate standardisation. The method of achieving this varies from study to study, but a few factors are considered below—

(a) Use of multiple drugs can give misleading data—it is essential that the drug scheduled for study is, in effect, the one actually studied. One recalls the misleading conclusions of the action of chlorpromazine derived from the use of the lytic cocktail, or the mistaken opinion of the efficacy of papaveretum from the use of Omnopon-Scopolamine.

(b) Elimination of variables: In addition to pathological conditions certain factors, such as sex, age and genetic make-up may affect the response to drugs. An obvious example of this is the sex difference in tendency to post-operative sickness, or the importance of ambulation in affecting the toxicity of analgesics.

(c) Drug Variables: Here one has to consider such things as dose-response curves, potentiation and synergism, as well as the topical subject of enzyme induction. This refers to the ability of a drug to stimulate enzymes which alter the metabolism of a drug administered subsequently. One must also consider drug stability and realise that some preparations deteriorate in aqueous solution (such as diamorphine) or on exposure to heat (such as suxamethonium).

(d) Measurement: This is important, particularly with respect to subjective responses, when patient-observer estimate have both to be considered. Standardisation can be achieved to some extent by reducing the number of observers—there is something to be said for the use of non-medical trained observers in long term studies. Under this subject one has to consider proper statistical analyses of data.

(e) Use of standard drugs and placebos. While not everyone will agree with the need of the latter (or even the justification of its use on ethical grounds), it is essential to prove the validity and sensitivity of the method of evaluation employed. Since there are useful standard preparations available for most purposes, one should compare new drugs with these—preferably at more than one dose level, and in comparisons of old and new preparations, special emphasis should be placed on side effects.

(f) Elimination of Observer Bias: This is a major problem in clinical trials, particularly for the enthusiast, and attention should be paid to the value of blind (or double blind) methods of administration and randomisation of sequence of drug administration, as well as the best use of 'cross-over' studies where possible.

(g) Number of patients: Many planned clinical trials fail to reach fruition because of inadequacy of numbers—either because sufficient patients are not available or because the observer has not sufficient time to study them. Here attention should be given to sequential studies in which the results of each administration determine the number still needed and also 'in depth' studies, where the largest possible amount of information is obtained from each subject. This has much to commend it, especially early on in a clinical trial, since one should not subject a person to the risk of a new untried preparation without learning as much as possible from this experience.

The above is not a comprehensive list, but it draws attention to some of the problems in clinical trials and suggests how they can be overcome.

The Registrar's Prize

THE Society awards annually a prize of £50 for the best original paper submitted by an anæsthetist in Scotland, holding the grade of Senior Registrar or under. A second prize of £20 or a third of £10 may be awarded for other papers of particular merit at the discretion of the assessors. It is not necessary that the Registrar be a member of the Society.

The conditions attaching to the award are as follows:—

1. The paper must be original, i.e., it should not have been read previously at any meeting or published in any journal. The winning of the prize is in no way a bar to the subsequent publication of the paper.

2. It is desirable that papers submitted show evidence of personal work, but papers consisting of surveys of the literature are eligible for consideration. The Council of the Society wishes to stress that intending competitors should not be discouraged through fear of their efforts being judged elementary. It is fully realised that junior anæsthetists in some peripheral hospitals may not have opportunities to deal with special types of cases or to employ advanced anæsthetic techniques.

3. Papers for adjudication *must* reach the Secretary by the *end of February* at the latest.

4. The winner of the prize will be required to give a digest of the paper at the Annual General Meeting of the Society towards the end of April.

The Secretary places all entries in the hands of the Award Committee which consists of the President, Vice-President and Past President. The members of this Committee have expressed the desire to be able to adjudicate without knowing the name or hospital of the writer: it is requested therefore that the name, address, etc., of the entrant be submitted on a separate covering page. This will be retained by the Secretary, but otherwise the essay itself should give no indication as to its source: acknowledgment to colleages, etc., should not be included.

The Prize for 1970 was awarded to Dr. G. J. B. Robinson of the Royal Infirmary, Glasgow, for a paper entitled "Thiopentone Blood Levels immediately after Injection." The following is a summary of the paper:—

THIOPENTONE BLOOD LEVELS IMMEDIATELY AFTER INJECTION

In 1960 Price and others published a paper which interpreted the course of thiopentone anæsthesia in terms of its distribution immediately after injection mainly to the well-perfused vital organs, the so-called vessel rich group, and its subsequent redistribution first to the muscle mass comprising 50% of the body mass, and later to the body fat which, because of its high affinity for thiopentone, is an even larger reservoir in functional terms. Finally, detoxification occurs, mainly in the liver, but this is slow —about 15% of the body content per hour— and plays little part in recovery from anæsthesia in ordinary clinical practice.

This scheme fits the findings after the first fifteen minutes, but not within that period when arterial levels fell at first more rapidly and later less rapidly than predicted.

Evidence has been presented to show that the liver delays the passage of thiopentone through it (Robinson and Joss, 1968). One reason why this must occur is that the bulk of liver blood flow passes through the other organs of the portal circulation first. However, hepatic vein blood contains practically no thiopentone whatever for upwards of three minutes after injection in most subjects. Therefore, even the thiopentone in the hepatic artery blood is held up and it is suggested that the liver itself is capable of delaying the entry of foreign substances into the general circulation in order to keep the concentration high locally in it and to allow more time for detoxification to occur.

The mechanism of this delaying power is considered to be analogous to a chromatography column. Here, a fluid carrying a bolus of foreign material is brought into contact with finely divided particles with a large surface area at one end of a long column. If the foreign material is soluble in the material of the column, the bolus is carried through the column at a rate slower than the carrier gas. If the column is efficient it will appear at the other end occupying a volume of carrier gas little larger than the volume it occupied on entering.

In the liver the sinusoid is considered to be the column, the liver cells the stationary

phase and the blood moving through the sinusoid the mobile phase. Sinusoids are about one-third of a millimetre long, and although this may seem a short distance it is a very long way for a molecule the size of thiopentone to diffuse in a liquid. In gas chromatography columns have to be much longer because diffusion speeds are much greater. In the liver all the sinusoids are arranged as chromatography columns in parallel, giving the same effect as a single large column.

The delay imposed on the passage of thiopentone is then identical with the retention time of a chromatograph. It can be calculated and if liver blood flow is normal it is of the order of two minutes, using Price's data. Under actual anæsthesia it appears to be longer.

Arterial blood levels computed according to this model show two special features—firstly, an elbow in the curve at just under a minute, and a striking increase in concentration when the initial arterial peak traverses the liver and re-enters the general circulation.

The initial elbow is due to rapid filling of the kidney, heart and brain which at this point reach their maximum concentrations and begin to redistribute their thiopentone.

The clinical significance of the secondary rise will depend on the effect it has on central nervous system levels. The calculated effect shows that the rise is not great enough in the normal subject to cause a secondary rise in the brain. However, it does prevent continuing lightening of depth for a short period and when it resumes it is at a slower rate.

In a person with any degree of fatty infiltration of the liver as in the early changes seen in alcoholism, however, it may be of considerable clinical importance. It is predicted that the secondary arterial rise is delayed and when it occurs its relative effect is much greater, leading to an actual increase in depth lasting some minutes. As fatty infiltration of the liver may occur in obesity alone, this could well be more common than one might expect.

Four patients were studied. They all show a decrease in the rate of fall at roughly two minutes after injection, but this is seen best in the subject who was given the injection rapidly. As the computer solution predicted this to occur at about one minute after injection, it seems reasonable to assume that the drug and the premedication have resulted in a greatly reduced cardiac output as has been reported (Fieldman, Ridley and Wood, 1955). As a result of this, the secondary rise may be expected to occur at a later time not covered by the sampling period.

The patients selected were all having intra-arterial pressure recordings during surgery. At induction blood was allowed to drip into a series of 36 bottles which were then analysed for thiopentone.

This study is of necessity preliminary and incomplete. However, it is consistent with the hypothesis that the liver takes up thiopentone rapidly in the initial period and therefore it may well later be released in patients with fatty livers in amounts sufficient to cause secondary deepening of anæsthesia.

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News from the Regions

Western Region

We note with pleasure the opening of the magnificent new dental hospital in Glasgow. It will certainly require a much extended provision of anæsthetic services for radical and conservative dental surgery. In addition, the new centre for Neurosurgery, Neurology, Neurophysiology (and Neuro-everything else) is due to open at the Southern General at the end of 1970, as is the new theatre suite at Stobhill.

The Registrars' Meeting of the Association of Anæsthetists was held in Glasgow this year, the first time ever outside London, and resulted in many flattering comments from those attending it. Many had never been to Scotland before, and we believe they were very favourably impressed with all aspects of the meeting.

The West was also visited during the year by the Hickman Society who, having ascertained that the anæsthesia was fully up to Hickman's standards, sampled the local waters and other fluids with evident satisfaction.

Dr. Winifred E. I. Finlay has become the first lady Consultant at the Western Infirmary. It is believed that this appointment was made in self defence owing to the increasing number of ladies in the junior ranks. "Set a thief . . ." There is no such shadow over the appointment of Dr. Harvey Maule at the Victoria. Dr. Kirsteen Dewar has gone to work in Bristol, and in exchange we have Dr. John Alexander up here to work on respiratory physiology on a grant from the Home and Health Department. The Bristolians, however, are craftier than us — Dr. Alexander has a return ticket. Dr. Bill Hamilton is in Nairobi for a year or two, and is obviously deriving much satisfaction from exercising small resources in complete clinical freedom.

At the Royal Infirmary we welcome the return of Dr. Elizabeth Bradshaw as Lecturer and the elevation of Dr. David Steel to an M.R.C. Research post. Dr. Dan Thomson is visiting South Africa for a year on an exchange basis.

We learned with deep regret of the death of Dr. Forbes of Falkirk.

South-East Region

The past year has seen more members taking up consultant appointments outside the region. Dr. Jean Horton, having returned from Nigeria, has moved to Cambridge, Dr. James Wilson has gone to Leeds, Dr. Peter Lord to Worcester, Dr. David Turner to Yarmouth, and Dr. George Stephen to Queen Charlotte's, London. Nearer home, Dr. Duncan MacNaught has moved to Peel, Dr. John Mason has gone to Dumfries, Dr. Sheila Donald to Falkirk and Dr. Colin Small to Bangour. We wish them all well in their new appointments.

Dr. Margaret Riddoch, back from India, now has an unusual post — part-time general practice in Livingstone and part-time consultant anæsthetist in Bangour.

Dr. Peter Jebson and Dr. Evan Lloyd have returned from North America enthused but not lured by their experiences there.

Early in the year Prof. Robertson had a successful world tour when he was guest speaker to anæsthetic societies in Australia and New Zealand.

The Society's Registrars' Meeting was held in the Royal Infirmary in October when a good turn-out saw video tapes of local analgesic techniques and heard a discussion on intensive care. In February we were again hosts to a British Council Course who were impressed not only by our anæsthetics but also by our piping and Highland dancing.

The Primary course has been so successful that there are already applicants not only for the next course but also for the one following, and this demand has led to the initiation of a Final F.F.A. course which will be held in November.

For the first time in memory the weather for the picnic was less than perfect — Miss Taylor must be losing her touch. However, she promises to make amends with a bigger and better Christmas Party which will be held at the same venue as last year on 12th December.

Northern Region

At the end of last year's Newsletter, Phase One of the Central Inverness Hospital and the new Nurse Training School were mentioned as building projects. It is pleasant to be able to record that both are now open and functioning.

Phase One, which houses all the laboratories, out-patient departments and the Blood Transfusion Service, opened in the late spring.

Contrary to our expectations while it was being built, it has turned out to be an attractive building, modern in style and nicely proportioned. It is set in pleasantly landscaped grounds right next to Raigmore Hospital on the outskirts of the town, forming a striking contrast to the squat ex-E.M.S. brick pavilions of the old hospital. Looking at it, we find ourselves becoming all the more anxious to hear a firm starting date for the next phase.

The Nurse Training School opened only a few weeks ago, bringing all the nurse training under one roof, and replacing the series of inadequate temporary premises.

Due to the co-operation of the School, the medical staff is to benefit very considerably from this new building. We have always felt very acutely the need for a large and well equipped lecture theatre for medical meetings, and the main auditorium of the School is being placed very substantially at our disposal.

The building also contains a spacious library. This accommodation we are also to share pending the building of a postgraduate centre.

These are two important considerations to us, because they will allow us to provide a more adequate library service than our present premises permit, and to intensify our postgraduate training and expand our programme of medical society meetings.

North-East Region

The past year has been fairly uneventful for us here in the North-East. We have had few staffing changes, but those have been significant ones. We greatly regret the departure of Dr. David White who was a consultant with us in Aberdeen for six years and who contributed tremendously to the academic and clinical work of our department. Dr. White has gone to the new Northwick Park Hospital, London, where he will have increased opportunities to pursue his main research interests in the mode of action of anæsthetics, working with Professor Nunn in the M.R.C. Research Unit. His interests in Intensive Care will also be served as he will run the Intensive Care Unit at Northwick Park.

However, we are most fortunate that Dr. White's post has been filled by Dr. C. R. Dundas who has been Senior Registrar with us, and, indeed, has been in the department in Aberdeen since 1960 in a variety of appointments. Dr. Dundas and Dr. White worked closely together, shared many of the same clinical and research interests, and it might be said that in Dr. Dundas we had almost a natural successor for the appointment.

It is with great regret that we have to record the untimely death of Dr. Mackay McLeod in Lerwick, Shetland, where as a general practitioner he has also had a large share in provision of the anæsthetic services to the Gilbert Bain Hospital. He is succeeded by Dr. George Smith who spent some time in the Anæsthetics Department in Aberdeen before taking up his appointment.

Dr. Rollason is, at the time of writing, on a tour which takes him to the Australasian Congress of Anæsthesiology in Canberra and, under the auspices of the W.H.O., a visit to Sarawak to advise on anæsthesia training there. He is also lecturing in, and visiting, a number of other centres in the Antipodes and North America.

Three of the five registrars from our department in Aberdeen sitting the recent primary F.F.A.R.C.S. examination were successful. We feel that this is a good record and would like to think that it is in some measure due to our course of teaching for this examination which has been evolving over the past few years, with much help from various University Departments.

Finally we welcome the agreement that building of phases two and three of the hospital development on the Foresterhill site in Aberdeen will commence in April 1972. This will eventually provide for our department new and expanded accommodation as well as new operating theatres, an Intensive Care Unit and accommodation close to the operating theatre labelled at present on the plans "Human Physiology"—surely relevant to our interests.

Eastern Region

Professor E. A. Cooper, Department of Anæsthesia, Royal Victoria Infirmary, Newcastle-upon-Tyne, has been appointed Eastern Regional Hospital Board Visiting Lecturer in the Department of Anæsthesia, Dundee Teaching Hospitals. He will spend two weeks in Dundee in November 1970, taking part in the various activities of the Department, including the teaching of junior staff. He will also deliver an Open Post-graduate Lecture in the University of Dundee entitled "Breaths of Change."

A conference on the teaching of General Anæsthesia and Analgesia to dental students was held in the Dundee Dental School on 28th and 29th September, 1970. Papers were presented by Professor W. W. Mushin, Professor E. A. Cooper, Dr. J. I. M. Lawson and several other prominent anæsthetists and dentists. The proceedings of this conference will be published in extenso.

On the obstetrical side we are now able to offer continuous epidural analgesia to women in labour. Shortage of staff has restricted the indications for this technique to some extent, but an average of two cases each week receive it. This service has been provided mainly by the efforts of one consultant anæsthetist, with assistance from some of the junior anæsthetic and obstetrical staff.

To encourage our operating theatre attendants to prepare for the Diploma examination of the Institute of Operating Theatre Technicians, a two-year course of training has been started in Dundee. It will consist of lectures, demonstrations and visits to specialist departments.

At the European Congress of Anesthesiologists in Prague, Dr. Lawson took part in a Symposium on "The Risks of the Anesthesiologic Profession" under the chairmanship of Professor Dundee.

Editorial Notes . . .

Dr. W. NORRIS

THE past year has been an active one not only for our own Society but for other bodies connected with the specialty. In common with other Anæsthetic Societies set up for scientific and social purposes, we are becoming entangled—temporarily many hope—in semi-political affairs. There are rumours in the air of the formation of a College of Anæsthetists and of closer co-operation between regional societies and the Association of Anæsthetists. Problems have arisen and are arising in ensuring that our specialty—now the largest in the country—is represented side by side with the other older and traditionally more vocal and powerful groups. These bodies have evolved through the years a mechanism by which their advice is sought and given in all matters — education, staffing and policy-making. In time we, too, may have such a body, but it is clear that until then the Scottish Society of Anæsthetists may have to devote some time and energy to ensuring that the views of the specialty in Scotland do not go unheeded.

It seems likely that the business part of our Annual General Meeting may well be partially concerned with such matters for—one hopes—a limited time, and therefore it is in all our interests that there is a good attendance at such meetings to hear and to be heard! It would be a tragedy if changes which may affect us all for many years were to be passed by default.

It is encouraging to see our Society grow as the number of doctors entering the specialty grows. This augurs well for our continuing success in furthering section two of our constitution. Few associations in a season offer such a combination of scientific and social fare. Possibly fewer still enjoy the harmonious blending of interests of an entire country. It is a pleasure and honour to serve a Society such as ours. Next year will bring a new hand to the Editorial pen to continue in his own way the good work started by our Past President, Dr. Shaw. Please remember that the Newsletter exists to keep *you* in touch with *your* friends and colleagues. It will always be as good as you help to make it.

THE ELECTRICAL EVALUATION OF MUSCLE RELAXATION IN ANESTHESIA

Prof. J. F. CRUL, M.D.
Dept. of Anæsthetics, University of Nijmegen

A wide variety of local, inhalational and intravenous anæsthetics as well as central and peripheral muscle relaxants interfere with muscle tone and contraction during almost every anesthesia. Superimposed narcotics and anesthetics can depress impulse formation in motor neurons.

Just as with respiration and circulation the degree of muscle relaxation should be carefully monitored during and after anesthesia. As the different drugs depress muscle function at a wide variety of levels of impulse transfer, a differentiation of causes should also be aimed at but is still impossible to achieve.

An overall clinical estimation of muscle activity in conscious patients postoperatively is easy to achieve. In unconscious patients, however, only spontaneous and reflex muscle activity can be used for evaluation. Study of reflex activity is the more useful. Setting up an indirect muscle stimulation somewhere in the body can at least differentiate between central and efferent peripheral muscle relaxation. Several types of nerve stimulators are commercially available.

The effects of motor nerve stimulation can be evaluated either by direct vision, by measuring evoked electromyographic response and by measuring force of muscle contraction with displacement transducers. For routine clinical practice the first method is sufficient. The other two remain research tools, the mechanically evoked response more closely resembling the spontaneous muscle power than the electrical.

Technical difficulties may prevent studying the muscles around the operative field during operation and the respiratory muscles after, therefore superficial nerves and muscles are better tested and a correlation found between these and the muscles around the operative field and those of respiration. The most popular is the ulnar nerve hand muscle stimulation.

Single twitch pulses as well as tetanic pulses have to be used for good evaluations. Both are reduced by peripheral muscle relaxants. Single twitches should be given not faster than 1 per 4 seconds as they are otherwise depressed by "fading" with the use of non-depolarising relaxants. Trains can be given in frequencies from 50 to 200 cycles per second. When using lower frequencies the twitch height is the better estimate of the degree of muscle block. With higher frequencies the tetanus becomes the more sensitive indicator. Depolarising and non-depolarising relaxants show a different pattern of blockade. The depolarising ones give no depression of contraction at low frequencies of twitch contractions (1—0.25 c/sec), minor fading of tetanic contraction and no post-tetanic facilitation. The non-depolarising ones give a depression of contraction at twitch frequencies above 0.25 c/sec, causing a post-rest facilitation and a strong fading at tetanic stimulation followed by a more than two-fold increase in twitch contraction after the tetanus. After prolonged administration of depolarising relaxants the block pattern more closely resembles the non-depolarising without being identical (desensitization block). Sufficient relaxation of abdominal muscles is achieved with non-depolarising agents with a 80-90% reduction of twitch height of the hand muscles. Sensitivity of the particular patient and the need for subsequent doses can so be titrated.

For depolarising agents the tetanic contraction heights are a better estimate, but even then are a poorer indicator of abdominal relaxation than with non-depolarisers particularly with the short-acting depolariser, succinylcholine.

Only in the stage of desensitization block the correlation is better. Fully recovered twitch height and fully sustained tetanus even at high frequencies (150 c/sec) are the best signs of complete reversal of the peripheral neuromuscular blockade. Persistent lack of spontaneous muscle activity then points at more centrally located causes.

The cause of apnoea in operations terminated unexpectedly early could be well differentiated with this nerve-muscle stimulation.

MONITORING IN POSTERIOR FOSSA CRANIOTOMIES

Dr. D. C. WHITE, Aberdeen

Monitoring of vital functions during posterior fossa craniotomies is concerned with detecting possible interference with centres in the floor of the 4th ventricle controlling cardiac and ventilatory function. The former may be monitored from the ECG and the latter by allowing spontaneous ventilation and observing the ventilatory pattern. It is not always entirely satisfactory to permit spontaneous ventilation as respiratory acidosis tends to occur, and the use of controlled ventilation in this situation has been justified by the statement that ECG abnormalities may always be seen before or at the same time as ventilatory ones.

To test this assumption in a series of posterior fossa craniotomies the ECG and the spontaneous ventilatory pattern (as shown by airway pressure changes) throughout the operation were recorded on magnetic tape. The slowly changing nature of the ventilatory signal necessitated the use of a Frequency Modulated type of recorder. Portions of the recording in which ventilatory abnormalities had been detected could be played back and recorded on paper before the tape was wiped clean for re-use.

In two cases (of acoustic neuroma), periods of apnoea occurred without any detectable ECG abnormality. This evidence shows that the ECG cannot be relied on to reveal interference with the respiratory centre.

A further concern of monitoring in these cases is the detection of air embolus which is particularly a hazard, if the patient is placed in the sitting position. The possibility exists that the presence of air in the circulation could be detected by observation of changes in the pattern or excretion of CO_2 during the ventilatory cycle (as seen by an infra-red CO_2 analyser). Some changes would be expected if portions of the pulmonary circulatory bed were occupied by air. Further work is required to determine the sensitivity of this method.

CO_2 output monitoring with a fast response analyser would also be a satisfactory method of monitoring spontaneous ventilation for the purposes set out in the first part of this paper and such monitoring would then fulfil two functions.

CARDIOVASCULAR MONITORING DURING ANÆSTHESIA —A PHYSIOLOGIST'S VIEWPOINT

By G. R. KELMAN

Professor of Human Physiology, University of Aberdeen

Before and during the administration of any general anæsthetic the anæsthetist must try and assess the state of his patient's cardiovascular system. He may be helped in this task by various instruments, such as the sphygmomanometer and electrocardiograph; but, even in the most advanced centres, the anæsthetist has nothing like the range of monitoring equipment which is available to, for example, an airline pilot.

If it were possible to provide the anæsthetist with all the information which he could possibly want about the state of his patient's cardiovascular system, what parameters would he choose to have displayed before him? My list would be as follows:

(i) **Blood flow to all the major organs**—the brain, heart, kidney, gut, liver, skin and skeletal muscles—and the relationship between their blood flow and oxygen consumption as reflected in the oxygen tension of the local venous blood.

(ii) **Cardiac output** and, if this is normal, the extent to which it is being so maintained by the body's compensatory mechanisms. I call this the cardiac reserve.

(iii) **The degree of filling of the peripheral circulation** and, if this appears satisfactory, the extent to which it is so only because of the body's compensatory mechanisms — the peripheral circulatory reserve.

(iv) **Arterial blood pressure.** As regards this last parameter many workers would argue that it is blood *flow* which is important, not blood pressure. This is probably true in the main, although pressure *is* important in maintaining the cerebral circulation in the upright posture, and in maintaining renal filtration. It may also be important in the maintenance of an adequate cerebral circulation, even in the horizontal position, because, although in the normal person the physiological phenomenon of autoregulation can maintain cerebral perfusion even when the arterial pressure falls to quite low levels, this is not necessarily the case when the vessels have been damaged by disease.

The technical difficulties in the way of making many of these measurements are great, therefore in normal clinical practice, cardiovascular monitoring is limited to 5 parameters which can be measured fairly readily:

(i) **Arterial blood pressure** may be measured by a sphygmanometer or an oscillotonometer ("oscillometer") or an electromanometer connected to an arterial canola. There is said to be a slight morbidity associated with the technique of arterial cannulation; my feeling is, however, that a patient ill enough to need continuous assessment of his arterial pressure is ill enough for the (minute) risk of arterial cannulation to be fully justified.

(ii) **The electrocardiogram** can be recorded and displayed either by a pen writer or on a cathode ray tube. It can also be made to work a warning device such as a flashing light or a "bleep."

(iii) **Central venous pressure** can be measured by a simple saline manometer connected to a percutaneously-introduced central venous catheter. This technique, of course, gives only mean pressure; to obtain the various peaks and troughs which interest the cardiologist it is necessary to use an electromanometer, but this complexity is not necessary for routine purposes.

(iv) **Finger tip blood flow** can be assessed by a photoelectric or other type of plethysmograph. This is a particularly valuable measurement because, unlike the electrocardiogram, it gives information about actual blood flow through part of the circulation. As is the case with the renal micro-circulation the small vessels of the fingers rapidly shut down when the body's cardiovascular system comes under stress, e.g. by blood loss or depressed cardiac function.

The interpretation and fallacies of the measurements in the above list are, in the main, well known and do not need repetition here. The interpretation of central venous pressure, however, needs a few words of explanation. The present treatment is dogmatic and, although it relates fairly well to clinical reality, it should be applied to clinical problems with due caution; physiological dogmatism can never replace clinical skill. (Nor can clinical experience compensate for a lack of knowledge of clinical physiology).

Guyton suggests that, for many purposes, the heart and pulmonary circulation may be regarded as a single system in which an increase of right atrial pressure — central venous pressure—causes an increase of cardiac output. This is an application of Starling's law of the heart, an increase of right atrial pressure stretches the ventricular muscle during diastole and increases the force of its subsequent contraction, thus causing an increase of cardiac output. Overfilling of the circulation, e.g. by overtransfusion, causes an increase of pressure in the peripheral circulation—what Guyton refers to as the mean systemic pressure—and this pressure is transmitted to the right atrium, thus causing a rise of central venous pressure and of cardiac output. Conversely, loss of blood from the circulation causes a decrease of cardiac output. This is, of course, the familiar clinical condition of hypovolaemic shock.

A decrease of efficiency of the cardiac pump has the opposite effect on central venous pressure. The maintenance of an adequate cardiac output then requires an increase of right atrial pressure; the failure of the cardiac pump causes blood to be dammed back in the peripheral circulation with a consequent rise of central venous pressure. This is the condition of cardiogenic shock, as seen after a severe myocardial infarction.

In summary, it is possible to measure, simply and cheaply, the following parameters — arterial blood pressure, central venous pressure, finger tip blood flow and urine flow. Knowledge of these parameters, plus some knowledge of applied physiology, should enable the clinician to form a useful opinion about the state of his patient's cardiovascular system.

THE MONITORING OF THE ELECTRICAL ACTIVITY OF THE HEART

By W. N. ROLLASON, F.F.A.R.C.S.
Department of Anæsthetics
The Royal Infirmary and University of Aberdeen

About 340 B.C. Aristotle wrote "The torpedo narcotizes the creatures it wants to catch, overpowering them by the strength of a shock that is resident in its body . . ." Thus electrical phenomena associated with living tissues were observed even by ancient man.

In 1856 Kölliker and Müller placed a frog's nerve muscle preparation in contact with a beating heart and were able to demonstrate twitches of the frog's muscle with each contraction of the ventricle; thus the electromotive phenomena of cardiac muscle became well established. That this was measurable was demonstrated by Waller in 1887 using Lippmann's capillary electrometer.

The development, however, of the string galvanometer by Einthoven in 1901 was one of the outstanding achievements in medicine. By 1910 physicians began to realise that electrocardiography was not only very useful in the laboratory but also in clinical practice, and since 1918 it has found an important place in the operating and more recently in the intensive care suites throughout the world.

My personal interest in electrocardiography followed on the publication in Anæsthesia of the paper by Griffith and Gillies in 1948 on the "Anæsthetic procedure for thoracic-lumbar splanchnicectomy and sympathectomy." Here hypotension was achieved by total sympathetic blockade resulting from the subarachnoid injection of procaine.

As one of the organs principally at risk during hypotensive anæsthesia is the heart, the effect of this technique on the cardiovascular system assumed major importance.

While the young and healthy with reactive cardiovascular systems may have their pressure lowered to the region of 30 mm Hg with impunity for limited periods in the supine position, the same procedure in the elderly with advanced arterio-sclerosis and hypertensive vascular disease may result in catastrophe. Monitoring accordingly assumes greater importance in the older age groups.

While what really matters is, of course, not blood *pressure* but blood *flow* it is still difficult to measure this directly under routine clinical conditions. It is accordingly necessary to fall back on indirect monitors such as the E.C.G. to detect evidence of cardiac ischaemia and arrhythmia.

In an endeavour to assess the E.C.G. changes which occur during increasing normovolaemic hypotension a series of 10 dogs were monitored until cardiac arrest ensued. Halothane was the hypotensive agent used. Adequate oxygenation by I.P.P.R. and a near constant pCO_2 were maintained through a series of steady states. Five of the dogs developed ventricular fibrillation and five asystole. Cardiac failure was preceded by an increasing ST depression and a slowing of the heart rate.

In clinical work E.C.G. changes have been more associated with the pulse rate and the rate of fall of the blood pressure rather than with the degree of hypotension produced during the low pressure phase. A combination of a rapid rate of fall and tachycardia can be associated with a profound depression of the ST segment.

Occasionally, an improvement in the E.C.G. pattern may be seen during the hypotensive phase in patients with left ventricular strain associated with hypertension.

In 1965 Kaufman related E.C.G. changes to the moment of extraction of the teeth. This led to a study of the incidence of cardiac arrhythmia during dental anæsthesia using the technique of radio-telemetry. The results using four different techniques are shown in Table I.

More recently still the incidence of arrhythmia associated with E.C.T. has been assessed and an endeavour has been made to compare methohexitone with propanidid using each patient as his or her own control. Table II suggests there is little to choose between the two agents.

Finally, it should be stressed that monitoring devices are no more than ancillary aids. They are no substitute for skill or for keen and constant clinical vigilance.

TABLE I

Incidence of Cardiac Arrhythmia during Dental Anaesthesia

Group	Anaesthetic Technique	No. of Cases	Average age (yrs)	Average duration (mins)	% incidence of Cardiac arrhythmia		
					Major	Minor	Total
1	I.V. only ..	314	27.7	6.2	0.3	2.5	2.8
2	N_2O/O_2/HAL .. (Nose piece)	202	23.6	5.8	1.5	17.2	18.7
3	N_2O/O_2/HAL .. (Face piece-Marrett)	126	28.1	7.4	3.2	15.1	18.3
4	N_2O/O_2/HAL .. (Intubated)	204	34.2	26.8	4.9	21.1	26.0

TABLE II

Comparative incidence of Cardiac Arrhythmia during E.C.T. Therapy (50 patients)

		V.E.S.	Tachycardia > 159
Methohexitone ..	NOT Propanidid	3	1
	AND Propanidid	1	3
	Total	4	4
Propanidid ..	NOT Methohexitone	3	3
	AND Methohexitone	1	3
	Total	4	6

LIBERATION OF HISTAMINE AND ANAPHYLACTIC REACTIONS IN ANÆSTHESIAS—BIOCHEMICAL AND CLINICAL ASPECTS

By Profs. A. DOENICKE and W. LORENZ

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Introduction

Examinations relating to the liberation of histamine by drugs have rarely been carried out in man. The riskiness of experiments of this kind is only one reason for what has been left undone. Since the side-effects of some drugs suggest that histamine is involved, one is astonished at the very rare attempts made to clarify this question through histamine determination. According to our own experience, the reasons for that might be due to the difficulty of identification and quantitative determination of histamine in the various body fluids. We have, for obvious reasons, examined some anæsthetics with regard to their effect on the liberation of histamine.

Methods

According to the method of Lorenz et al. (1970), histamine was determined fluorometrically after isolation by ion-exchange chromatography in Dowex 50W-X8 and subsequent extraction in butanol.

The examinations were carried out in volunteers who had agreed to undergo several anæsthesias.

Results: General Preliminaries

In the "allergy" following the application of drugs, one has to distinguish between three possible modes of action.

(1) Chemical liberation of histamine—a direct effect on the reacting organs,

(2) anaphylaxis, an antigen-antibody reaction and

(3) contact allergy, a very rare phenomenon in case of intravenous anæsthetics. It is much more frequently observed in case of other drugs, such as, for example, procaine or penicillin.

In order to prove a chemical liberation of histamine by drugs, we use the following parameters:

(1) Increase of the histamine level in the plasma or in the whole blood,

(2) increased gastric secretion and increase of acidity of the gastric juice,

(3) a more or less marked decrease in blood pressure,

(4) negative prick test for allergy and partly also

(5) a decrease of the basophilic leucocytes in the venous blood.

We examined the liberation of histamine following the administration of Epontol, the solute cremophor EL, thiopental, haemaccel as well as, in animal experiments, further expanders. After the administration of Epontol a decrease in the mean blood pressure occurred. In addition, we were able to demonstrate an increase in the acidity of the gastric juice as well as an increase in the histamine content of the whole blood. The histamine level increases after 3 and 6 minutes and has increased by 30% 10 to 20 minutes after injection. After 30 minutes it may still be increased, although no longer significantly.

Six minutes after Epontol injection, the pH value of the gastric juice decreases and it is still significantly decreased after 10 and 20 minutes.

For a long period of time the solute of the propanidid, cremophor EL, was considered as causing a decrease in blood pressure on account of possible histamine liberation. These opinions were probably based on the analogous conclusion that wetting agents might lead to histamine liberation in man, as this is the case in dogs. This is, however, not true. Blood pressure was not decreased significantly after intravenous injection of cremophor EL, the histamine content of the blood and the pH value of the gastric juice were unchanged.

In one typical case during anæsthesia the histamine content of the plasma rose by a maximum of 230% after 6 minutes, returning approximately to its initial value after the 30th minute.

After application of thiopental, we could also demonstrate an increase in the plasma histamine level, in some cases up to 700% in the first few minutes. The average increase in the 3rd minute amounted to 500%. Sometimes the initial value had not been regained 20 to 30 minutes after the injection had been started. Following the administration of thiopental all subjects revealed a marked increase in the acidity of the stomach, which corresponded to that following the application of Epontol.

Also in case of the gelatinous preparation haemaccel, which is used as a blood-substitute solution, histamine liberation was proved in man (by the same method of determination) which, quantitatively, corresponded to that of Epontol, after quick infusion of 500 ml (within 5 minutes). As we mentioned at the beginning, changes in the blood picture, especially in the basophilic and eosinophilic leucocytes, may, in some cases, also indicate histamine liberation. The basophilic leucocytes, counted in venous blood per 500 cells, show maximum decrease in the 10th minute after application of thiopental. The drop is dependent on the injection speed: With an injection period of 20 seconds the drop is significant in the 3rd minute, with an injection period of 100 seconds it is significant in the 20th minute. These findings following the application of thiopental are new, because neither *Adriani* nor *Lee* described changes in the white blood picture after the administration of thiopental.

Histamine liberation may be the cause of various symptoms. More or less marked hypotension is frequently observed. An erythema, blepharoedema or urticaria may occur. Oedema of the glottis or oedemas of the trachea are rare, whereas bronchospasm is quite a frequent complication. In animal experiments, *Felix* demonstrated an increase in the pressure of the pulmonary artery in 1966; it has in the meantime also been observed in clinical practice.

All these symptoms may appear separately as well as jointly. In case of massive histamine liberation, a circulatory collapse occurs due to the drop in blood pressure. Death may occur due to cardiac standstill within a few seconds.

Treatment promising success in case of histamine liberation may be derived from the following findings:—Histamine produced in larger quantities (induced histamine) in the region of the endothelial cells (in allergic processes, X-ray therapy, burns, septic conditions) shows a strong effect on microcirculation. The glucocorticoids reduce induction of the enzyme "histidindecarboxylase" and thus prevent increased histamine production. They further act as functional antagonists of histamine in the vascular endothelium.

Histamine liberated from the mast cells acts on the receptors. Antihistamines just block this effect. However, in case of massive liberation of histamine and simultaneous considerable production of histamine, which we have experienced in individual cases, the antihistamine alone cannot prevent the effect of the histamine. Decisive success only comes with the combination of gluco-corticoid and antihistamine. We will report on these observations in more detail on another occasion.

From the scheme described we can deduce the therapy in case of histamine liberation.

In the first place, there is the administration of gluco-corticoids, such as dexamethasone or prednisolone, followed by that of antihistamines. When a complication occurs without preceding administration of antihistamine or a cortisone derivative, a glucocorticoid should be given first, then an intravenous antihistamine and finally infusions to fill up the circulation. Vasoconstrictors, such as intravenous noradrenaline, have proven their value as functional antagonists against the effect of histamine. Broncholytics (alupent) are indicated in case of bronchospasm.

We have recently been informed of a contact allergy in an anæsthetist following the handling of Epontol. We tested him for allergens. The remarkable thing is that only the agent propanidid induced contact allergy, whereas the solute cremophor EL and the other allergens usually submitted in serial tests did not. The plasma histamine level was not increased.

We have recently been informed of another interesting case. Complications probably due to histamine liberation were quite frequently observed when certain ready-for-use syringes for one application only were used. These complications occurred only in those cases in which Epontol had been stored ready for injection in these plastic syringes for quite a considerable length of time before anæsthesia was effected. We will soon report on our examinations carried through in animal experiments.

We have to conclude from these clinical observations that the storing of Epontol in ready-for-use syringes for one application only over a considerable length of time must be avoided.

Summary

(1) Massive circulatory reactions following the administration of drugs used for intravenous induction of anæsthesia (dosage according to effect) may be attributed to a liberation of histamine. This is substantiated by an increased plasma histamine level, a stimulation of the secretion of gastric juice, as well as the possibility to prevent or influence hypotension by prednisolone and antihistamines.

(2) Histamine liberation is mainly brought about by a direct effect of drugs on the mast cells. It is not effected with an antigen-antibody reaction acting as an agent, because:

(a) graded reaction can be recognised (relation between dosage and effect) and

(b) cutaneous tests were negative in those volunteers or patients who had shown massive histamine liberation after the administration of the drug.

EDINBURGH AND EAST OF SCOTLAND SOCIETY OF ANÆSTHETISTS

Syllabus 1970-71

1970

Saturday, October 31

Combined Meeting with Glasgow and West of Scotland Society of Anæsthetists will be held in the University Staff Club, Chambers Street, Edinburgh, at 5.30 p.m.

"Sleep"—Dr. Ian Oswald, Senior Lecturer, Department of Psychiatry, University of Edinburgh.

A Buffet Supper will follow the Meeting.

Tuesday, November 10

"New Views of Muscle Relaxants"—Dr. S. A. Feldman, Consultant Anæsthetist, Westminster Medical School.

Tuesday, December 8

Presidential Address—Dr. A. C. Milne.

1971

Tuesday, January 12

"Cardiac Irregularities and Anæsthesia"—Dr. D. B. Scott.

Tuesday, February 9

Members' Short Papers.

Friday, February 26

Informal Dinner at University Staff Club.

Tuesday, March 9

"Problems and Mechanisms of Post-operative Hypoxaemia"—Dr. A. A. Spence, University of Glasgow.

Tuesday, April 27

Annual General Meeting.

* * *

Meetings will be held in the Royal College of Surgeons, Nicholson Street, on the **second Tuesday** of each month, unless otherwise specified.

GLASGOW AND WEST OF SCOTLAND SOCIETY OF ANÆSTHETISTS

Syllabus 1970-71

1970

Saturday, October 31, 5.30 p.m.

Combined Meeting with Edinburgh and East of Scotland Society.

"Sleep"—Dr. Ian Oswald, Senior Lecturer Department of Psychiatry, University o Edinburgh.

University Staff Club, Chambers Stree Edinburgh.

A Buffet Supper will follow the Meeting.

Tuesday, December 1

"Experiences in a Pain Clinic"—Dr. J. E Riding, Department of Anæsthesia, Univer sity of Liverpool.

1971

Wednesday, January 13

Symposium on Resuscitation—Dr. J. D Briggs, Renal Unit, Western Infirmary; D C. R. M. Prentice, Department of Medicin Royal Infirmary; Dr. J. G. B. Hendry Department of Anæsthetics, Victoria In firmary.

Thursday, February 18

"Underwater Medicine"—Surgeon Com mander E. E. P. Barnard, Royal Navy Physiological Laboratory, Alverstoke, Han

Wednesday, March 17

Presidential Address—Dr. Peter Stuart.

Tuesday, April 20

Annual General Meeting.

* * *

Unless notified otherwise, Meetings will b held in the Lister Lecture Theatre, Glasgo Royal Infirmary, at 8.15 p.m. Tea will b served in the Board Room at 7.45 p.m. Notic of each meeting will be sent to members.

NORTH-EAST OF SCOTLAND SOCIETY OF ANÆSTHETISTS

Syllabus 1970-71

1970

Thursday, October 15—Stracathro

"The Author and the Editor"—Dr. J. E Riding.

Thursday, November 19—Aberdeen

"The Avoidance of Oxygen Toxicity"— Surg. Cdr. E. E. P. Barnard.

1971

Thursday, March 25—Dundee

"Lesser Known Therapeutic Effects o Nitrous Oxide"—Dr. A. Tindal.

Thursday, May 13—Stracathro

Presidential Address—Dr. D. C. White. Annual General Meeting.

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