bronchial tree when these cannot be effectively moved by ciliary action. The unhurried tracheostomy, with a clear airway maintained by the bronchoscope, contrasts sharply in ease of performance with the difficulty found in the congested neck of a semi-asphyxiated patient.

In any case of respiratory obstruction cardiac arrest may occur. When possible, we feel that such emergencies should be managed by "two-surgeon" teams as described above. One operator watches the carotid pulse and is prepared to undertake cardiac massage at any time, while the other concentrates on the bronchoscopic work and the continuous supply of oxygen through the bronchoscope. Oxygen under pressure should also be administered at regular intervals, using the bronchoscope as an endotracheal tube. This is of the utmost importance, and should not be forgotten by the operator who is engrossed in attempting to clear the airway.

It is stressed that time should not be wasted trying to ascertain the presence of the heart beat, either by palpation at the apex or by auscultation. The time available once arrest has occurred is very limited. Greenfield (1938), quotes Gildea and Cobb in their conclusion that cortical neurones may suffer irreparable damage from five minutes of circulatory arrest. When arrest occurs in the presence of anoxia, a much shorter period would suffice. Therefore, once the carotid pulse is no longer palpable, the chest or abdomen should be opened immediately and rhythmic cardiac massage started. In the above case a trans-abdominal approach was used, as this was the route most familiar to the surgeon concerned. It is only fair to state, however, that cardiac massage through an anterior incision in the fourth left intercostal space is no more difficult or time-consuming to perform. It is easily learnt and should be within the scope of all surgeons regardless of their specialty. The thoracic approach has the added advantage of more effective "massage," since the pericardium can be incised to get more effective compression. This also allows the surgeon to observe whether the ventricles are inert or fibrillating, for, if the latter is found, an electric defibrillator as described by McMillan *et al.* (1952) should be used.

Pneumothorax as a complication of tracheostomy and neck incisions has been well described by several authors (Macklin, 1937, 1939; Neffson, 1942; Morgan and Wishart, 1947; Reading, 1949; Michels, 1951). In the present case there were three possible causes: (1) rupture of an emphysematous bulla on the left lung when this lung was inflated during the cardiac arrest; (2) injury to the bronchial wall during removal of the secretions; and (3) mediastinal emphysema with rupture into the pleural cavity, or an extrapleural spread causing an extrapleural pneumothorax secondary to suction of air through the tracheostomy wound. This last cause is the most likely, for even with the bronchoscope in position there was a degree of obstruction still remaining in the smaller bronchi due to the exudate. At no time during the post-operative period had the tracheostomy tube slipped out of the tracheal opening—the usual cause of air being sucked into the mediastinum.

The use of alevaire almost continually for the first three post-operative days was of great help in liquefying the secretions and rendering them more easily aspirated.

Summary

A case of acute and severe respiratory obstruction and its management is described.

The cause was thought to be acute tracheobronchitis added to an already present partial obstruction, this obstruction being caused by a previous respiratory infection.

Immediate treatment by bronchoscopic aspiration and tracheostomy was given. Cardiac arrest, which occurred during this treatment, was dealt with satisfactorily by cardiac massage.

The possibility of cardiac arrest occurring in these cases is stressed and its treatment discussed. This part of the management is greatly facilitated by a second surgeon being available.

Pneumothorax as a post-operative complication is discussed.

The value of alevaire in the immediate post-operative period is mentioned.

We are indebted to Dr. E. C. Allibone, under whose care the patient was admitted, for permission to publish this report. We thank Professor P. R. Allison, Dr. G. A. W. Neill, and Mr. G. S. Seed for their encouragement and their many helpful criticisms.

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A COLORIMETRIC METHOD FOR THE DIAGNOSIS OF PHAEOCHROMOCYTOMA

BY

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It is well known that a patient suffering from phaeochromocytoma excretes a large amount of noradrenaline in the urine. Such urine, or an extract made from it, produces a rise in blood pressure when injected into a cat (von Euler and Hellner, 1951; Burn, 1953): in our opinion this biological method is reliable for quantitative assay (Burn, 1954). However, it is expensive, and recently there has been a dearth of suitable cats. Accordingly we have developed a chemical method of estimating noradrenaline in urine with which we have been able to diagnose two cases of phaeochromocytoma.

Method

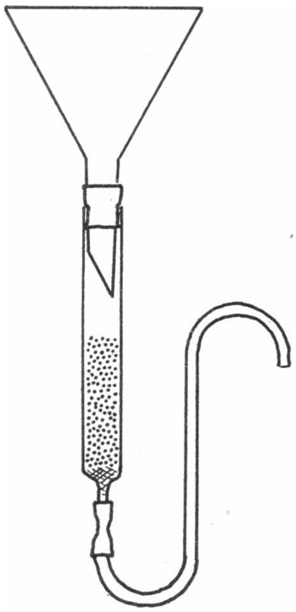
At *p*H 6.5 noradrenaline can be adsorbed from urine on the cation-exchange resin "amberlite IRC-50" (Bergström and Hansson, 1951), and can be eluted with excess of hydrogen ions. This stage gives a relatively large volume of solution free from the urinary pigments. Concentration of the extract is effected by adsorption on aluminium hydroxide, followed by solution in a small volume of acid and precipitation of the aluminium.

The colour reaction employed is the condensation of noradrenaline with ethylene diamine (Natelson, Lugovoy, and Pincus, 1949); the reaction produces a yellow colour with an absorption maximum of 405 mμ and a millimolar extinction coefficient of 10.

Preparation of Urine.—Urine was collected for 24 hours into a Winchester bottle containing 5 ml. of conc. HCl. An aliquot of 100 ml. was adjusted to *p*H 6.5 with *N* NaOH, using a glass electrode.

Construction of Amberlite Column.—The amberlite column was set up as shown in the Diagram. The glass tube containing the amberlite was of 18-mm. bore and about

14 cm. long. It had a constriction at the lower end, which was plugged with either glass or cotton-wool and which was connected to an S-shaped piece of glass tubing having a capillary bore. This tubing was arranged so that its outlet corresponded approximately with the level of the amberlite. The filter funnel set up above the tube could accommodate about 200 ml. To fill the column the filter funnel was removed and the apparatus was filled with water. Then 6 g. of dry amberlite IRC-50 was poured into the tube and stirred to dislodge air bubbles. The filter funnel was then replaced.



Construction of amberlite **column.**

Preparation of Amberlite Column.—The column was washed with successive 25-ml. portions of 2 *N* H_2SO_4, demineralized water, *N* NaOH, water, 0.5 *M* phosphate buffer *p*H 6.5, water, in that order, each fluid being allowed to run through the column before the addition of the next one. The flow rate was about 2 ml. per minute. The column was used repeatedly, the washing being sufficient to clean and regenerate it.

Adsorption and Elution of Noradrenaline. — After the column had been prepared 100 ml. of urine adjusted to *p*H 6.5 was passed through it followed by 25 ml. water. The filtrates were discarded. The noradrenaline was eluted with 30 ml. of 2 *N* H_2SO_4.

Purification with Aluminium Hydroxide.—To the eluate there was added 1 ml. of 20% $Al_2(SO_4)_3.18H_2O$ and the solution adjusted to *p*H 8 by the use of a glass electrode. 5 *N* NaOH was added until aluminium hydroxide began to precipitate and then *N* NaOH was added until *p*H 8 was reached. The precipitate was centrifuged down and the supernatant discarded. The precipitate was partly dissolved and partly suspended in 1 ml. of *M* H_3PO_4 by stirring with a glass rod. The mixture was transferred to a 15-ml. centrifuge tube. A further 1-ml. portion of *M* H_3PO_4 was used to dissolve up the remaining precipitate adhering to the large tube, and this was also transferred to the 15-ml. centrifuge tube. Complete solution of the precipitate was achieved by shaking this tube. The aluminium was precipitated as the phosphate by the addition of 1 ml. of *M* sodium acetate, giving a final *p*H of 4.5 to 5.5. The precipitate was separated by centrifugation. The supernatant was transferred to another tube calibrated at 10 ml. The aluminium phosphate precipitate was washed with 1 ml. of water by stirring with a glass rod and again centrifuged. The second supernatant was also transferred to the calibrated tube.

Colour Reaction.—To the solution in the calibrated tube there was added 0.5 ml. of ethylene diamine (redistilled under reduced pressure). The solution was adjusted to *p*H 11, using alizarin yellow G as an external indicator (no adjustment was usually necessary), and made up to 10 ml. with water. The precipitate of hydroxides that formed on addition of ethylene diamine did not interfere with the colour reaction. Gaseous oxygen was bubbled through the solution for about three minutes. The solution was heated on a waterbath at 50° C. for one and a half hours and centrifuged. The extinction was determined on a "unicam" spectrophotometer at 405 mμ in a 1-cm. glass cell.

Alternative Colour Reaction.—An alternative colour reaction involves the formation of a purple complex between reduced noradrenaline (or adrenaline), ferric ion, and ethylene diamine in alkaline solution. The colour forms at a reaction above *p*H 7.5. At this *p*H it is stable for at least one hour, but its stability diminishes with increasing *p*H.

To the solution obtained after precipitation of aluminium phosphate (and including the washings) was added 1 ml. of saturated potassium oxalate. The precipitate (of calcium oxalate) was centrifuged off and the supernatant was transferred to a calibrated tube. Now 0.1 ml. of conc. H_2SO_4 followed by 0.1 ml. of 5 mM ferric alum were added and mixed; 0.5 ml. of ethylene diamine was added and mixed, and the optical density was read at 550 mμ after 10 minutes. The millimolar extinction coefficient of the purple complex was 2.

Results

Recovery of Noradrenaline Added to Normal Urine.—To 100 ml. of normal urine was added 100 μg. of noradrenaline. The urine was adjusted to *p*H 6.5 and subjected to the extraction procedure. A second aliquot of the normal urine to which no noradrenaline had been added was extracted as a control. A third aliquot was also extracted and 100 μg. of noradrenaline added to the final extract: this solution served as the standard. The mean recovery in 14 experiments was 58% (S.D. 9.7%).

Normal Subjects.—Extracts of 100-ml. samples of urine from normal subjects gave extinctions of up to 0.15. If a recovery of 58% is assumed, an extinction of 0.15 corresponds to about 50 μg. of noradrenaline. Assay of such an extract on a spinal cat showed no pressor effect (less than 5 μg. of noradrenaline).

Diagnosis of Phaeochromocytoma.—We have examined 100-ml. samples from the 24-hour collections of 29 patients who were suspected of suffering from phaeochromocytoma. In 26 cases the extinction was less than 0.15; the mean extinction was 0.086 (S.D. 0.020). In three cases the extinction was greater than 0.15.

Case 1 gave an extinction of 0.29; a duplicate estimation gave 0.33. A duplicate extract was assayed on a spinal cat, but the extract had no pressor effect (less than 5 μg. of noradrenaline).

Case 2 gave an extinction of 0.47. Biological assay showed that the extract contained 50 μg. of noradrenaline. Taking account of the recovery, and of the volume of the urine, we found the excretion was 2,000 μg. of noradrenaline per 24 hours. At operation a right adrenal tumour was removed, but the patient did not obtain a remission of his symptoms. A further sample of urine (after operation) gave an extinction of 0.65; biological assay showed the presence of 70 μg. of noradrenaline. Subsequently a left adrenal tumour was removed.

Case 3 gave an extinction of 1.35. Biological assay showed 150 μg. of noradrenaline; this corresponded to an excretion of 4,000 μg. of noradrenaline per 24 hours. A phaeochromocytoma was found at operation.

The alternative colour reaction was also performed on Cases 2 and 3. The extinctions were 0.07 and 0.19 respectively (corrected for reagent blank), corresponding to 125 μg. and 350 μg. of noradrenaline per 100 ml. urine.

The results are shown in the Table.

Results in Three Cases

Method of Estimation of Extract	Recovery of 100 μg. Noradrenaline from 100 ml. Normal Urine	Abnormal Urine. μg. Noradrenaline per 100 ml. Urine			
		Case 1	Case 2		Case 3
Biological assay ..	50%	Nil	100	140	300
Colour reaction 405 mμ ..	58%	43	100	160	400
Alternative colour reaction 550 mμ ..	55%	—	125	—	350

Discussion

Recovery.—Examination of the stages of the extraction procedure indicated that about 15% of added noradrenaline was lost on the amberlite column, that there was no appreciable loss as a result of the use of aluminium hydroxide, and that there was a loss of 20 to 30% on the precipitation of aluminium phosphate. Both these losses can be reduced: in the first case by increasing the volume of sulphuric acid used to elute from the amberlite resin; and in the second case by repeated washing of the aluminium phosphate precipitate with sodium acetate buffer of *p*H 5. However, these procedures result in dilution of the extract.

Specificity.—The extraction procedure favours cations, whereas the colour reactions take place with catechols. Catecholamines possess both of these properties. Consequently the reaction is also given by "corbasil," isoprenaline, and "epinine," substances which are used medicinally and excreted in the urine in sufficient quantity unchanged. The false-positive result obtained in Case 1 was due to the administration of "neo-epinine."

Normal Values.—The values given by normal urine are thought to be due to the presence of biologically inactive catecholamines (von Euler *et al.*, 1955). Accordingly we prefer to express our results in terms of the extinction itself rather than by conversion into a quantity of noradrenaline which would give the same extinction. We have taken the value of 0.15 as the upper limit of normal.

Alternative Colour Reaction.—The alternative colour reaction with ferric ion has two advantages; it is less sensitive to *p*H and the colour develops rapidly at room temperature. However, the extinction coefficient is only one-fifth of that obtained by the first method. We have occasionally observed the formation of a precipitate on adding the ethylene diamine, which did not dissolve in excess of the reagent and which depressed the development of the purple colour.

Summary and Conclusion

A colorimetric method is described for the diagnosis of phaeochromocytoma.

Two cases of phaeochromocytoma have been diagnosed by this method, and the results were confirmed by biological assay.

In our opinion the chemical method can be relied upon to exclude the diagnosis of phaeochromocytoma. On the other hand, when a positive result is obtained we think it should be confirmed by biological assay.

We wish to acknowledge the help and encouragement given by Mr. J. R. P. O'Brien; we are indebted to Mr. H. W. Ling, of the department of pharmacology, for the biological assays.

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The committee for Commonwealth University Interchange has published a report on its work over the last eight years. Its object has been to facilitate the movement of university teachers and graduates within the Commonwealth. Eighty-five universities and university institutions in the United Kingdom, Canada, Australia, New Zealand, South Africa, India, Pakistan, Malta, Ceylon, Hong Kong, Malaya, Singapore, the Gold Coast, Nigeria, East Africa, and the West Indies participated in the scheme, and a total of 389 visits were arranged. The members of the university staffs whose visits have been assisted have ranged from vice-chancellors and scholars of international repute to young postgraduate workers at the outset of their academic career. About 6% of the visitors were medical or working in allied fields of science. The scheme is administered in co-operation with the British Council and financed by grants from the Commonwealth Relations Office, the Colonial Office, and the committee of Australian Vice-Chancellors. The chairman of the committee is Sir CHARLES MORRIS, Vice-Chancellor of the University of Leeds. The report may be obtained from the British Council, 65, Davies Street, London, W.1.

INTRACRANIAL HAEMATOMA CONCEALED BY LEAKAGE OF CEREBROSPINAL FLUID*

BY

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Persistent leakage of cerebrospinal fluid from the nose or ears, resulting from fractures involving the nasal air sinuses or middle ear, may greatly alter the classical clinical picture of acute intracranial haematoma and may confuse the diagnosis. The usual clinical picture of acute intracranial haematoma consists essentially of a head injury, in most cases associated with immediate loss of consciousness and followed by a lucid interval or lightening of consciousness. Later, deterioration of the state of consciousness occurs, and this is often accompanied by dilatation and inactivity of the pupil on the side of the clot and weakness of the limbs on the opposite side. In such cases it is unusual for the lucid interval to last for more than a few hours, although cases have been described in which this interval has been prolonged.

King and Chambers (1952) recorded eight cases of extradural haematoma in which operation was not required until 24 hours to 11 days after the injury. They thought that the bleeding was probably venous in origin in four cases. All their patients recovered, and they made the point that the prognosis was better when pressure symptoms were slow in developing, as compression of the brain was less rapid. None of their cases had any associated leakage of cerebrospinal fluid from the nose or the ears. Jackson and Speakman (1950) described a case of extradural haematoma which came to operation on the thirty-sixth day after the injury. In the meantime, before the case reached them and before the presence of the haematoma was determined, there had been intermittent severe headache, which had been relieved by repeated lumbar puncture and drainage of cerebrospinal fluid. They did not, of course, advocate such a dangerous procedure.

Persistent leakage of cerebrospinal fluid from the nose or ears will tend to lower intracranial tension so that the formation of intracranial blood clots may be facilitated. A large haematoma may form in this way, but while the leakage of cerebrospinal fluid continues the intracranial tension may remain within normal limits. The brain, although displaced, may not be compressed, so that its function may remain unimpaired. A large intracranial blood clot may thereby show no evidence of its presence on clinical examination. Johnson and Dutt (1947), in a paper discussing treatment of wounds involving the dura overlying the air sinuses, mention the case of a Gurkha soldier who sustained a gun-shot wound involving the right mastoid temporal region and who, when operated upon five days after the injury for dural repair to stop the leakage of cerebrospinal fluid, was discovered to have a large intracerebral haematoma which had apparently been unsuspected.

*Based upon a paper read at a combined meeting of the Association of British Neurologists and the Society of British Neurological Surgeons, 1953.