All these three cases recovered full function of the limb involved within a maximum of four sessions. In two cases the same or similar symptoms returned soon afterwards, but these were handled successfully in an identical manner during one session. No patient was seen for more than 10 interviews. Follow-up of these patients at 21, 12, and 9 months respectively found them all well adjusted and asymptomatic.

Discussion

Failure to make an early and correct diagnosis of hysterical contracture inevitably raises the problem of irreversible secondary change in the affected limbs. Traditional psychotherapeutic management, which for the most part ignores the symptom, may in this instance be a luxury the physician cannot afford.

The claim of psychoanalysts that symptom removal cannot hope to effect a "cure" except in very recent cases is repudiated by Wolpe (1961), who has advocated that the concepts of motivation and gain be replaced by a theory of the neuroses based on the principles of learning. Without denying that psychological distress may be instrumental in initiating the symptom in these cases, one is still able to offer an alternative explanation for their subsequent potentiation and prolongation.

Startling, bizarre, and incomprehensible symptoms may produce considerable anxiety in a physician who is puzzled over their aetiology. Should this be communicated to a patient, particularly a child, already in psychological distress, puzzled and frightened by the evidence of disordered function which her own body displays, there will be a reinforcement of the mode of behaviour, and the pattern for a prolonged and intractable illness is set. Viewed in this light, hysterical contracture can clearly be an example of "maladaptive learned behaviour" (Wolpe, 1958). Repeated investigations and emphasis on symptoms in any situation, but particularly a structural interpretation, as is most often the case, will serve time and again to reinforce the neurotic behaviour.

The three patients who were treated by reassurance and re-education all had associated psychiatric problems and all

required careful handling. These cases were, however, amenable to straightforward psychotherapy or environmental manipulation which could have been given by any psychiatrically sophisticated physician.

The practice of leaving the symptom to sort itself out is, in the case of hysterical contracture, fraught with the extra dangers raised by the possibility of irreversible secondary changes. While such a danger exists, and until early diagnosis can be assured, a more energetic approach to the handling of conversion symptoms of this order must be advocated.

Summary

Six cases of hysterical contracture in children are described. The need for early recognition and rapid institution of appropriate therapy is outlined, and a method of treatment based on early removal of symptoms is advocated.

Thanks are due to Dr. J. J. Fleminger, physician in psychological medicine, Guy's Hospital, for his encouragement at the initiation of this project; and to Dr. G. F. Vaughan, physician in child psychiatry, Guy's Hospital, for his advice in the preparation of the paper and for permission to include the case material. This article was prepared while I was in receipt of a grant from the Bloomfield Charitable Trust.

REFERENCES

- Babinski, J., and Froment, J. (1918). In *Hysteria or Pithiatism*, edited by E. Farquhar Buzzard, London.
 Briquet, P. (1859). *Traité clinique et thérapeutique de l'hystérie*. Baillière, Paris.
 Brodie, Sir Benjamin (1837). *Lectures Illustrative of Certain Local Nervous Affections*. London.
 Charcot, J. M. (1890). *Cliniques des Maladies du Système Nerveux*, 1, 96. Paris.
 Finesinger, J. E. (1948). *Amer. J. Psychiat.*, **105**, 187.
 Fraser, A. C. (1919). *Med. J. Aust.*, **2**, 436.
 Hurst, Sir Arthur F. (1918). *Brit. J. Surg.*, **6**, 579.
 — (1941). *Clin. J.*, **70**, 29.
 Macalpine, I., and Ross, Sir James Paterson (1956). *Lancet*, **1**, 78.
 Steindler, A. (1935). *Int. Clin.*, **4**, 221.
 Wolpe, J. (1958). *Psychotherapy by Reciprocal Inhibition*. Stanford Univ. Press, Stanford, California.
 — (1961). *Amer. J. Psychiat.*, **118**, 35.

Effects of Arterial and Venous Pressure Changes on the Electroencephalogram During Cardiac Operations

ANN HARDEN,* B.Sc.

Brit. med. J., 1965, **1**, 23-27

The value of the electroencephalogram (E.E.G.) as a sensitive indicator of changes in cerebral function during cardiac operations has been recognized (Arfel *et al.*, 1961; Storm van Leeuwen *et al.*, 1961; Thies-Puppel and Wiemers, 1961). It is known that a fall in blood-pressure during operations on the heart and main vessels may result in an inadequate blood supply to the brain; this is immediately followed by E.E.G. changes when the circulatory alteration is of sufficient duration and severity. The superior vena caval pressure has also been studied during cardiac surgery. Obstruction of venous outflow from the brain by clamping the superior vena cava was shown by Pampiglione and Waterston (1958) often to be followed within 20 to 30 seconds by increasing slow activity in the E.E.G.

Other workers (Brechtner *et al.*, 1959; Kavan and Brechtner, 1961) have also said that the level of superior vena caval pressure had an important effect on the electrical activity of the brain during open-heart surgery. It is possible that venous congestion of the brain may be followed by E.E.G. changes whenever the increased venous pressure prevents an adequate supply of arterial blood to the brain (Pampiglione and Waterston, 1961). It has also been suggested that in conditions such as congestive heart failure, in which there is an increase in systemic venous pressure, there is a reduction in cerebral blood flow (Kety, 1950), though no measurements have been reported.

In experiments on dogs, Duffy and Caliva (1961) have shown that an increase in venous pressure is accompanied by a decrease in oxygen availability to the cerebral tissues, probably as a result

* Department of Electroencephalography and Clinical Neurophysiology, the Hospital for Sick Children, Great Ormond Street, London.

of decreased blood flow. Hitherto other workers (Moyer *et al.*, 1954) had found that cerebral blood flow in man was not affected by increasing the jugular pressure, though the venous pressure may not have been significantly elevated in their experiments. Arfel *et al.* (1961) have attached importance to simultaneous variations of arterial and venous pressures in assessing the haemodynamics of patients during open-heart surgery; they suggest that if the venous pressure is increased while the arterial pressure falls there may be circulatory standstill in the brain, although they report no measurements. The effect on the E.E.G. of changes in arterial and venous pressure in animals, especially dogs, is not strictly comparable to that found with human studies because of anatomical differences, particularly in venous drainage.

It has become the practice in this hospital to record continuously the E.E.G. as well as the electrocardiogram from each patient during open-heart surgery. Over the last two years the mean arterial pressure and the pressures of both superior and inferior vena cava have also been continuously recorded. Arterial and superior vena caval pressures were simultaneously measured during these operations, and the purpose of this study has been to correlate the occurrence of E.E.G. changes with mean arterial and venous pressures.

Material and Methods

Fifty-two children aged between 1 and 14 years had E.E.G. studies during open-heart surgery requiring cardiopulmonary by-pass. Silver disk electrodes were placed in standard positions on the scalp with collodion (Pampiglione, 1956). An E.E.G. was recorded the evening before the operation. After premedication on the morning of operation anaesthesia was induced with either intravenous sodium thiopentone or in some cases with cyclopropane and oxygen. In all cases anaesthesia was maintained at a very light plane by endotracheal administration of nitrous oxide and oxygen, and small doses of curare were given intravenously. The E.E.G. (seven channels) was recorded throughout the operation on an Offner type T apparatus with a time constant of 0.3 second. On the eighth channel an electrocardiogram was recorded from electrodes placed over the right and left deltoid regions as a modified Lead I. On another polygraph the arterial pressure was continuously recorded through a catheter inserted via the radial, internal mammary, or femoral artery. The venous pressures were recorded from the superior vena cava (by a catheter advanced from the median cubital vein to the superior vena cava) and from the inferior vena cava (via the saphenous and femoral veins).

During the initial period of the operation, before the beginning of perfusion from the pump-oxygenator, the temperature of the patient was near normal, and the level of anaesthesia and the blood pH and PCO_2 were maintained fairly constant by the anaesthetist. It was only during this pre-bypass period that the arterial and venous pressure changes were correlated with the E.E.G. features in the present study, as too many unknown factors were likely to complicate the interpretation of the results once the patient was on cardiopulmonary bypass.

The E.E.G. was recorded continuously and the occasional alterations in mean venous and arterial pressure levels were written on the tracing. Because this study was concerned with cerebral activity, the inferior vena caval pressures were of limited interest and

only superior vena caval (S.V.C.) pressures have been studied. In selecting suitable material for this study the following criteria were fulfilled: (1) the background E.E.G. activity was relatively stable; (2) values of synchronously recorded arterial pressure and venous pressure were known; and (3) the transitory pressure changes were of rapid onset, of more than 5 seconds in duration and greater than 5 mm. Hg (except

FIG. 1.—Degree of E.E.G. changes plotted against the A-V difference (mean arterial pressure minus mean superior vena caval pressure) at periods during operative procedures when there had been a fall in mean arterial pressure and/or a rise in superior vena caval pressure.

FIG. 2.—Case 1. (a) No change in the E.E.G. features (grade 0) when arterial pressure 70 mm. Hg and S.V.C. pressure raised to 30 mm. Hg. (b) No change in the E.E.G. features (grade 0) when arterial pressure decreased to 50 mm. Hg and S.V.C. pressure to 15 mm. Hg. (c) Minor change in E.E.G. features (grade I) when arterial pressure 50 mm. Hg and S.V.C. pressure increased to 30 mm. Hg. (d) E.E.G. returned to previous pattern when arterial pressure increased to 80 mm. Hg and S.V.C. pressure decreased to 17 mm. Hg.

for arterial pressure values above 70 mm. Hg, when only a fall greater than 20 mm. Hg was considered significant).

The E.E.G. features during the periods of fluctuation in arterial and/or venous pressure were classified into four grades:

Grade O: no change in the background pattern.

Grade I: minor change, with diminution of fast activities and some increase in amplitude and amount of 4–7 c/s intermediate slow activity.

Grade II: marked change, showing disappearance of fast components and appearance of high-amplitude slow activity (1–6 c/s).

Grade III: gross change, with marked increase in amplitude of very slow activity (less than 1/sec.) whether or not followed by flattening of the traces.

The surgical techniques which sometimes produced fluctuations in arterial and/or venous pressure in the preliminary prebypass phase of the operation were: (a) dissection around the great veins and the passing of snares under the superior vena cava and inferior vena cava; (b) insertion of caval drainage-tubes through the right atrium; (c) the draining of blood from the patient just before beginning the cardiac bypass, with simultaneous transfusion from the pump-oxygenator; and (d) unexpected circumstances. In all cases the pressure changes were transitory and the E.E.G. changes reversible.

Results

In these 52 children relevant fluctuations in pressure occurred 75 times (in 33 children). In general a fall in arterial pressure beyond a critical level (which appeared to vary from one individual to another) produced changes of a varying degree in the E.E.G. However, the changes in the E.E.G. which occurred with a fall in arterial pressure were partly related to the level of the S.V.C. pressure recorded at the same time. When the S.V.C. pressure was moderately high, the E.E.G. changes occurred more readily for an equivalent fall in arterial pressure than when the venous pressure was at a low level. Moreover, when the arterial pressure was at a steady, moderately low level—though not producing E.E.G. changes—a small rise in S.V.C. pressure was often followed by alterations in the E.E.G. pattern.

A value for the arterial-venous (A-V) difference could be expressed by subtracting the value of the S.V.C. pressure from that of the mean arterial pressure. E.E.G. changes were more closely related to the A-V difference than to the arterial or S.V.C. pressures alone. In Fig. 1 the E.E.G. changes have been plotted against the A-V difference and an increase in slow activity in the E.E.G. was found to be associated with a decreasing A-V difference. There were never changes in the E.E.G. when the A-V difference was above 45 mm. Hg. When the difference was between 20 and 30 mm. Hg some E.E.G. changes occurred. With an A-V difference of less than 20 mm. Hg marked or gross E.E.G. changes were always seen.

The interdependence of arterial and S.V.C. pressures in determining E.E.G. changes may be illustrated by the following examples.

Case 1

The patient was a 7-year-old boy with pulmonary stenosis. The E.E.G. trace (Fig. 2) showed persistent fast activity and no change (grade O) when the arterial pressure was 70 mm.

Hg and the S.V.C. pressure was simultaneously raised to 30 mm. Hg (while placing a snare under the superior vena cava). At a later stage, when cannulae were placed in the right atrium, the arterial pressure fell to 50 mm. Hg while the S.V.C. pressure was 15 mm. Hg; yet there was no change in the E.E.G. features (grade O). However, on another occasion, when the arterial pressure fell to 50 mm. Hg for a short time and the S.V.C. pressure rose to 30 mm. Hg, there was a definite though minor E.E.G. change with a diminution in the fast activity and some increase in 6 c/s activity (grade I). The E.E.G. returned to the previous pattern when the arterial pressure and the S.V.C. pressure were restored to more normal values. When the S.V.C. pressure was not raised, a fall in the arterial pressure to 50 mm. Hg did not cause E.E.G. changes. When the arterial pressure was moderately high a considerable rise in the S.V.C. pressure also failed to alter the E.E.G. features. Only when the A-V difference was lowered were changes produced in the E.E.G. which were rapidly reversed when the pressures improved.

Case 2

The patient was an 8-year-old girl with a ventricular septal defect. The E.E.G. (Fig. 3) showed generalized fast rhythms together with some 4 to 7 c/s components and did not change when the arterial pressure was 50 mm. Hg while the S.V.C. pressure was 13 mm. Hg (grade O). However, when the arterial pressure fell to 40 mm. Hg after blood loss while cannulating the right atrium marked slowing of the E.E.G. occurred (grade II), although there had been no increase in S.V.C. pressure. Later in the operation when the arterial pressure fell from 75 to 50 mm. Hg and at the same time the S.V.C. pressure rose from 20 to 30 mm. Hg, the E.E.G. again changed from predominantly fast rhythms to an increasing amount of slow activity progressing to very gross changes (grade III). The importance of the A-V difference rather than the actual value of the arterial pressure is shown in this patient. When the arterial pressure fell to 40 mm. Hg the A-V difference

FIG. 3.—Case 2. (a) No change in E.E.G. features (grade O) when arterial pressure fell to 50 mm. Hg and S.V.C. pressure 13 mm. Hg. (b) Marked change in E.E.G. features (grade II) when arterial pressure fell to 40 mm. Hg and S.V.C. pressure 13 mm. Hg. (c) No change in E.E.G. features (grade O) when arterial pressure 75 mm. Hg and S.V.C. pressure 20 mm. Hg. (d) Marked change (grade II) in E.E.G. features when arterial pressure fell to 50 mm. Hg and S.V.C. pressure increased to 30 mm. Hg. (e) Gross change (grade III) in E.E.G. following (d).

was 27 mm. Hg, but later the A-V difference was only 20 mm. Hg, the arterial pressure having fallen to 50 mm. Hg while the S.V.C. pressure had increased to 30 mm. Hg.

Case 3

This patient was a 6-year-old boy with a ventricular septal defect. The E.E.G. (Fig. 4) showed predominantly fast rhythms when the arterial pressure was 65 mm. Hg and the S.V.C. pressure was 10 mm. Hg. While placing a snare under the superior vena cava there was a marked fall in arterial pressure to 40 mm. Hg and a marked rise in S.V.C. pressure to 35 mm. Hg, and high-amplitude very slow waves appeared in the E.E.G. (grade III). There was a very rapid recovery after this manipulation when the arterial pressure rose to 55 mm. Hg and the S.V.C. pressure decreased to 20 mm. Hg. Later, while adjusting the cannula in the heart, the arterial pressure fell to 50 mm. Hg with an S.V.C. pressure of 20 mm. Hg, but there was only a minor change in the E.E.G. with higher amplitude 4 to 7 c/s activity appearing (grade I). Just a small rise in arterial pressure to 55 mm. Hg was enough to restore normal electrical activity, although the S.V.C. pressure remained at 20 mm. Hg for a few more seconds. The delicate balance between the arterial and S.V.C. pressures within a narrow range is seen in this patient. In fact, when the arterial pressure dropped again to 50 mm. Hg there was no slowing in the E.E.G., as by this time the S.V.C. pressure was 15 mm. Hg.

Discussion

Although no measurements of cerebral blood flow have been possible in these patients, changes in the E.E.G. patterns have been regarded as indicating some impairment of cerebral function resulting from an inadequate blood supply to the brain. The children in this study were anaesthetized and lying flat. The haemodynamic disturbances which were followed by E.E.G. changes were presumably too sudden or too severe for the homeostatic mechanisms regulating cerebrovascular resistance and cardiac output to compensate for them.

The pressure difference between the cerebral arteries and veins is the driving force of the cerebral circulation. Since under normal circumstances the venous pressure is only a few mm. Hg above atmospheric pressure, the mean arterial pressure at head level usually adequately represents cerebral perfusion pressure. However, under the special conditions of these observations the gradient between the cerebral arteries and veins was reduced not only by a fall in the arterial pressure but also on occasions by an increase in the venous pressure. It appears that the difference in A-V pressure measured in these patients represents more closely the effective cerebral perfusion pressure than the arterial pressure alone.

Cerebral perfusion pressure may decrease without apparent alterations in cerebral function until the A-V pressure difference reaches a critical level. At this critical level the blood supply to the brain is reduced just enough for cerebral function to be impaired and minor E.E.G. changes follow (grade I). Any further decrease in A-V pressure difference progressively impairs cerebral function, with increasingly marked E.E.G. changes (grade II-III). The critical value of the A-V difference as measured by the occurrence of minor E.E.G. changes seems to differ from one patient to another, as can be seen by comparing Case 1 with Case 3.

The A-V pressure difference was reduced to 20 mm. Hg in Case 1 before E.E.G. changes occurred, but in Case 3 a difference of 30 mm. Hg was sufficient to produce E.E.G. changes. Fig. 1 demonstrates that minor E.E.G. changes, reflecting critical A-V differences in all the material studied, occurred at values varying from 20 to 45 mm. Hg. This individual range is probably complicated by the fact that all these children suffered from congenital heart defects with somewhat abnormal haemodynamic states. The total duration of each episode of pressure change as well as the abruptness of onset were other variable factors in this study. All the pressure changes that occurred were incidental to various operative procedures and no attempt was made to change experimentally the levels of arterial and venous pressure.

Summary

Mean arterial and/or superior vena caval pressures have been studied in relation to E.E.G. features in 52 children undergoing open-heart surgery. Relevant fluctuations in pressure occurred 75 times in 33 of these patients. E.E.G. changes, presumably related to the cerebral blood supply becoming inadequate, were seen 36 times, in all cases being reversible.

An arterial-venous difference, probably representing the effective perfusion pressure, was calculated by subtracting the mean superior vena caval pressure from the mean arterial pressure. Changes in pressure difference were more closely related to the appearance of particular E.E.G. features than either a fall in arterial pressure or a rise in venous pressure alone.

When this arterial-venous pressure was greater than 45 mm. Hg E.E.G. changes were not seen. Minor E.E.G. changes occurred when the arterial-venous difference reached a critical value. This showed considerable variation from one patient

FIG. 4.—Case 3. (a) E.E.G. pattern when arterial pressure 65 mm. Hg and S.V.C. pressure 10 mm. Hg. (b) Gross change (grade III) in E.E.G. when arterial pressure fell to 40 mm. Hg and S.V.C. pressure increased to 35 mm. Hg. (c) Return of previous pattern when arterial pressure increased to 55 mm. Hg and S.V.C. pressure fell to 20 mm. Hg. (d) Minor change (grade I) when arterial pressure 50 mm. Hg and S.V.C. pressure 20 mm. Hg. (e) Return of previous pattern when arterial pressure 55 mm. Hg and S.V.C. pressure 20 mm. Hg. (f) No change in the E.E.G. (grade 0) when arterial pressure fell to 50 mm. Hg and S.V.C. pressure fell to 15 mm. Hg.

to another, but was between 20 and 45 mm. Hg in the children studied.

This work was supported by a grant from the Joint Research Board of the Hospital for Sick Children. I am grateful to Mr. D. J. Waterston, Mr. E. Aberdeen, Dr. G. R. Graham, Dr. M. Hawksley, Dr. W. J. Glover, and Dr. R. W. Cope, whose interest and co-operation in the operating-theatre have made this work possible. I am especially grateful to Dr. G. Pampiglione for his invaluable help and encouragement.

REFERENCES

Arfel, G., Weiss, J., and Du Bouchet, N. (1961). *Cerebral Anoxia and the Electroencephalogram*, edited by H. Gastaut and J. S. Meyer, Chapt. 24. Thomas, Springfield, Ill.

Brechner, V. L., Kavan, E. M., and Dillon, J. B. (1959). *J. thorac. Surg.*, **37**, 352.
Duffy, P. E., and Caliva, F. S. (1961). *Neurology (Minneap.)*, **11**, 742.
Kavan, E. M., and Brechner, V. L. (1961). *Anesth. Analg. Curr. Res.*, **40**, 418.
Kety, S. S. (1950). *Amer. J. Med.*, **8**, 205.
Moyer, J. H., Miller, S. I., and Snyder, H. (1954). *J. appl. Physiol.*, **7**, 245.
Pampiglione, G. (1956). *Proc. Electrophysiol. Technol. Ass.*, **7**, 80.
— and Waterston, D. J. (1958). *Electroenceph. Clin. Neurophysiol.*, **10**, 354.
— (1961). *Cerebral Anoxia and the Electroencephalogram*, edited by H. Gastaut and J. S. Meyer, Chapt. 25. Thomas, Springfield, Ill.
Storm van Leeuwen, W., Mechelse, K., Kok, L., and Zierfuss, E. (1961). *Ibid.*, Chapt. 27.
Thies-Puppel, H., and Wiemers, K. (1961). *Ibid.*, Chapt. 28.

Cushing's Syndrome Associated with Carcinoma of the Bronchus in a Patient with Normal Plasma Electrolytes

M. FRIEDMAN,* M.B., B.CH., M.R.C.P.ED.; J. R. MIKHAIL,† M.R.C.S., L.R.C.P.;
K. D. BHOOLA,‡ M.B., B.CH., B.A.O., PH.D.

Brit. med. J., 1965, **1**, 27–29

The original description of the association between bronchogenic carcinoma and Cushing's syndrome was given by Brown (1928). Since Thorne (1952) reported two cases, 24 additional reports of similar cases have appeared in the literature, which is reviewed by Allott and Skelton (1960). In most cases the clinical features of Cushing's syndrome have been absent. Hypokalaemic alkalosis was found in all cases with the notable exceptions of the single cases reported by Rosenthal (1957), MacPhee (1959), and Billingham *et al.* (1961). Weakness or paralysis due to low potassium has often been the presenting and predominant symptom of the disease.

This report concerns a patient who presented with an oat-cell carcinoma of the bronchus and who was found to have biochemical evidence of Cushing's syndrome, the diagnosis subsequently being confirmed at necropsy. However, throughout the period of observation no abnormality in her plasma electrolytes was observed.

Many investigators have used the plasma potassium and bicarbonate as a screening procedure for Cushing's syndrome in patients with carcinoma of the bronchus. Reliance on this alone is bound to lead to cases being missed, and hence the recognition that the disease can occur in the presence of normal plasma electrolytes is of some practical importance.

Case Report

A 59-year-old woman was seen at the Willesden Chest Clinic in June 1963, having been referred after a routine mass chest x-ray examination at her place of work. She gave a history of a cough, wheezing, and dyspnoea on exertion of three to four months' duration. One month before being seen she had a small haemoptysis followed by slight blood-staining of her sputum for a few days. She had smoked 10–20 cigarettes a day for the past 20 years. On examination she had signs of collapse in the right lower zone of the chest. There was no clubbing. No glands, liver, or spleen were palpable. B.P. was 160/90. X-ray examination showed an opacity in the hilar region of the right lung. Sputum cytology

revealed no carcinoma cells. Bronchoscopy demonstrated a tumour of the right-lower-lobe bronchus, which was proved histologically to be an invasive oat-cell carcinoma. Early in July 1963 an exploratory thoracotomy (Mr. J. Jackson) revealed a globular neoplastic mass invading the apical and posterior segments of the right middle and upper lobe. The carinal and peribronchial glands were greatly enlarged. Infiltration of the oesophagus was present. The neoplasm was thought to be inoperable. The patient was discharged home after an uneventful post-operative recovery. She was not given radiotherapy because of the known danger of temporary enlargement of mediastinal glands due to oedema, giving rise to tracheal compression.

At the beginning of September she was readmitted to hospital. She complained of chest pain, dyspnoea, wheezing, a productive cough, and anorexia. On examination at this time she was in poor condition. There were signs of collapse at the right base. Both the supraclavicular and cervical glands were enlarged. The liver was palpable 5 cm. below the costal margin. B.P. was 98/60. There was no pigmentation, no signs of Cushing's syndrome, and no muscular weakness.

Investigations.—Haemoglobin 13.5 g./100 ml.; E.S.R. 55 mm. in one hour; W.B.C. 10,400/c.mm. Total protein 6.5 g./100 ml. Thymol turbidity 1.2 units. Alkaline phosphatase 16 K.A. units; sodium 133 mEq/l.; potassium 4.5 mEq/l.; chloride 92 mEq/l.; bicarbonate 27.4 mEq/l.; blood urea 26 mg./100 ml.; serum calcium 8.9 mg./100 ml.; plasma phosphorus 2.7 mg./100 ml.; fasting blood glucose 96 mg./100 ml.; blood glucose two hours after a meal 98 mg./100 ml. Absolute eosinophil count 8/c.mm.

Adrenal Function.—Because of the patient's low blood-pressure and lethargic state the plasma cortisol was measured, as a hypoadrenal state due to destruction of the adrenal glands by secondary carcinomatous deposits was suspected. This was performed by one of us (M. F.) by the method described by Mattingly (1962). Much to our surprise this revealed a level of 37.1 µg./100 ml. (normal at 9 a.m. 8–26 µg./100 ml.). Furthermore, there was a loss of the normal diurnal rhythm of plasma cortisol with a mid-night level of 21 µg./100 ml. (normal less than 6 µg./100 ml.). The 24-hour total urinary 17-hydroxycorticosteroids (17-OHCS) were 34 mg./24 hours. An A.C.T.H. stimulation test was performed, using known biologically active gel at a dosage of 40 units 12-hourly intramuscularly. This produced a rise in the total 17-OHCS to 165 mg. on the second day and to 215 mg. on the third day of the test. There was also an abnormally large rise in the plasma cortisol to 83 µg./100 ml. on the first day, 178 µg./

* Medical Unit, University College Hospital, London.

† Willesden Chest Clinic, London.

‡ Central Middlesex Hospital, London.