findings in the parents of two Norwegian cases of Refsum's syndrome (Eldjarn, personal communication, 1966).

The remarkable variability of the clinical course of Refsum's syndrome is now well known. Of Refsum's original cases, one presented after an acute febrile illness, and one apparently began as a sequel to the physical exertion of fishing near the Lofoten Islands. In both cases the worsening immediately after a febrile episode had led to their first hospital admission. Another of Refsum's cases relapsed regularly in the spring-time; in the light of our present knowledge it is tempting to speculate that this might have been associated with seasonal dietary variations. A member of one of Refsum's original families has recently been reported to have improved after long-term mental hospital admission, possibly again associated with low vegetable intake (Eldjarn *et al.*, 1966). Following preliminary reports on the value of a diet low in phytanic acid (Eldjarn *et al.*, 1966) in the condition, this diet was given to our Case 1, but without improvement. Because of the patient's intolerance the diet was relaxed, and on moderate restriction he was at the time of writing showing steady improvement.

A fluctuation in C.S.F. protein was evident in our cases, and reference to Fig. 3 might suggest that there was a relation between the activity of the disease and the C.S.F. protein in Case 1 over the nine-year period of study. The C.S.F. protein in Case 2 has dropped from 400 mg./100 ml. in 1958 to 83 mg./100 ml. in 1966. Since 1964, a year after her hysterectomy, she has improved markedly and steadily. This is of interest as it might indicate that an alteration in hormone balance after hysterectomy may have favourably influenced the course of the disease.

The only biochemical abnormality consistently described so far in Refsum's syndrome is that of phytanic acid accumulation. While the C.S.F. phospholipid, lecithin, and globulin increases here recorded may simply reflect this abnormality, abnormalities of copper metabolism in the condition have been reported by several workers (Richterich *et al.*, 1965; Rake and Saunders, 1966). In Case 1 and a sib with optic atrophy (II 6) the caeruloplasmin was raised (see Table). The significance of this finding is at present obscure.

Continued follow-up of patients with Refsum's syndrome, with phytanic acid estimations being compared to clinical state, would seem a fruitful field for study. While alteration in phytanic acid intake may well affect the disease process, there may be physiological factors influencing the metabolic pathways of phytanic acid breakdown which also affect the course of the disease. Such a hypothesis would fit the observations above regarding the effect of intercurrent illness and improvement in a woman after the child-bearing period.

Summary

The results are reported of a clinical and biochemical study of two sibs with Refsum's syndrome who have been studied over a period of nine years. Three generations of the family were investigated, and no significant evidence of biochemical abnormality was found in any of the unaffected members. The serum phytanic acid level was raised in both patients, and high levels of phytanic acid in cerebrospinal fluid were present in one.

Fluctuations in the severity of the condition are compared with C.S.F. protein levels, and possible explanations for this characteristic variation discussed.

REFERENCES

- Alexander, W. S. (1966). *J. Neurol. Neurosurg. Psychiat.*, **29**, 412.
 Carrell, R. W., Scott, P. J., and McLellan, G. H. (1966). *N.Z. med. J.*, **65**, 766.
 Cori, G. T., and Cori, C. F. (1952). *J. biol. Chem.*, **199**, 661.
 Eldjarn, L. (1965). *Scand. J. clin. Lab. Invest.*, **17**, 178.
 — *et al.* (1966). *Lancet*, **1**, 691.
 Gordon, N., and Hudson, R. E. B. (1959). *Brain*, **82**, 41.
 Gubbay, S. S., Walton, J. N., and Pearce, G. W. (1966). *J. Neurol. Neurosurg. Psychiat.*, **29**, 500.
 Kahlke, W. (1964). *Klin. Wschr.*, **42**, 1011.
 — and Richterich, R. (1965). *Amer. J. Med.*, **39**, 237.
 Klenk, E., and Kahlke, W. (1963). *Hoppe-Seyler's Z. physiol. Chem.*, **333**, 133.
 Rake, M., and Saunders, M. (1966). *J. Neurol. Neurosurg. Psychiat.*, **29**, 417.
 Refsum, S. (1946). *Acta psychiat. scand.*, Suppl. No. 38, p. 9.
 Richterich, R., van Mechelen, P., and Rossi, E. (1965). *Amer. J. Med.*, **39**, 230.

Medical Memoranda

Perforated Duodenal Ulcer Presenting as Acute Respiratory Failure

Brit. med. J., 1967, **3**, 779–780

Respiratory failure in patients with chronic bronchitis and emphysema is usually part of a generalized cerebral depression from hypoxia and hypercapnia. It may come on suddenly, however, as a result of bronchial blockage from plugs of inspissated secretions (Simpson, 1962). In the following case a generalized peritonitis induced acute respiratory failure in a severely emphysematous patient.

CASE REPORT

A man aged 48 was admitted to hospital with bronchopneumonia and congestive cardiac failure complicating his long-standing chronic bronchitis and emphysema. His blood gases at the time of this admission were: pH 7.35 units, Pco_2 72.5 mm. Hg, base excess +8 mEq/l., standard bicarbonate 31 mEq/l., and Po_2 79 mm Hg. Chest x-ray examination showed appreciable generalized emphysema with bullous formation affecting both left and right apical zones

together with recent inflammatory shadowing at the left base. After a period of bed rest associated with diuretics, digoxin, and antibiotic therapy, he made a satisfactory recovery but was still considerably disabled by his emphysema. His blood gases on 19 April 1966—that is, the day before his discharge—showed an established ventilatory insufficiency as well as impaired alveolar-arterial gas exchange (see Table).

He was advised to stop smoking, as this was considered the only thing likely to delay progression of his emphysema.

On 6 May at 4.15 p.m. he was readmitted in acute respiratory failure with complete apnoea. Emergency treatment in the casualty department consisted of endotracheal intubation with positive-pressure oxygen respiration, intravenous infusion of 7.5% bicarbonate, and hydrocortisone also administered by the intravenous route. The pH on admission was 7. Treatment was continued in the intensive care unit, where the patient was put on an East-Radcliffe respirator. Two hours later his general condition improved and he regained consciousness. By this time he had received 1 litre of 7.5% bicarbonate and was on tetracycline 100 mg. intramuscularly six-hourly. Investigations produced the following results: P.C.V. 60%; Hb 128%; serum electrolytes—Na 137 mEq/l., K 4.7 mEq/l., Cl 81 mEq/l.; blood urea 83 mg./100 ml. The blood gases at 6.30 p.m. are shown in the Table.

He now complained of severe abdominal pain and was found to have a rigid and silent abdomen. A previous long-standing history

of dyspepsia suggested the diagnosis of a perforated peptic ulcer. This was confirmed by the presence of free gas under the right diaphragm shown on an x-ray film of the abdomen.

At laparotomy a perforated anterior duodenal ulcer was found with established generalized peritonitis. The perforation was closed with three chromic catgut sutures and an omental patch. After toilet of the peritoneal cavity, it was drained by tubes in the right

Table Showing Blood Changes

Date	Time	Treatment	pH	PCO ₂ (mm. Hg)	Base Excess (mEq/l.)	Standard bicarbonate (mEq/l.)	PO ₂ (mm. Hg)
19/4/66			7.33	72.5	+8	31	58
6/5/66	4.15 p.m.		7.0				
6/5/66	6.30 "	E.R. res- pirator. Bicarb. 1 litre	7.42	65.0	+13		300
7/5/66	11 a.m.	O ₂ tent	7.34	80.0	+10.5	33.0	56
8/5/66	12 noon	O ₂ "	7.34	68.5	+6.0	29.0	53
9/5/66	4.00 p.m.	O ₂ "	7.34	72.0	+8.5	31.0	58

subphrenic space and in the pelvis. After a further 14 hours on the respirator he was transferred to an oxygen tent. Tracheostomy was decided against, as he was by this time breathing well and was able to cough satisfactorily.

The Table indicates the blood gases during the immediate post-operative days. The patient showed steady improvement, but on the sixteenth postoperative day had a complete dehiscence of his abdominal wound. This was resutured under general anaesthesia without complications affecting the respiratory system. Ten days later he developed Friedlander's pneumonia and despite all attempts at resuscitation he died on 3 June. Unfortunately a post-mortem examination was refused.

COMMENT

There are two main types of respiratory failure: (1) ventilatory failure in which the PCO₂ is increased, and (2) impaired

alveolar-arterial gas exchange with decreased oxygen saturation but without hypercapnia (Fletcher, 1962). The most severe cases of respiratory failure are usually encountered in patients with advanced emphysema and bronchitis. These patients usually show a composite picture of both underventilation and impaired alveolar-arterial gas exchange.

The above patient had advanced chronic respiratory insufficiency and was relying on his diaphragmatic movements for his tidal exchange. The duodenal perforation with its attendant peritonitis "splinted" his diaphragm and thus precipitated an acute respiratory failure. On 9 May 1966, three days post-operatively, he was breathing spontaneously and his blood gases gave almost identical values to those carried out on 19 April—that is, the accepted normal for him (see Table).

A pronounced increase in arterial PCO₂ causes cerebral vasodilatation and increased intracranial pressure (Comroe *et al.*, 1962). It is possible that hypercapnia might have been a contributory cause towards the perforation of a duodenal ulcer in this case; the CO₂ engendered raised intracranial pressure, stimulating the vagus centre with consequent gastric hyperacidity. Also hypercapnia stimulates release of adrenaline from the adrenal medulla.

We would like to thank Mr. J. Moroney, under whose care this patient was admitted, for permission to treat and publish this case.

A. CUSCHIERI, M.D., F.R.C.S.ED.

K. F. EDWARDSON, M.B., CH.B., B.SC., F.R.C.S.

Broadgreen Hospital,
Liverpool.

REFERENCES

- Comroe, J. H., Forster, R. E., Dubois, A. B., Briscoe, W. A., and Carlsen, E. (1962). *The Lung: Clinical Physiology and Pulmonary Function Tests*, 2nd ed., p. 157. Chicago.
- Fletcher, C. M. (1962). *Proc. roy. Soc. Med.*, **55**, 565.
- Simpson, T. (1962). *Ibid.*, **55**, 569.

Lupus-like Syndrome Induced by Procainamide

Brit. med. J., 1967, **3**, 780-781

Many drugs have been associated with the onset of a syndrome resembling systemic lupus erythematosus. Among the drugs implicated are hydrallazine; sulphonamides; anticonvulsants of the phenytoin group, and troxidone; penicillin; phenylbutazone; tetracycline; streptomycin and isoniazid; griseofulvin; thiouracil derivatives; and procainamide.

Since the first description of a syndrome closely mimicking, if not identical with, systemic lupus erythematosus, and occurring after the administration of procainamide (Ladd, 1962), 13 cases have been reported—12 in patients receiving the drug for cardiac disease (Hahn, 1964; Colman and Sturgill, 1965; Kaplan *et al.*, 1965; Paine, 1965; Carabia and Fortney, 1965) and one in a patient with dystrophia myotonica (Prockop, 1966). All previous reports have appeared in the American literature.

CASE REPORT

A 50-year-old widow attended hospital in May 1965 with symptoms suggestive of angina of effort, and was subsequently found to be hypertensive, with a blood pressure of 260/150 mm. Hg. Investigation showed no cause for this, and a diagnosis of essential hypertension was made. She was initially treated with antihypertensive drugs, but these were withdrawn when she had a myocardial infarction. In September 1965 she developed paroxysmal ventri-

cular tachycardia and was given quinidine sulphate, but because of a drug rash occurring within 24 hours this was replaced by procainamide 500 mg. q.i.d.

In January 1966 she was readmitted to hospital complaining of left-sided pleuritic pain of sudden onset. She had no cough, sputum, or haemoptysis. She had a pleural rub at the left costophrenic angle and signs of a small left-sided pleural effusion. Her pulse was in sinus rhythm and her blood pressure was 160/100 mm. Hg. E.S.R., blood picture, and blood urea were within normal limits. Serum aspartate aminotransferase and serum lactate dehydrogenase were also normal. X-ray examination showed a small pleural effusion at the left costophrenic angle and marked cardiac enlargement. Though there was no obvious source of emboli, an initial diagnosis of pulmonary embolism was made and anticoagulation was started. Procainamide was continued as prophylaxis against further cardiac arrhythmia.

Initially there was some improvement, but three weeks after admission the patient began to complain of severe pain in the small joints of both hands and in the muscles around the shoulder girdles. Subsequently she had a further episode of left-sided pleuritic pain, followed by pain and a pleural rub on the right side. X-ray examination showed an increase in the left-sided pleural effusion and the presence of fluid at the right base. The E.S.R. was 70 mm. in one hour and the serum gammaglobulin 1.5 g./100 ml. The most likely diagnosis was thought to be multiple pulmonary emboli, and the oral anticoagulants were supplemented by high doses of intravenous heparin. However, no clinical improvement was noted.

The possibility of a collagen disease—a procainamide-induced lupus syndrome—was then considered. Positive L.E.-cell preparations were found on several occasions, the L.E. latex fixation and Jones tests were positive, and the antinuclear factor was demonstrated.