Clinical Course.—Deterioration was rapid; the patient developed purpura, haemoptysis, and epistaxis, and died on March 19.

Necropsy Findings.—The right lung weighed 1,010 g. The bronchus to the right middle lobe was occluded by a mass of whitish growth 3 by 2 cm. in diameter. The remainder of the right lung and the left lung were not involved in growth. The liver weighed 5 kg. and showed widespread secondary deposits, as did the pancreas. Microscopy of primary and secondary tumours showed an oat-celled carcinoma. Section of the sternum revealed metastatic carcinoma.

Discussion

The main interest of the two cases is that they provide further unequivocal instances of the occurrence of Bence Jones proteinuria in secondary carcinomatosis. Both were cases of bronchial carcinoma of oat-cell type accompanied by secondary deposits in bone. Study of previously reported cases of Bence Jones proteinuria in skeletal secondary carcinomatosis does not indicate any special association with bronchial carcinoma.

Case 1 further illustrates that multiple myelomatosis may on occasion be simulated by secondary carcinoma if undue reliance is placed on the finding of Bence Jones proteinuria together with the presence of a high percentage of plasma cells in the marrow smear. That carcinoma cells infiltrating marrow can arouse a plasma-cell response is well known, and several recent papers have emphasized the occurrence of a "myeloma-like" marrow reaction in such cases. Rohr and Hegglin (1936), Nordenson (1940), Stöger (1941), and Delcourt (1946) have all reported this association. Coste *et al.* (1948) described a case under the heading "Pseudomaladie of Kahler," while Marchal and Mallet (1948) reviewed the subject under the heading "Plasmacytose Cancereux." Hardisty (1952) published a further case in which metastatic breast cancer gave a marrow picture indistinguishable from that of myelomatosis.

The possibility that multiple myelomatosis and carcinoma of the bronchus may have coexisted in these two cases requires consideration. In both cases microscopical examination of post-mortem material showed generalized carcinomatosis. In addition to the histological study of the primary tumour, sections were taken in Case 1 of adrenal, kidney, and sternum, and in Case 2 of liver, spleen, kidney, sternum, and vertebrae. In each case the pathology was typical of secondary carcinoma, with no histological evidence to support a diagnosis of multiple myelomatosis.

The validity of methods for the detection of Bence Jones protein has occasioned much discussion. Snapper (1949), in a brief review, said that the careful examination, under controlled conditions of temperatures, of precipitation and solution affords the most suitable method for the routine examination of urine for this substance. The methods outlined by Jacobson and Milner (1944) and recommended by Snapper were followed in the examination of the above cases. In each case a substance fulfilling the criteria laid down by these authors was demonstrated. Temperatures of precipitation were from 50 to 55° C., whilst the precipitate was completely redissolved at a temperature of 100° C.

It is interesting to note the increase in serum globulin in both these cases. Such an increase was reported by Delcourt (1946) in a case of metastatic abdominal cancer in which the globulin was 3.8 g. per 100 ml. Coste *et al.* (1948) describe a case of breast cancer in which the globulin was also 3.8 g. per 100 ml. In their case the myelogram showed that plasma cells formed 80% of the nucleated cells. The sternal marrow of Case 1 had the characteristic appearance associated with multiple myelomatosis, and this case adds further weight to the growing opinion of the non-specific nature of such a marrow picture.

Summary

Two cases of carcinoma of the bronchus with Bence Jones proteinuria are reported.

The simulation of multiple myelomatosis is commented upon.

Alternative explanations of the findings are discussed. The literature is briefly reviewed.

I am indebted to Dr. M. D. Milne and to Dr. R. W. Luxton for permission to publish these cases and to Dr. J. Davson for help and encouragement in the preparation of this report.

REFERENCES

- Copeland, M. M. (1931). *Arch. Surg., Chicago*, 23, 581.
Coste, F., Bourgeois, P., Delbarre, F., and Blatrix, C. (1948). *Bull. Soc. méd. Hôp. Paris*, 64, 364.
Delcourt, R. (1946). *Sang.*, 17, 202.
Geschickter, C. F., and Copeland, M. M. (1928). *Arch. Surg., Chicago*, 16, 807.
Hardisty, R. M. (1952). *Acta med. scand.*, 142, 64.
Jacobson, B. M., and Milner, L. R. (1944). *Amer. J. clin. Path.*, 14, 138.
Jones, H. B. (1848). *Phil. Trans.*, 138, 55.
Marchal, G., and Mallet, L. (1948). *Sang.*, 19, 457.
Nordenson, N. G. (1940). *Nord. Med. (Hygiea)*, 6, 834.
Rohr, K., and Hegglin, R. (1936). *Disch. Arch. klin. Med.*, 179, 61.
Snapper, I. (1949). *Medical Clinics on Bone Diseases*, 2nd ed., p. 245. Interscience Publishers Inc., New York.
Stöger, R. (1941). *Disch. med. Wschr.*, 67, 1389.

ACUTE SUPRARENAL FAILURE

BY

JOSEPH SMART, M.D., F.R.C.P.

Physician, London Chest Hospital and Connaught Hospital, London

The occurrence of acute suprarenal failure in cases of Addison's disease is not uncommon, but in cases in which previous adrenal insufficiency was unsuspected it is not very usual. The following case is reported because of its interest, as there were practically no signs or symptoms of suprarenal failure until within five days of the patient's death.

Case Report

A man aged 30 was seen on September 8, 1953, with a history of loss of weight for one year (approximately 1 st.—10.9 kg.), lassitude, some dizziness, and a feeling of faintness for the last three months. He had previously had a tuberculous lesion of the left knee, which had responded well to treatment, there having been no evidence of any pulmonary lesion at that time. In view of the lassitude and loss of weight, the possibility of reactivation of the knee or of a pulmonary tuberculous lesion was considered. There was no evidence of active disease in the knee either clinically or radiologically, this being confirmed by an orthopaedic surgeon, but an x-ray examination of his chest showed a minimal lesion at the left apex. The clinical findings were negative apart from limitation of range of movements of the left knee. His blood pressure was 130/85, he had no sputum to test, but his stools did not contain tubercle bacilli. The rapid onset of further symptoms prevented gastric lavage from being done. His E.S.R. at this time was 20 mm. in the first hour (Westergren).

It was thought that the loss of weight and the lassitude were probably accounted for by the tuberculous lesion in the chest, although at the time it was felt that the lesion was not sufficient to cause such toxic symptoms. The patient was put on to streptomycin, 1 g. twice a week, P.A.S., 12 g. daily, and isoniazid 150 mg. twice daily. Forty-eight hours after starting this regime vomiting began, but his general condition appeared to be good. Vomiting continued the following day (September 20), and as this was thought to be probably due to the P.A.S. that drug was stopped. On September 21 his general condition rapidly deteriorated; he became dehydrated, felt thirsty, had marked oliguria, and his blood pressure had dropped considerably, being only 95 systolic, the diastolic pressure not being readable. His alkali reserve was 24 vols. CO₂ and his chlorides 450 mg. per 100 ml. as sodium chloride. His blood urea was 100 mg. per 100 ml.

The probability of the condition being an acute Addisonian crisis was considered, and his suprarenals were x-rayed, but there was no definite calcification in this area. He was given a glucose-saline drip, but as the response was poor and his general condition unsatisfactory he was put on to cortisone and "eucortone" (50 mg. of cortisone 12-hourly and 20 ml. of eucortone into his intravenous drip every three hours). Marked clinical improvement was now seen, his blood pressure, which had fallen to 60 mm. Hg systolic, rising to 140 mm., and between 80 and 90 diastolic. During the first twelve hours of this treatment his fluid intake was 4,400 ml. while his total loss by vomiting and urine was 310 ml. During the next twelve hours his total intake was 2,600 ml. and his total output 2,325 ml. This initial high intake and poor output was due to his extremely dehydrated condition; but, unfortunately, his general condition, which had at first improved rapidly, began to deteriorate during the next twenty-four hours, and his blood pressure fell again, his urine output decreased, and by midnight on September 22 his blood pressure had fallen to 80/60. Cortisone was thereupon increased to 50 mg. six-hourly, which resulted in a further temporary improvement in blood pressure to about 120/80, but his urine output, which had fallen, did not improve. Fluid intake on September 22 was 5,500 ml. while the output was 1,900 ml. This was accompanied by changes in the lungs, where there was evidence of marked engorgement, both clinically and radiologically, particularly on the left side. He died on September 23.

Biochemical Findings.—Blood urea on admission (September 15) 27 mg. per 100 ml.; blood count normal; Hb, 107%; white cells, 8,000 (polymorphs 67%, lymphocytes 32%, hyaline cells 1%); E.S.R., 20 mm. in first hour. On September 21, after the initial vomiting, the blood urea was 100 mg. per 100 ml., his alkali reserve was 24.2 vols. CO₂, and his plasma chlorides as sodium chloride 450 mg. per 100 ml. The following day his alkali reserve was 31.9 vols. CO₂ and plasma chlorides as sodium chloride 505 mg. per 100 ml.; the blood urea was 68 mg. per 100 ml. During this time the urinary chlorides were: September 21, 8.15 p.m., pH 5.0, chlorides 238 mg. per 100 ml.; September 22, 1.30 a.m., pH 4.8, chlorides 278 mg. per 100 ml.; 8 a.m., pH 5.0, chlorides 350 mg. per 100 ml.; September 23, serum potassium 22 mg., serum sodium 295 mg. per 100 ml.

Post-mortem Examination.—This showed no abnormality apart from the lungs and suprarenals. Both lungs were adherent to the parietal pleura; the left lung was greatly enlarged and of a rubbery consistence, exuding frothy fluid. Numerous haemorrhages were present on the pleural aspect; and the upper lobe, on section, contained a caseous encapsulated nodule, about 15 mm. in diameter. There were greyish-white trefoil areas scattered throughout the lungs, suggestive of miliary tuberculosis. The right lung was similar to the left but less voluminous, and it also contained an apical upper-lobe lesion about 1 cm. in diameter. The liver was congested; the spleen was one and half times its normal size, moderately firm; the left suprarenal was grossly enlarged, indurated, and distorted in shape, and was completely replaced by an opaque, caseo-calcareous tuberculous lesion. The right suprarenal was adherent to the liver and four times its normal size, and also replaced entirely by fibro-caseous tuberculosis.

Histology.—There was fibro-caseous tuberculosis in both lungs, with a moderately well defined fibroblastic "capsule," and with new tubercle formation elsewhere in the lung. The suprarenals were completely replaced by caseo-calcareous disease, and the sections were too friable and broke up on cutting. Remnants of the sections, however, showed caseo-calcareous debris and fibro-granulomatous tuberculosis.

Discussion

This case is interesting because of the abrupt onset of suprarenal failure, especially as at necropsy the patient's suprarenals appeared to have been completely replaced by tuberculous caseous material, and it is surprising that there

was no previous stage when there were signs of a relative insufficiency. Doubtless the lassitude complained of was associated with this, but there were no corollary signs such as a lowering of the blood pressure or pigmentation of the skin to help in the diagnosis, and the minimal chest lesion might have accounted for this lassitude. A further difficulty, which delayed the giving of cortisone for just over twenty-four hours, was the onset of vomiting shortly after P.A.S. had been started, and which was therefore thought to be due to this drug, especially as during this period the blood pressure remained up. Valuable time was consequently lost before cortisone was given, and the patient became dehydrated. It is possible that as the P.A.S. was given in the soluble form it may have upset the potassium balance, causing the acute onset, or, again, the P.A.S. may have caused vomiting, leading in turn to dehydration, with some alkalosis, which might have been the precipitating factor.

It would appear from this case that the amount of suprarenal tissue necessary for maintaining a practically normal life must be very small, since the tuberculous process must have been present for some months.

Summary

A case of acute suprarenal failure is described, due to destruction of the suprarenals by a tuberculous process, there being no evidence of suprarenal failure previously. Difficulty in arriving at an accurate diagnosis was encountered because of a minimal chest lesion, which might have accounted for the patient's symptoms, and the treatment with cortisone was delayed, as the vomiting, when it started, was thought to be due to P.A.S.

THROMBOCYTOPENIA FOLLOWING SULPHADIMIDINE

BY

DUNCAN MACAULAY, M.D., B.Sc., M.R.C.P.
D.C.H.

Lecturer in Child Health, University of Manchester

Sulphadimidine is generally, and with good reason, regarded as one of the safest of the sulphonamide drugs. Thrombocytopenia is one of the rarer manifestations of sulphonamide toxicity. Its occurrence after sulphadimidine administration has not previously been recorded.

Case Report

A boy aged 3 was admitted to the Duchess of York Hospital for Babies, Manchester, on January 18, 1954. He was the fifth child of healthy parents and, except for chicken-pox in November, 1953, had always been well. Twelve days before admission he developed an upper respiratory infection with cough and sore throat. A mixture containing sulphadimidine was given in a dose of 1 g. twice a day, along with a cough mixture (mist. cod. pro infant. (N.F.), 2 dr. (7 ml.) thrice daily). The symptoms subsided, but the mother continued the sulphonamide mixture for seven days. The day after it was stopped the boy became hot and flushed with a temperature of 104.6° F. (40.3° C.). At the same time a rash appeared on the shoulders. The sulphadimidine was prescribed once more, and the mother, not realizing that it was the same medicine, also gave what was left of the original mixture. For four days the child had 4 g. of the drug daily. During this period the rash spread all over the body, anorexia was very marked, and the child was constipated. He also became drowsy and was unable to stand because of dizziness. On the day before admission a swelling appeared in the right side of the neck.