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

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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. coden. 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.

On the day of admission his breathing was rapid for short periods. He passed only small amounts of urine, without pain and with no obvious haematuria.

On admission he was drowsy and fretful, lying curled up when left alone. There was a widespread morbilliform rash, and the face was flushed. Two small bruises were noted in the lumbar region. Many glands were palpable in the neck, and on the right side there was a large soft swelling overlying the middle of the sterno-mastoid muscle and extending forward over the angle of the lower jaw. The axillary and inguinal glands were also palpably enlarged. The liver edge was palpable two fingerbreadths below the costal margin. No other abnormalities were discovered.

A provisional diagnosis of sulphonamide toxicity was made and penicillin administration was begun in a dosage of 1.5 mega units daily. Potassium citrate was also given in a daily dose of 6 g., and the fluid intake was pushed to 2 pints (1,140 ml.) a day. The haematological findings are summarized in the Table.

On the second hospital day the boy's temperature rose to 103° F. (39.4° C.). He was passing urine plentifully—21 oz. (200 ml.) plus two wet beds in the first 24 hours—and drinking freely, but remained very drowsy. The urine contained a trace of albumin, but no red cells or crystals were found; the chemical test for sulphonamides was strongly positive. In the afternoon of this day he passed a very large tarry stool which gave a strongly positive benzidine reaction.

The temperature settled within 12 hours, and in the course of the next few days the child became brighter and more

rested itself by very slight bruising and profuse melaena. The cerebral state was probably also the consequence of sulphonamide intoxication.

Thrombocytopenia after sulphonamide administration has been infrequently reported. In 1943 Kracke and Townsend reviewed the literature and found reports of 10 cases, to which they added two of their own. Since then there have appeared reports of another 21 cases, making 33 in all. The drugs responsible were sulphanilamide, 4 cases; sulphapyridine, 8 cases; sulphathiazole, 12 cases; sulphadiazine, 7 cases; sulphamerazine, 1 case; and sulphafurazole, 1 case. The frequency with which preparations appear on this list reflects their popularity rather than their toxicity, and it is noteworthy that the number of reports, after reaching a peak in 1943, 1944, and 1945, has fallen off sharply—presumably following the more general use of penicillin and other antibiotics. It would appear that almost all of the more soluble and absorbable sulphonamides are capable of producing thrombocytopenia.

In the present case there was an obvious depression of the bone marrow affecting all elements. This was almost certainly due to the sulphonamide in view of the rapid recovery following withdrawal of the drug, the failure to discover any other cause, and the associated symptoms of sulphonamide toxicity. This case underlines the potential toxicity of even the best of the sulphonamides. It would appear to be advisable that these drugs be prescribed in quantities sufficient for a definite short period only, and that opportunities for excessive medication be not given to parents of patients by supplying more than is needed. The over-dosage in this case arose from a misunderstanding, and though the outcome was favourable it might not have been.

I wish to thank Professor W. F. Gaisford for criticism and advice.

REFERENCE

Kracke, R. R., and Townsend, E. W. (1943). *J. Amer. med. Ass.*, **122**, 168.

Haematological Findings

Date	Hb	W.B.C.					Platelets
		Total	Poly-morphs	Lympho-cytes	Eosino-phils	Mono-cytes	
19/1/54	78%	3,980	66%	33%	—	1%	45,000
20/1/54	78%	4,600	48%	51%	—	1%	55,000
21/1/54		5,400	45%	53%	1%	1%	60,000
22/1/54		6,300	38%	60%	1%	1%	110,000
23/1/54		8,700					135,000
25/1/54		12,600					275,000
26/1/54		9,600					360,000
27/1/54	74%	9,000	55%	42%	—	3%	400,000

alert, the rash gradually faded, and the lymph-node swelling subsided. Melaena stools were passed for three days, but on the ninth day after admission the faeces gave a negative benzidine reaction. The urine never contained red cells or crystals, but the chemical test for sulphonamides remained positive until the third day.

A throat swab taken on admission gave a scanty growth of normal upper respiratory flora. A Paul-Bunnell test on the third day gave no agglutination and a 1:1,000 Mantoux test was negative. Chest x-ray films taken on admission showed slight enlargement of the right hilar shadow but no pulmonary lesion. Bone marrow was obtained on the second day in hospital by iliac crest puncture. There was definite hypoplasia—total nucleated cell count of 46,800 per c.mm. (normal for children of 2 to 10 years, 70,000–700,000 per c.mm.)—with general reduction in the number of all types of nucleated cells; myeloid/erythroid ratio 12:1 (normal ratio in children 4:1 to 13:1); megakaryocytes were plentiful—1% of the nucleated cells.

The child was finally discharged after 12 days in hospital in apparently normal health.

Discussion

This child received a total of 30 g. of sulphadimidine in 11 days. He had not, so far as his parents were aware, ever received a sulphonamide before, and there was no family or personal history of allergy or idiosyncrasy. The effects were presumably, therefore, a direct toxic action of the overdose. These effects were fever, rash, lymph-node enlargement, moderate granulocytopenia (total polymorph count of 2,600 per c.mm.), and marked thrombocytopenia. The last mani-

Medical Memoranda

Treponematoses in Gambia: Preliminary Communication

Investigations have been made into the forms of treponematoses occurring in Gambia, and two forms have been encountered. These are yaws and another treponemal disease which shows many similarities with the endemic syphilis described among the Arabs and the people of Bosnia.

This second disease, as found in Gambia, usually appears first on the mucous membranes at the angles of the mouth in young children, or it can appear on the tip of the penis in small boys. These lesions contain large numbers of spirochaetes morphologically identical with *Treponema pallidum*, and the patients give strongly positive Wassermann and Kahn reactions. There is little doubt that the disease is mainly transmitted by the use of a common drinking-cup and, less often, by close personal contact. The use of a common drinking-cup is prevalent in Gambia, and the people themselves, when asked if the disease could be transmitted from one person to another, volunteered the information that they believed the drinking-cup to be responsible for passing on the disease.

The secondary manifestations of the disease which have been observed are (a) florid eruptions on the vulva and in the anal cleft, and (b) circularly arranged groups of papules which may coalesce to form rings; these can occur on any part of the skin. These lesions contain large numbers of spirochaetes.

The most common tertiary lesion observed is a hyperkeratosis of the palms and soles associated at a later stage with depigmentation of the hands and feet. Destructive lesions of the nasal septum are fairly common, but lesions of the long bones are rarely seen.