synthetic compounds of a similar structure. Nikethamide (coramine) = pyridine- β -carboxylic acid diethylamide. Cycliton = diethylamide of 3:5-dimethyliso-oxazol-4-carboxylic acid.

No information has been obtainable about the detailed pharmacological action of cycliton. Faust (1925) has shown that nikethamide causes vasoconstriction by local action on the vessels, a property not found when Curtis and Wright (1926) investigated lobeline. Possibly the vasoconstriction produced locally by cycliton, associated with the vasoconstriction and slowing in arterial blood flow that accompanies asphyxia, precipitates the development of thrombosis. Beyond this we can only say, as Cohen does of thiopentone, that the arterial intima appears to be particularly sensitive to cycliton.

An attempt to reconstitute the lesion in animals was made by Professor R. A. Gregory (Department of Physiology). One millilitre of cycliton was injected into the internal iliac arteries of six adult cats, under light ether anaesthesia at aseptic operation, with negative results. The experiments were then repeated, but before injecting the cycliton the animals were kept in a state of asphyxia. Again the results were negative. Finally, in order to make conditions as comparable as possible to those obtaining in the newborn infant, small amounts of cycliton (0.05–0.5 ml.) were injected into the umbilical arteries of four newborn kittens; none of these animals survived longer than 24 hours.

Summary

Twenty cases of unilateral sciatic paralysis in the newborn, sometimes accompanied by cutaneous gangrene, are described. Accidental injection of cycliton into an artery instead of the vein in the umbilical cord is suggested as the possible cause of the lesions.

Experimental proof is as yet lacking, but the evidence in favour of this theory is as follows:

1. The cases occurred only in the hospitals in the city of Liverpool in which cycliton was in use.
2. The only common factors were asphyxia at birth and injection of cycliton into a cord vessel.
3. The lesions are consistent with the results of ischaemia due to disturbance of blood flow in the internal iliac artery, and are comparable to the lesions produced by intra-arterial injection of thiopentone.
4. No further lesions have occurred since cycliton has ceased to be used. (Cycliton is not now sold in England, although it is used extensively on the Continent and in other parts of the world.)

We would like to thank Professor R. A. Gregory for the considerable amount of thought and time that he has given in an attempt to establish experimental evidence, and Professor N. B. Capon and Mr. Bryan McFarland for their interest and help in the preparation of this article. We also wish to thank Professor T. N. A. Jeffcoate for permission to publish three of the cases, and Dr. S. E. Keidan (paediatric registrar) for his interest in the problem and help in recording the clinical details of many of the cases.

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ANAPHYLACTOID PURPURA IN PULMONARY TUBERCULOSIS

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The occurrence of purpura in association with pulmonary tuberculosis is generally considered to be a rarity. Instances of it in sanatoria reports are not common, and references to it in the literature do not seem to be numerous, most of them appearing in publications from other countries. In view of this we feel it justifiable to report five cases which all attended a general medical clinic within the space of twelve months.

The association of purpura with pulmonary tuberculosis was described as early as 1801 by Willan in his treatise on cutaneous disease. He had noted the occurrence of purple spots in the skin in the last stages of pulmonary consumption, and considered it to be a forerunner of death. In contradistinction to this, in 1890 Rendu described a purpuric eruption especially prone to occur on the dorsum of the hands and wrists, which he considered was a premonitory sign of tuberculosis. Sixteen years later Bensaude, Carnot, and Harvier reported a case of purpura as a pre-tuberculous manifestation. In that year also, Bensaude and Rivet (1906) produced their monograph on this subject. They have classified four main groups: (1) Purpura haemorrhagica occurring in the course of miliary tuberculosis—and this was more common if the miliary state was superimposed on chronic disease. (2) Purpura haemorrhagica occurring in the course of chronic pulmonary tuberculosis, usually in terminal and cachectic states. (3) Purpura haemorrhagica occurring in the course of latent tuberculosis. (4) Purpura haemorrhagica occurring in the course of extrapulmonary tuberculosis.

They also considered that purpura may occur as a pre-tuberculous manifestation, though they did not classify it as such, and they stress the importance of searching for a tuberculous focus in the presence of chronic or recurring purpuric eruptions. Single cases found in the literature—such as that of Gossner, who reported the occurrence of purpura in a man with a tuberculous testis, the eruption disappearing with the removal of the organ—can be fitted into the classification.

The gravity of purpura as a symptom in pulmonary tuberculosis was stressed by Cruice (1912), who considered that it marked either a terminal stage or an exacerbation from which the patient might die, or if recovery occurred the state of the lesion would be found to be more advanced.

The purpura may be due to a symptomatic thrombocytopenia, be a simple symptomatic purpura, or be of the Henoch-Schoenlein group. The last-mentioned form is suggested by Bauch (1916). Wits (1946) considers that in all cases the endothelial lining of the vessels is damaged, and states that the platelet count varies from case to case. Greengard (1931), in his review of two cases, also considered capillary damage to be the most important factor in its development.

Case 1

A man aged 44 was admitted to hospital from the out-patient department. He gave a history of heaviness in the abdomen associated with nausea and loss of appetite of nine days' duration. Two days before admission he had noticed a generalized

rash on his legs, and next day had had severe colicky abdominal pain, with the passage of black motions, and his urine had become dark. He gave a history of bronchitis followed by pleurisy in 1936, since when he had had a slight cough, particularly in winter-time. Three months before admission he had had a small haemoptysis, but as he had felt well he had taken no notice of it.

On examination he looked thin and unwell, his temperature was 100.6° F. (38.1° C.), pulse 92, and respirations 20. Extensive areas of purpura were present over both legs with small purpuric spots on the thighs and arms. Percussion and air entry were impaired, and rales were heard at the right apex. No other abnormalities were found. A blood count showed: haemoglobin, 95%; red cells, 4,800,000; white cells, 18,300 (polymorphs 79%, lymphocytes 19%, monocytes 2%). The bleeding-time was four and a half minutes, clotting-time nine minutes, and the platelets numbered 240,000. Hess's capillary fragility test was strongly positive. The urine contained albumin and red blood cells, and the stools altered blood. The bone marrow was completely normal and the Wassermann reaction was negative. A radiograph of the chest revealed tuberculous infiltration at the right apex and mid zone with possible cavitation. Two cavities were demonstrated by tomography. The sputum contained tubercle bacilli, and the erythrocyte sedimentation rate was 60 mm. in the first hour.

Progress.—The patient was given complete rest in bed, and in the course of the next 48 hours the melaena ceased, the purpura disappeared in five days, and the haematuria stopped in ten days. By the end of a fortnight the temperature had settled, the leucocyte count was normal, and the erythrocyte sedimentation rate had fallen to 40 mm. in the hour. He was then transferred to a sanatorium, where after six months he was discharged symptom-free and feeling well; he has since resumed work.

Case 2

A woman aged 31 was seen in the out-patient department complaining of recurrent areas of discoloration of the skin of the legs for the preceding six weeks. Associated with the eruptions was cramp-like pain in her calves. At the onset she had also had severe colicky abdominal pain and had vomited a small amount of blood on two occasions. This condition had improved spontaneously after one week. She gave a history of pulmonary tuberculosis for the preceding four years, and had been discharged from a sanatorium some fifteen months previously.

On examination extensive purpura involving both legs and thighs was seen. The chest showed signs of consolidation at the right apex. Other systems were normal. The blood count was: haemoglobin, 84%; red cells, 5,000,000; white cells, 9,800 (normal differentiation). The bleeding-time was four minutes, the clotting-time eight and a half minutes, and there were 270,000 platelets. Hess's capillary fragility test was strongly positive. The urine contained albumin and red blood cells. A radiograph of the chest revealed chronic tuberculous infiltration at the left apex and mid-zone and the right mid-zone, while the trachea was displaced to the right. The right apical zone was completely opaque, probably owing to tuberculous consolidation. The sputum contained a large number of tubercle bacilli. The patient's general condition rapidly deteriorated, and after a short time she left the district to be looked after by relatives.

Case 3

A man aged 47 complained of a rash on both his legs which had first developed seven weeks previously, and had varied in intensity from day to day. At the onset he had had severe pain and swelling of the right knee and then of the right ankle, which lasted for two weeks, and some three weeks later both wrists had been similarly affected. He gave a history of pneumonia in 1948, but nothing else was relevant.

On examination an extensive purpuric eruption was seen on the legs, thighs, upper arms, and the lower part of the trunk. Both wrists were swollen and had limited movement. General

examination was negative. A blood count showed: haemoglobin, 87%; red cells, 4,200,000; white cells, 7,500 (normal differentiation). The bleeding-time was three minutes, the clotting-time eight minutes, and there were 190,000 platelets. Hess's capillary fragility test was negative. A radiograph of the chest revealed several calcified foci in the left lung, with calcification in the corresponding glands. A soft opacity was present at the left apex and was thought to represent active tuberculosis.

Progress.—The purpura disappeared in one month without specific therapy. At the end of two months his platelets had risen to 270,000 and the erythrocyte sedimentation rate was 3 mm. in the hour. A chest radiograph was unchanged. When seen at the end of a further six months he was feeling well, had not had any further purpura, and had gained 5 lb. (2.3 kg.) in weight. The chest radiograph showed calcification in the opacity at the left apex, and the blood count was normal.

Case 4

A man aged 53 was referred to the out-patient department following the sudden development 24 hours previously of extensive purpura involving his legs, arms, face, and mouth. He felt well in himself, but for many years had been subject to a cough with sputum, which had become rather worse in the past winter. On account of this cough an x-ray examination of his chest had been made by the tuberculosis authorities three years previously and had revealed a calcified focus which was said to be inactive.

On examination he looked ill and was very thin. There were large bullae containing blood on both lips, with smaller ones on the tongue and on the mucous membrane of the mouth. The face, arms, and legs showed a widespread fine purpuric eruption with several larger areas of bruising about the size of a shilling. General systems were normal. The blood count showed: haemoglobin, 92%; red cells, 4,600,000; white cells, 5,400 (normal differentiation). The bleeding-time was two minutes, the clotting-time four minutes, and the platelets numbered 150,000. Hess's capillary fragility test and the blood Wassermann reaction were negative. A radiograph of the chest revealed tuberculous infiltration of both apical zones, some showing calcification. The sputum contained tubercle bacilli. The erythrocyte sedimentation rate was 10 mm. in the hour.

Progress.—The purpura started to go at the end of one week and had disappeared in a further 14 days. His general condition remains unchanged.

Case 5

A man aged 67 was admitted as an emergency case. He gave a history of loss of weight and cough for three months. In the two days before admission he had lost his appetite, had felt very ill, and had at times been irrational.

On examination he was seen to be a thin, pale, cyanosed, dyspnoeic man who was apyrexial. The chest showed signs of cavitation at the right apex, with consolidation of the rest of the right lung. A purpuric eruption, consisting of large reddish-purple blotches, was present on the dorsum of the hands, wrists, and forearms. A radiograph of the chest revealed cavitation at the right upper zone and patchy bronchopneumonic changes throughout the right lung field and in the left upper zone. The sputum was positive for tubercle bacilli. The blood count showed: haemoglobin, 52%; white cells, 16,100 (87% polymorphs). The bleeding-time was one and a half minutes, the clotting-time four and a half minutes, and the platelets numbered 190,000. Hess's test was negative. There was no microscopical haematuria, and the blood urea was 42 mg. per 100 ml.

Progress.—The patient rapidly deteriorated, and died in 10 days. The necropsy confirmed the pulmonary finding. There was no evidence of endocarditis. The liver and spleen were normal. The left kidney contained several infarcts.

Immediately before the development of the purpura none of the cases had been receiving any medication.

Discussion

In all cases the diagnosis of pulmonary tuberculosis was made on the radiological findings and was confirmed by the presence of tubercle bacilli in the sputum of all except Case 3, in which no sputum was obtained. The first four cases presented as extensive purpuric eruptions requiring diagnosis. In Case 2 only was there a definite previous history of tuberculosis, although Case 1 had had a haemoptysis three months before and Case 4 had been investigated for tuberculosis three years previously and the lesions then found were thought to be healed. In Case 5 the presence of purpura in association with the clinical findings in the chest pointed to tuberculosis as the likely cause, and this was subsequently confirmed.

In the first three cases the platelet count was within normal limits, and in the last two it was only just below the lower limit of normal. Consequently, it does not seem likely that thrombocytopenia could have been responsible. The appearance of arthritis and the occurrence of haemorrhages from the bowel and haematuria in some cases led us to consider that this purpura was allergic in nature.

The importance of capillary damage as a mechanism was borne out by the strongly positive capillary fragility test in the two cases that had gastro-intestinal bleeding and haematuria. These cases would seem to belong to the type described by Henoch, while Case 3 belongs to the Schoenlein type. With the exception of Case 5 the general condition of the patients was good when they were first seen, and their blood counts were within normal limits; this strengthened our belief that it was a sensitivity manifestation rather than a toxic effect in the bone marrow.

The findings in this small series do not support the suggestion of Cruice that the development of purpura is either a terminal condition or one marking a serious exacerbation. Only two of the five cases described showed marked deterioration, although Case 1 seems to have had a temporary progression of his pulmonary lesion. The two remaining cases had few signs of activity, being afebrile, with normal erythrocyte sedimentation rates, and evidence of subsequent calcification ensued without treatment.

The continuance of their general well-being, with quiescence of the lesion in two cases and only very transient deterioration in a third, supported the suggestion that toxæmia was unlikely.

Summary

A brief review of the literature on the occurrence of purpura in pulmonary tuberculosis is given.

Five cases of purpura occurring in the course of pulmonary tuberculosis are described in which the bleeding involved not only the skin but also the gastro-intestinal tract and kidneys.

In two cases the appearance of the eruption does not seem to have been the grave omen that the literature would have us believe.

These cases stress the importance of searching for a tuberculous focus on the incidence of unexplained purpura, as originally suggested by Bensaude and Rivet in 1906.

We wish to thank Dr. D. H. G. MacQuaide for permission to report these cases and for helpful advice in the preparation of this paper.

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Medical Memoranda

A Case of Stevens-Johnson Syndrome

This syndrome was first noted by Alibert and Bazin in 1822, and was described in 1922 by Stevens and Johnson, who recorded two cases. Few cases have been recorded in Britain; the majority have appeared in American and Canadian journals. Inquiry among colleagues, however, leads me to suppose that the condition is commoner than the number of recorded cases suggests.

CASE REPORT

On September 17, 1948, a young man aged 20 was admitted with severe malaise, sore throat, cough, and haemoptysis. Twelve days previously he had contracted a cold, with sinusitis and a productive cough. Two days before admission he had a feeling of constriction in the chest and roughness in the mouth, and his face and eyes became swollen. The following day he had a rigor, and his symptoms became worse. On the day of admission he had itching of the legs, and his sputum became offensive and heavily blood-stained.

On examination he was seen to be extremely ill. His temperature was 102.6° F. (39.2° C.). The lips and buccal mucous membrane were excoriated and covered with white pseudo-membrane. The gums were ulcerated and bleeding (see Figure). There was bilateral conjunctivitis, with a film of

The patient on admission.

pus covering the right eye; the left pupil was smaller than the right. Both pupils reacted sluggishly to light and accommodation, and there was nystagmus to the right. A maculo-papular eruption was present on both lower limbs, the right forearm, and the left wrist. The papules varied in diameter from 0.25 to 1 cm., and were surrounded by a purplish-red areola. In both lungs there were signs of patches of consolidation. The liver and spleen were not enlarged. The knee-jerks, ankle-jerks, and abdominal reflexes were absent; all other reflexes were present and equal. Sensation was unimpaired. Swabs from the throat, gums, and conjunctiva yielded no growth on