which, however, were associated with haematemesis and haematuria, and followed cases of septic scarlet fever. Goodall and Washbourn² have recorded four cases of fulminating purpura haemorrhagica, and they regarded the condition as a rare complication of scarlet fever. The cases of Rolleston and McCririck³ were characterized by the absence of haemorrhage from mucous membranes, and in this respect they resembled the one under discussion. However, the period of illness from the first appearance of ecchymosis till the fatal termination was in the present case extremely short. The total duration was only thirty hours. These features bring the present case into the category of purpura fulminans.

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A CASE OF ELEPHANTIASIS NEUROMATOSA.

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VON RECKLINGHAUSEN in 1882 drew attention to an association of lesions affecting the skin and nervous system—namely, soft tumours of molluscum fibrosum, cutaneous pigmentation (freckles and maculae) scattered all over the body, and multiple fibrous tumours of nerves. Since then two other manifestations, occasionally present, were found to be classifiable in the same group—namely, plexiform neuro-fibroma and elephantiasis neuromatosa of Virchow.

Diffuse neuro-fibromatosis, or von Recklinghausen's disease, consists essentially of a diffuse overgrowth of the connective tissue of the nerves, especially that of the endoneurium separating out the nerve fibres. The fibrous overgrowth may be confined to a single nerve or a plexus, or it may be generalized to include cranial, spinal, and sympathetic nerves—large or small, superficial or deep. When the small nerves in the skin and subcutaneous tissues are affected the overgrowth spreads beyond the nerve filament in which it originates, causing soft fibrous tumours of the skin (molluscum fibrosum), which may be few and widely spread, or so abundant as to cover every inch of an individual except his palms and soles. They vary from the size of a pin's head to a fig, and may be sessile or pedunculated.

Plexiform neuro-fibroma is a fibromatosis affecting a group of contiguous nerves, commonly those of the head and neck (fifth and superficial cervical). Commencing shortly after birth, it gradually forms a pendulous mass composed of convoluted, thickened, or beaded nerve cords held together by connective tissue.

FIG. 1.—The patient. Note the pendulous scalp in the occipital region and subcutaneous nodules in the affected limb.

Elephantiasis neuromatosa of Virchow is closely allied to plexiform neuro-fibroma and molluscum fibrosum. Here the fibromatosis of the cutaneous nerves merges into a diffuse overgrowth of the skin and subcutaneous tissue, uniformly enlarging the affected region, such as a limb, as in other forms of elephantiasis. The overlying skin may be normal, thickened, or pigmented, and may sometimes

contain palpably thickened and coiled nerves, as in plexiform neuroma. The condition is usually congenital and starts at a pigmented spot or a molluscum fibrosum.

In many cases of neuro-fibromatosis death results from sarcoma, the change manifesting itself clinically by rapid enlargement of the lesions. The only treatment is excision of removable masses.

The case here reported is remarkable for the colossal growth of a limb.

The patient, a male Tamil, looks more like a boy of 15 than the man of 20 he is said to be. His outstanding feature is the gigantic size of the left lower limb, which forms a pendulous mass representing about a third of his body weight, and prevents

FIG. 2.—The affected portion of the limb before amputation.

him from walking except with the very greatest difficulty. The abnormality is said to have been present at birth and to have progressed with the growth of the boy, especially during the last fifteen years. In addition, he presents the following lesions: small, soft, freely movable, painless, subcutaneous tumours scattered all over the body, particularly on the abdomen, but absent in the palms and soles; a small pachydermatocoele of the occipital scalp; pigmentation of the skin in the form of freckles and larger maculae—the palms are pigmented, the soles less so; pigmentation of the mucous membrane of the mouth, and muddy discoloration of the conjunctivae as in argyrosis. He complains of some pain in the affected limb. His mental faculties are not impaired.

Skiagraphy showed a marked atrophy of the epiphyses and smaller bones resulting in distorted outlines. The shafts of the long bones showed an irregularly distributed thickening of the cortex, and greater elongation than on the sound side.

Treatment consisted of amputation at the upper third of the thigh, under spinal anaesthesia. Considering the amount of tissue removed the patient stood the operation very well. The amputated limb weighed 35 lb., the rest of the patient 65 lb.

Dissection of the Amputated Limb.—Apart from the enormous increase in the connective tissue of the soft parts there was also an increase in the bony development, as evidenced by the greater length of the affected limb. The normal tibia (right) was 12 inches long, the abnormal one 15½ inches. The normal fibula was 12 inches, the abnormal one 16½ inches, its lower end curving round the astragalus like a smoker's pipe bowl, and thrusting up the foot bones into a position of talipes equinus (Fig. 3). The skeleton of the affected foot was only a quarter of an inch longer than the other. Both tibia and fibula were bowed, rough, and pitted, the latter especially about its middle. The periarterial sympathetics of the femoral artery at the site of amputation were visibly enlarged. Professor A. G. Smith, to whom I sent a section of it, reported as follows:

"The lumen of the artery seemed to be small. It, and to a lesser extent the vein, were completely ensheathed in a mass of flattened, hypertrophied, tortuous nerve cords—evidently greatly enlarged periarterial sympathetics. The individual nerve bundles were clearly to be distinguished."

Histological examination by Professor Ellison confirmed that the hypertrophied nerves belonged to the autonomic system. He said they were the finest example of non-medullated nerve tissue he had ever seen.

FIG. 3.—Skeleton of amputated limb.

It is interesting to consider what part the autonomic hypertrophy played in the overgrowth of the limb. Were they parts of the same process, or were the hypertrophied sympathetic nerves responsible, even partially, for the generalized overgrowth of the limb, through disordered vaso-constrictor and secretory impulses?

FIG. 4. Patient's mother.

leg, which was stated to be similar to the initial lesion affecting her son.

The patient's mother (Fig. 4), who was about 40 years of age, was 5 feet in height, and her physique suggested achondroplasia. The patient was her only child. Despite a certain degree of deformity of her infant's limb at birth, there was no special trouble at the confinement. She said that her parents were normal, but that her grandmother showed similar lesions to hers, which consisted of over 2,000 minute cutaneous tumours and scattered subcutaneous swellings; freckles and patchy pigmentation of the skin; and a diffuse swelling on the dorsum of the right

few cases, where repeated blood counts were carried out, considerable fluctuations in the degree of eosinophilia were observed. One case showed 17 per cent. at one time and only 0.8 per cent. on another occasion four months later. It is possible, therefore, that eosinophilia may have been temporarily present in others of our series, but was not discovered by a single blood count. It was noticeable that an increase in the eosinophilia occurred in several cases during the very hot weather in July and August, 1928, being lower before and after these months. This observation we intend to confirm next summer if climate permits. It would be interesting to know the degree of eosinophilia in insulin cases in hot countries.

The Cause of the Eosinophilia.

So far we have only established the presence of eosinophilia in a large proportion of insulin-treated diabetics and its absence in non-insulin cases. No factor other than the insulin has been discovered to account for this eosinophilia. The following ways in which insulin may be responsible suggest themselves.

1. Insulin, by virtue of its physiological action, might produce an eosinophilia. This is hardly likely, and the fact that we have found an eosinophilia in a case of diabetes insipidus treated by injections of pituitary extract is against this possibility.

2. The eosinophilia may be an allergic phenomenon produced in susceptible patients by the protein nature of insulin or by protein impurities in the solution. The latter, however, are almost absent in the brands of insulin (B.D.H. and B.W.) used by most of our patients. Moreover, there has been no sign of local allergic phenomena, such as wheals and urticaria, in these cases.

3. Insulin, being an acid solution, has an irritative effect on the skin and subcutaneous tissues, manifested locally by stinging and oedema at the site of injection. Eosinophilia is possibly produced by this constant skin irritation in the same way that it is so frequently associated with skin disease.

No definite explanation of insulin eosinophilia can be offered at present. The possibilities are being further investigated.

SUMMARY.

An eosinophilia has been found in 10 out of 20 diabetics treated with insulin. It is absent in cases treated without insulin.

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EOSINOPHILIA IN INSULIN THERAPY.

A PRELIMINARY REPORT TO THE MEDICAL
RESEARCH COUNCIL.

BY

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THE occurrence of a high degree of eosinophilia in a diabetic patient treated with large doses of insulin was first observed in 1927.¹ Various blood counts gave percentages of 12, 20, 11, 15, and 17.5, and a thorough investigation showed none of the usual causes of eosinophilia to be present. It therefore seemed possible that insulin therapy *per se* might be responsible for the abnormal blood count, and this point has been investigated in other diabetics. It has been found that, of the 20 insulin cases examined, 10 show an eosinophilia varying between 4 and 20 per cent.

Non-Insulin Diabetics.

As far as we are aware, no abnormal eosinophilia has been reported in diabetics. To control this point blood counts have been carried out on 12 diabetics who were not having insulin. In only one (and he suffers intermittently from eczema) has an eosinophilia of over 4 per cent. been found. The others are mostly between 0.5 and 2 per cent., the same as in the non-diabetic population attending our out-patient departments. An eosinophilia of 4 per cent. or over has therefore been taken as a definite degree in classifying our results.

Insulin Cases.

Twenty insulin cases, of all ages and degrees of severity, have been investigated. Of these, 10 have an eosinophilia of 4 per cent. or over, and 5 of 9 per cent. or over. The highest observed is 20 per cent. In none has there been any evidence of parasitic or skin diseases, and the only asthmatic had a low count of 1.6 per cent. No factors have been observed to account for the production of eosinophilia in half these cases and its absence in the other half, such as general allergic tendencies, varying skin reactions at the site of insulin injections, or variations in the diet followed. On the whole the eosinophilia bore no relation to the size of insulin dose, although one insulin-resistant case, on 200 units a day showed the highest figure. In a

INSULIN FAT ATROPHY A TRAUMATIC ATROPHIC PANNICULITIS.

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A PECULIAR form of local fat atrophy in the subcutaneous tissues following repeated insulin injections has been described, and a case was shown by me before the Clinical Section of the Royal Society of Medicine.¹ In all cases, despite instructions to the contrary, the insulin has been repeatedly injected into the one area instead of varying the site. The situation of the atrophy varies with the site of injection, the arms, thighs, and abdominal wall having been affected. A dimpling of the skin first appears, the depression then spreading in area and extending deeply. As a rule the underlying tissues are not affected, but where the injections have been given deeply the underlying muscle may also atrophy; the skin may adhere to the underlying tissues, but does not itself undergo any change in texture. Neurological changes are generally absent,^{2,3} the integrity of the somatic and sympathetic nerve supply being demonstrated by the presence of all forms of sensation, and the pilomotor (goose-skin) reflex on faradic and direct galvanic stimulation⁴; impairment of pain, tactile and thermal sensation may, however, occur.⁵ In one of the cases reported no sign of the atrophy remained two and a half years after ceasing injections, though the depression had been deep and distinctly felt through the clothing.⁶ The