For comparison the structures of the anticonvulsants mentioned above, in the enol forms, are:

It will be seen that in primidone and in phenobarbitone there is a six-membered pyrimidine ring, and that there is also a pyrimidine ring in the pteridine nucleus of pteroylglutamic acid—at (A). In phenytoin there is a five-membered hydantoin ring, but the general structural similarity of all four substances can be seen above. Epilepsy is a common disorder and anticonvulsant drugs are used in large quantities; megaloblastic anaemia from the use of phenobarbitone alone has not been recorded and its occurrence after phenytoin or primidone therapy is very rare. Nevertheless, in view of the structural similarities it is possible that in certain circumstances these last two substances act as competitive inhibitors of some enzyme system normally involving folic acid as a co-factor. Whether or not the coincidental administration of phenobarbitone is important has not been established, but it is surprising that primidone therapy should lead to megaloblastic anaemia while prolonged administration of the closely related phenobarbitone alone does not appear to do so.

Summary

An account is given of a patient who developed megaloblastic anaemia while under treatment with primidone and phenobarbitone. There was no response to injections of cyanocobalamin, but a good response occurred to folic acid therapy. Tests for folic acid excretion gave no evidence of malabsorption of synthetic folic acid. It is possible that primidone or phenytoin may in certain circumstances act as competitive inhibitors of some enzyme system normally involving folic acid as a co-factor.

Our thanks are due to Dr. J. K. Slater for allowing these investigations to be carried out on this patient, who was under his care.

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In the Invalid Children's Aid Association's annual report for 1954-5 it is stated that 1,503 delicate children were placed in Homes during the year. Of these, 1,107 went to recuperative holiday homes, 213 to boarding special schools, and 183 to convalescent homes belonging to regional hospital boards. The majority of the applications reach the association through health or education authorities. The association's case department has continued its work of helping children who are suffering from ill-health, emotional disturbance, or physical handicap. The work has been carried out from headquarters and from 17 local offices in London and the Home Counties by the association's 29 trained social workers, experienced both in family case work and in tackling the special problems presented by a sick or crippled child in the family. These workers have been assisted by a number of experienced voluntary workers, including several who have married or otherwise retired from their professional social work.

NYLON STOCKING DERMATITIS

BY

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Although many millions now wear nylon stockings, contact dermatitis from them is extremely rare. The first reference to dermatitis from dyed nylon stockings was by Dobkevitch and Baer (1947a, 1947b). They described 13 cases seen in the United States; all these patients were found to be sensitive to the dye but did not react to pure nylon. In France the condition has been reported by Sidi and Dobkevitch-Morril (1951) and Vial-Weissenbach (1954), but there have been no previous case reports from this country. Failure, however, to recognize the characteristic pattern of a stocking dermatitis may cause the diagnosis to be missed, as happened in most of the present cases.

FIG. 1.—Diagrammatic representation of areas usually affected.

Three sites are commonly affected—the dorsa of the feet and toes, the backs of the knees, and the inner part of the upper thighs (Fig. 1). The eruption may also involve the heels, the soles, and the plantar surfaces of the toes. It is usually symmetrical and may be acutely vesicular and exudative, or dry and scaly.

Case Reports

Case 1.—A housewife aged 51 complained of patches of eczema on the right side of the forehead and the nape of the neck for the past seven weeks. Four weeks later she developed a rash on the thighs, the bends of the knees, and the feet. It was noticed that the distribution of the rash conformed to the areas contacted by her nylon hair-net and nylon stockings. It was particularly marked where the strap of her shoes had pressed the stockings against the skin of the feet. She was told to wear no more nylon and was treated with a bland cream. The rash slowly faded in the course of the next year. During this time she tried wearing nylons on several occasions. Each time an exacerbation of the rash occurred after about three days.

Case 2.—A housewife aged 46 had suffered from a retro-auricular dermatitis for the past 10 weeks. This was followed by a weeping dermatitis behind the knees and an erythematous rash on the inner surfaces of the thighs and on the dorsal surfaces of the toes. The rash behind the ears cleared when she stopped wearing her hair-net, but relapsed when she wore it again a week later. She had suffered from urticaria in the past, but had no other skin disease.

Case 3.—A factory worker aged 44 had been treated for tinea pedis intermittently over a period of two years. One month previously she developed a rash which began over the soles of the feet on both sides. It spread up the legs, being particularly severe on the medial surfaces of the thighs and producing weeping patches behind the knees. She was

patch-tested to nylon stockings of three shades and gave positive reactions to all of them. She discontinued wearing nylon stockings and the rash healed up in the course of the following month. Three weeks later she developed blisters on both heels and on the dorsal surfaces of the toes. She found that at the time she had been inadvertently wearing rayon stockings reinforced with nylon at heels and toes. On ceasing to wear these the blisters healed. In the course of the next year she has had no further attacks of acute

FIG. 2.—Case 5. Dermatitis of dorsa of feet and toes.

FIG. 3.—Case 5. Dermatitis of soles of feet.

dermatitis. She did, however, develop an area of lichenified eczema behind the left knee, which was the more severely affected. She has since then developed transient patches of neurodermatitis on the neck and elbows. The legs had remained clear for three months when last seen.

Case 4.—A housewife aged 51 had suffered from a rash on the feet for five years. The eruption was intermittent, with exacerbations on Sunday afternoons and evenings. In the previous four months it had extended to the legs, particularly the backs of the knees and sides of the thighs. The axillae were later affected, but the trunk remained clear. She was accustomed to parade with the Salvation Army on Sunday mornings, wearing black nylon stockings. On examination there was a severe dermatitis of the soles and dorsal surfaces of the feet, the calves, the popliteal spaces, and the inner sides of the thighs. Both axillae were similarly affected, but the rest of the body was clear.

Case 5.—A nurse aged 30 noticed a rash on the right big toe five months previously. This was followed by an eczematous eruption on the sole of the foot. She was treated for tinea pedis without improvement, and the rash spread to involve all the toes and both heels. The development of blisters on the soles of the feet caused her to be

admitted to the wards with a diagnosis of podopompholyx. She was first seen by one of us (H. T. H. W.) at this time and treated with baths of potassium permanganate. Recovery was followed by relapse soon after resumption of work. An eczematous eruption then developed on the dorsal surfaces of all the toes, being most marked over the big toe (Fig. 2). There was a scaling rash on the soles of both feet, most severe under the arch of the foot on each side (Fig. 3). A patch of weeping dermatitis appeared in each popliteal space and an erythematous rash broke out on the inner side of both thighs and spread to encircle the thigh on each side (Fig. 4). A few years previously she had had a dermatitis attributed to plastic spectacle frames, but no other skin trouble.

Case 6.—A housewife aged 25 had suffered from an intermittent rash on the feet and legs once or twice every fortnight for the previous seven months. The inner sides of the thighs, the popliteal spaces, the dorsal surfaces of the toes, the heels, and the soles were all affected. She was accustomed to wear nylon stockings, which she washed with detergents. There had been no previous skin disease. On examination there were weeping eczematous patches behind both knees. The inner sides of the thighs, the dorsal surfaces of the toes, and the centre of each sole were also affected.

FIG. 4.—Case 5. Dermatitis behind knees and spreading up the thigh (severe case).

Discussion

It is agreed that the great majority of patients with dermatitis from nylon stockings are allergically sensitive to the dye. Two types of dye are used for nylon—azo and anthraquinone derivatives—but all the manufacturers of nylon stockings in this country use the azo variety, which has proved more satisfactory in practice. Three dyes of the primary colours—red, blue, and yellow—are used in varying proportions.

The ease with which the skin becomes sensitized to compounds containing an amino-group in the para-position on the benzene ring is notorious. Meltzer and Baer's (1949) patient (R.R.), who developed dermatitis from benzocaine, sulphaguanidine, *para*-aminobenzoic acid, as a result of cross-sensitivity to this particular grouping, is now immortal in dermatological history. However, one must not assume that a patient sensitive to one such compound will necessarily react to any other. Only a minority do in fact show such cross-sensitization. None the less, when patch-testing these patients it may be rewarding to test for sensitivity to other commonly used substances containing the "para-amino" grouping.

The patch test results in our patients are shown in Tables I, II, and III.

TABLE I

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Stocking . . .	+	+	+	+	+	+
Pure nylon . .	—	—	—	—	—	—

TABLE II.—Dyes. 1% Aqueous Solution

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Blue . . .	±	—	—	—	—	—
Yellow . . .	+	+	+	+	+	+
Red . . .	±	—	—	±	±	—
Black . . .	—	—	—	+	—	—
Anthraquinone dye	—	—	—	—	±	—

TABLE III

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Paraphenylenediamine 0.1% . .	—	—	—	+	—	—
Procaine 1% . . .	—	—	—	—	—	—
Sulphanilamide 5% . . .	—	—	—	—	—	—
Liq. azorubri 1% . . .	—	—	—	—	—	—
Benzocaine 2% . . .	—	—	—	—	—	—

The yellow dye was the cause in the five cases with dermatitis from ordinary nylon stockings. The patient with trouble from black nylon stockings (Case 4) reacted to the black dye as well as the yellow one.

All the patients were tested for cross-sensitivity to procaine, sulphanilamide, liquor azorubri, paraphenylenediamine, and benzocaine. The only positive was Case 4, who reacted to paraphenylenediamine.

Another possible cause of dermatitis from nylon stockings is the coating of synthetic resin used to give the so-called "snag" finish. Outbreaks of dermatitis resulting from the resin fabric finish used on a synthetic silk substitute fibre have been reported from Canada and the U.S.A. (Schwartz *et al.*, 1940). These resins are usually of the urea formaldehyde or melamine formaldehyde type. Our patients were tested to these resins (1% in soft paraffin) with negative results. The reason why these known sensitizers do not often cause dermatitis is almost certainly the fact that they are so readily removed by washing.

Turning to the practical aspects, one may ask if any substitute is available. We have been unable to find a brand of nylon stockings incorporating anthraquinone dyes. However, one manufacturer has agreed to make such stockings at our request. Patch tests to these dyes were negative in our patients, and they have all been wearing this type of stocking without developing any further trouble.

Not all black nylon is dyed with azo dyes. Instead a logwood dye is used by some firms. The patient with dermatitis from black nylon stockings can wear stockings treated in this way.

Summary

Six cases of dermatitis from nylon stockings are presented. All showed a similar and characteristic pattern.

The dermatitis was traced to an azo dye. An alternative dye was well tolerated.

We are grateful to Dr. F. R. Bettley and Dr. R. H. Meara, who kindly allowed us to investigate two of their patients. We wish to acknowledge help and advice from Mr. Symons, chief chemist of Kayser Bondor Ltd., Baldock, Herts, and also of Imperial Chemical Industries.

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A FORM OF INTERSEXUALITY

BY

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In 1938 Broster *et al.* described several degrees of intersexuality and discussed the methods of control, especially in relation to the masculinizing effects of the adrenal cortex, its role as a bisexual accessory sex organ, and its relationship to the pituitary gland.

More recently the difficult question of sex determination in children has been advanced by more than a decade, from puberty to infancy, by the discovery by Barr (1955), of Canada, of the female speck of chromatin lying in relation to the nucleus of skin cells. The method offers a very high degree of accuracy, for in only one test—that of a hermaphrodite with bilateral ovotestes—did his result not conform to the predominant sex of the patient.

The diagnosis at an early age lies between: (1) The adrenal pseudohermaphrodite with adrenal hyperplasia, a high ketosteroid excretion, uterus, tubes, and impaired ovaries. (2) The true hermaphrodite, with either ovotestes or an ovary on one side and a testis on the other, uterus, and tubes. (3) The intersex with uterus, tubes, and embryonic testes in the position of the ovaries. (4) The cryptorchid with abdominal testes in various stages of maturity and descent, but with absent uterus. All these have hypospadias with an enlarged phallus.

This clinical generalization reflects a persistence to a varying degree of the foetal sexually undifferentiated condition.

Up to the 50 mm. (about the 11th week) stage of the human embryo the development of the male and female external genitalia is identical. In the female the external genitalia remain in a relatively undifferentiated state, while in the male the developing process is continued to its final form. From the walls of the cloaca and urogenital sinus the urethral plate grows forwards (Glenister, 1954). It gives rise to a groove bounded on either side by two urethral folds. In hypospadias these folds, in various stages of fusion, run forwards, diverging slightly to reach the under surface of the glans of a malformed phallus.

In the female these folds remain apart to form the labia minora, whereas in the male they fuse along the ventral aspect of the phallus, leaving a median raphe on the surface. The urethra may open along any part of its course. Boys with this form of anatomy may be brought up erroneously as girls.

It is obvious, however, that two extreme forms of hypospadias can be recognized. One predominantly female, with an open urethral groove and enlarged clitoris; and the other predominantly male, with a partly fused urethral groove and a small flexed penis with prepuce. To the former type the adrenal pseudohermaphrodites tend to conform, whereas the three cases under review belong to the latter.

In 1952 I was sent a child (Case 1) and made a diagnosis of the more common condition—adrenal pseudohermaphroditism. The only difference was that the clitoris was more penile in its development. It came as a surprise that the ketosteroid excretion was within normal limits and not raised as it should have been. A