

which did not persist for as much as three months in the year. Sitting height was not found to be significantly related with P.E.F. when allowance was made for age.

The College of General Practitioners (1961) also found a similar rate of decline of mean P.E.F. with age in non-bronchitic subjects, and their values were uniformly lower than those found among "normal" men as defined in this study. The College of General Practitioners gave figures for non-bronchitic women indicating a rate of decline of P.E.F. with age about half that experienced by the men.

Higgins (1960, personal communication) found that the decline of P.E.F. with age in symptom-free men in the population he studied was similar to that found in our sample, and parallel to the decline in P.E.F. in symptom-free women. His values for P.E.F. in symptom-free men were a little higher than those given here. The values for P.E.F. in symptom-free women were approximately 200 l./min. lower than values for symptom-free men in the same age-group.

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DERMATITIS MEDICAMENTOSA

BY

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Contact dermatitis caused by medicaments is a common complication in the treatment of skin diseases. It is this violent reaction to some topical application which often necessitates referral of the patient to hospital. While it is true that one cannot practise dermatology without occasionally causing dermatitis medicamentosa, it is as well to recognize and avoid those substances which are frequent sensitizers. In an attempt to assess the relative dangers of topical applications commonly used in the Sheffield area, a survey of all patients who attended the department of dermatology suffering from dermatitis medicamentosa between July, 1959, and July, 1960, has been undertaken.

Present Investigation

A total of 136 patients thought to be suffering from dermatitis medicamentosa were investigated. The diagnosis was confirmed by positive patch tests in 117. When a patch test was negative it was repeated on skin that had been stripped by repeated applications of "cellophane" tape (Wells, 1957). If multiple patch tests were indicated, these were performed a few at a time; none were performed in the presence of widespread active disease.

The offending applications were prescribed in this department in 9 cases, obtained without prescription in 21, and prescribed by a doctor in 87. The results of all patch tests are given in the Table. Of the applications

mentioned, only chlortetracycline cream, neomycin ointment, and cromitron ("eurax") cream are used in this department; the incidence of proved sensitization to these in a three-month period was 0.09%, 2.7%, and 4.6% respectively.

Results of Patch Tests

| Preparation | Offending Constituent | Positive Patch Test | | |
|-------------------|------------------------|---------------------|---------------|-------|
| | | Normal Skin | Stripped Skin | Total |
| "Chloromycetin" | Chloramphenicol Base | 18 1 | | 19 |
| | Cinchocaine | 16 | | 17 |
| "Locan" | Amethocaine | 1 | | |
| "Proctosedyl" | Cinchocaine | 12 | | 12 |
| "Caladryl" lotion | Diphenhydramine | 2 | 10 | 12 |
| "Anthisan" cream | Mepyramine maleate | 3 | 9 | 12 |
| "Aureomycin" | Chlortetracycline Base | 2 8 | | 10 |
| | "Eurax" | 6 | | 6 |
| "Menopax" | Benzocaine | 5 | | 6 |
| | Amethocaine | 1 | | |
| Neomycin ointment | Neomycin sulphate Base | 2* | 4 | 6 |
| | "Dettol" | 8 | | 8 |
| "Kilgerm" | | 5 | | 5 |
| "Germolene" | | 4 | | 4 |

*By exclusion.

Discussion

These results clearly confirm the known dangers of topical applications of local anaesthetics and antihistamines. Cinchocaine appears to be the most potent sensitizer among the former, though benzocaine and amethocaine may produce sensitization. The presence of hydrocortisone in the preparation does not prevent dermatitis medicamentosa, as proctosedyl was a common offender. Of the antibiotics, chloramphenicol still tops the list as the most potent sensitizer, though its dangers have been recognized for many years (Sneddon, 1957). Chlortetracycline seems to be the safest local antibiotic (cf. Sarkany, 1960); of the 10 patients in this series sensitive to this application only two were sensitive to the antibiotic itself. Sarkany (1960) has reported one case which was sensitive to parabens contained in the base of aureomycin cream, but six of our patients were sensitized to a locally produced chlortetracycline cream in which the base was anhydrous "eucerin."

Considerable difficulty was found in proving sensitivity to local antihistamines and neomycin. With regard to the former, it is interesting that trouble seemed to occur more often when the application was used on an eroded surface, and it was this observation that led us to use the stripping technique, which was found to be both easy and reliable. Calnan and Sarkany (1958) had the same experience with neomycin, and suggested the use of an intradermal test with neomycin sulphate (1%), while Phillips (1946) used a scratch test to confirm sulphonamide sensitivity. In the present group the intradermal test with neomycin sulphate was performed in all patients thought to have neomycin sensitivity, and the results were exactly similar to those obtained with the stripping technique.

It is, of course, impossible to assess the true incidence of sensitivity to those drugs not used in this department, though Eckersley, Dunlop, and Catterall (1960) have reported an 8% incidence of sensitization to locan in patients treated for trichomonal vaginitis with this preparation. In the case of the other preparations, we can only point out those which appear to give the greatest trouble.

Summary

A review of 117 patients suffering from dermatitis medicamentosa seen in the Rupert Hallam Department

of Dermatology in one year demonstrates the dangers of topical applications of local anaesthetics (especially cinchocaine), antihistamines, and chloramphenicol. Of the local antibiotic ointments, chlortetracycline seems to be the safest.

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Preliminary Communications

Favism in an Englishwoman

Favism is a form of acute haemolytic anaemia induced by eating broad beans (*Vicia faba*) or by contact with their pollen in sensitive subjects. There is an ethnic and familial predisposition to the disease, which is common in Mediterranean countries (Luisada, 1941) but rarely seen in north-western Europe.

In Britain the condition has been reported in a few patients of Mediterranean or Iraqi ancestry (Diggle, 1953; Discombe and Mestitz, 1956; Gower and Frommer, 1960), and McCarthy (1955) described the case of a 9-year-old English boy, with no known foreign antecedents.

It is now known that favism is one of a group of anaemias induced by chemical or vegetable substances, in which the common factor appears to be a metabolic defect, inherited in a sex-linked manner with incomplete dominance (Childs *et al.*, 1958). This abnormality is characterized by a deficiency of an enzyme, glucose-6-phosphate dehydrogenase (Carson *et al.*, 1956; Larizza *et al.*, 1958) in the red cells, resulting in a diminished glutathione level (Grignani and Brunetti, 1958).

CASE HISTORY

The patient, a companion housekeeper aged 52, has been a moderately severe but stabilized diabetic for 30 years. During routine visits to the diabetic clinic she reported seasonal attacks of malaise, diarrhoea, abdominal pain, and headache, usually associated with jaundice and occurring about June or July every year, starting in 1944. They were so regular that she deferred her annual holiday until September, when she felt "safe." She had always recovered by the time she next attended the clinic. On examination between attacks there were no abnormal physical signs, and blood counts and two cholecystograms were normal. She was asked to consult us again during her next attack, and we were called to see her at home on June 25, 1960. She had been in normal health, and had taken no drugs other than her usual brand and dose of insulin. On June 16 she ate broad-bean tops, cooked as a green vegetable, for the first time in that year. On June 20 she had a meal of cooked broad beans and a second meal of beans on June 22. That night her urine became dark in colour. The next day she developed headache and diarrhoea, with abdominal pain, especially in the left hypochondrium, and became jaundiced. She was admitted to hospital on June 25.

On examination she was deeply jaundiced, but no other abnormal physical signs were found, and the liver and spleen

were not palpable. Her urine was almost black, and contained large amounts of glucose, acetone, and methaemoglobin. The results of laboratory tests were as follows: blood sugar, 442 mg./100 ml.; haemoglobin, 6.9 g./100 ml. (47%); reticulocyte count, 15%; serum bilirubin, 6 mg./100 ml. The other usual liver-function tests were normal. Blood film showed the erythrocytes to be mainly normocytic and normochromic, but numerous disrupted cells were present, with some basophils and normoblasts. The Coombs antiglobulin reaction, the Wassermann and Kahn reactions, the Donath-Landsteiner test, and tests for red-cell sickling and cold agglutinins were negative. A diagnosis of favism was made. Two days later her incipient diabetic coma had been controlled, but the haemoglobin had fallen to 4.4 g./100 ml. (30%), red cells numbered 1,300,000/c.mm., and the reticulocyte count had risen to 21%. The total white-cell count was 32,000/c.mm. (neutrophils 84%, lymphocytes 16%).

She was treated by a transfusion of 1 litre of blood, prednisolone 5 mg. six-hourly, and promethazine hydrochloride ("phenergan") 25 mg. three times daily. She made a strikingly rapid recovery, her haemoglobin level being 9 g./100 ml. (62%) after 10 days, and she was discharged on the nineteenth day. The only further treatment was oral iron. She avoided all contact with broad beans, and soon returned to her usual good health with a normal haemoglobin level. Subsequent laboratory investigations have shown that the osmotic red-cell fragility and faecal urobilinogen excretion are normal; and no foetal haemoglobin, abnormal adult haemoglobin, or raised haemoglobin A₂ has been detected. A skin-sensitivity test using broad-bean extract by the scratch method was negative on July 14 and October 3, 1960.

More recently the test described by Beutler *et al.* (1955) for detecting "primaquine-sensitive" red cells has been carried out. Fresh heparinized blood is incubated with a buffered solution of acetylphenylhydrazine and glucose, then examined microscopically as a wet preparation with crystal violet for the presence of Heinz bodies. The test is regarded as positive if more than 32.5% of red cells show five or more Heinz bodies. The patient's blood was positive by this test, 38% of red cells containing multiple Heinz bodies, compared with 3% of a normal control.

The patient's erythrocytes have also been investigated for the presence of glucose-6-phosphate dehydrogenase, and no detectable level has been found by the dye method of Motulsky and Campbell (1961) nor by a quantitative assay method. This confirms the clinical diagnosis.

Family History.—The patient is a member of a large family whose records show that they have lived in the Hastings area of Sussex since the year 1820 at least. Many members of the family have now been interviewed. They insist that there are no known foreign antecedents, and there is no Jewish or gypsy blood in the family. An investigation of this family is in progress, and it has been found that glucose-6-phosphate dehydrogenase is greatly reduced in the father's red cells, and diminished in those of two of the patient's sisters. No brothers who have been examined are affected. No member has suffered from any similar illness. It is hoped to report this study in detail later.

DISCUSSION

Broad beans, in common with aspirin, phenacetin, sulphonamide, primaquine, and many other compounds listed by de Gruchy (1960), may produce haemolysis in patients with this genetic abnormality. The title "enzyme-deficiency haemolytic anaemias" has been suggested by Larizza *et al.* (1960) to include all these conditions. In addition Doxiadis *et al.* (1961) have described a type of neonatal jaundice which falls into the same category. Not all subjects with this defect are sensitive to the fava bean (Roth and Frumin, 1960), and the first attack may not take place until late in life.