T. 98° F. (36.7° C.); P. 82. 10/5/46: T. 97° F. (36.1° C.); P. 80. Breasts normal. Penicillin discontinued. Total dosage, 300,000 Oxford units.

Case 8.—Primipara, aged 25. Delivered at another hospital and admitted 9/5/46 on account of an infected perineal laceration, for which she was being treated with sulphamezathine. The baby was not admitted. 10/5/46: T. 100° F. (37.8° C.); P. 100. Tender flushed left breast. Lactation suppressed with stilboestrol. Penicillin begun and sulphamezathine discontinued. 11/5/46: T. 100° F. (37.8° C.); P. 104. Slight flush and tenderness over an area the size of a penny. 12/5/46: T. 99.6° F. (37.55° C.); P. 86. Breasts normal. 15/5/46: T. 98° F. (36.7° C.); P. 80. Penicillin discontinued. Total dosage, 500,000 Oxford units.

Case 9.—Para-3, aged 32. 5/6/46: Normal delivery. Breast-feeding begun. 12/6/46: T. 99.6° F. (37.55° C.); P. 90. Outer and lower quadrant of left breast flushed and tender. Penicillin started. 13/6/46: T. 97.6° F. (36.4° C.); P. 88. Flush almost gone. Slight tenderness. 14/6/46: T. 97.8° F. (36.55° C.); P. 86. Breast normal. 18/6/46: T. 97° F. (36.1° C.); P. 80. Penicillin discontinued. Total dosage, 500,000 Oxford units.

Case 10.—Para-2, aged 26. 9/6/46: Normal delivery. Breast-feeding begun. 17/6/46: T. 100° F. (37.8° C.); P. 120. Flush, tenderness, and induration in inner and lower quadrant of right breast. Penicillin started. 18/6/46: T. 98° F. (36.7° C.); P. 110. Severe pain in breast. Stilboestrol 3 mg. As breast-feeding did not increase the pain it was continued. 19/6/46: T. 97° F. (36.1° C.); P. 84. Flush decreased. Localized hardening the size of a walnut. 20/6/46: T. 97.6° F. (36.4° C.); P. 84. Breast normal. 22/6/46: T. 97.6° F. (36.4° C.); P. 72. Penicillin discontinued. Total dosage, 500,000 Oxford units.

Comment

The above constitute the total number of cases of acute puerperal mastitis seen in the Princess Mary Maternity Hospital between November, 1945, and July, 1946, during which time 1,537 deliveries took place. In these cases there was quick resolution, with no prolonged disorganization of the breast; in only one instance did suppuration occur, and this was treated by closed aspiration. Lactation was not interfered with, and breast-feeding was maintained except in Case 8, where the baby was not admitted to hospital. The total period of disability was not longer than 7 days, and discomfort was never present for more than three days. The following table shows the length of time taken to achieve a cure as judged by the disappearance of all signs.

2 cases were cured in 2 days	
4 " " "	3 "
1 case was "	4 "
1 " " "	5 "
1 " " "	6 "
1 " " "	7 "

No baby became infected as a result of the continued suckling. There were no recurrences after the cessation of treatment.

These results are in such great contrast to those of the usual methods that the treatment seems worthy of an extended trial, for it appears that, provided early treatment is instituted, penicillin can abolish the morbidity of this painful and crippling puerperal complication. Our results are in agreement with those of Hodgkinson and Nelson, who suggest that, owing to the ineffectiveness of sulphonamide therapy in this disease, it should be entirely replaced by penicillin.

We wish to thank Dr. Jean Grant and Dr. G. I. Isaacs for their assistance in treating these cases.

REFERENCES

- Hodgkinson, C. P., and Nelson, R. E. (1945). *J. Amer. med. Ass.*, **129**, 269.
Hudson, R. Vaughan (1944). Progress Report to the Penicillin Committee. Middlesex Hospital.

Two motion pictures on tuberculosis case-finding with miniature film mass radiography of the chest have just been completed for the U.S. Public Health Service, under the supervision of the Tuberculosis Control Division. The films demonstrate the techniques, the staff, procedures, and equipment required for: (1) routine admission miniature film chest x-ray examination of all patients and personnel entering general hospitals; (2) miniature film mass radiography in community tuberculosis case-finding programmes. These are teaching and orientation films for an audience of professional, technical, or administrative personnel, or trainees, in the fields of medicine, public health, and hospital care. The film prints are 16 mm. size, black and white, with sound. They may be purchased from Castle Films, Inc., 30, Rockefeller Plaza, New York 20, N. Y.: routine admission chest x ray in general hospitals, \$23.00 per print; techniques of group chest x ray services, \$21.00 per print.

USE OF "BENADRYL" FOR PENICILLIN URTICARIA

PRELIMINARY REPORT

BY

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"Benadryl" (β -dimethylaminoethyl benzhydryl ether hydrochloride) is a synthesized chemical compound said to possess both anti-allergic properties and antispasmodic activity capable of relieving spasms of smooth muscle. This antihistamine agent is administered orally in the form of capsules, the dose for an average adult being one capsule (50 mg.) three or four times daily. Its toxic effects are said to be minimal but include a sensation of drowsiness and nausea. In consequence the simultaneous administration of barbiturates or opium derivatives should be conducted with caution. During the past year this drug has been undergoing extensive trials in the United States of America, and has shown encouraging results as a palliative for urticaria, angioneurotic oedema, serum sickness, and erythema multiforme; while hay-fever and vasomotor rhinitis have also been treated.

One of its uses in the U.S.A., and doubtless soon on this side of the Atlantic too, is the symptomatic treatment of urticaria occurring in patients undergoing penicillin therapy. This condition, which may arise at any time during treatment, often becomes apparent at the end of a 7½- or 12-day course in the treatment of syphilis. Generalized urticaria may be associated with oedema of the eyelids, swellings of the ankles or wrists, and effusions into joints, and, when treated symptomatically by means of adrenaline and ephedrine, usually takes 3 to 5 days to subside completely. The frequency of this complication depends to some extent on the particular batch of penicillin used or on the medium in which it is prepared. In America the early penicillin in oil-beeswax mixtures were said to be more liable to cause urticaria than penicillin in aqueous solution. It is therefore likely that this drug will be widely used in this connexion and the preliminary reports from America are most encouraging.

The following describes the action of "benadryl" on six cases of urticaria, five of which were considered to be due to intramuscular penicillin therapy. The penicillin used throughout was manufactured on Feb. 6, 1946, by the Distillers Company, Ltd.; the batch number was 0025.

Case I

A young man of 24, suffering from congenital syphilis with interstitial keratitis. The blood Wassermann was strongly positive and the quantitative Kahn 10 units. The cerebrospinal fluid had a protein value of 80 mg. per 100 ml. and contained a slight excess of globulin, but was otherwise normal. There was no history of previous allergy. In April, 1946, he received 720,000 units of penicillin in 36 three-hourly injections for a septic throat following dental extraction.

Present Attack.—Between Aug. 3 and 3 a.m. on Aug. 16, 1946, he was given a total of 4,000,000 units of penicillin (40,000 units every three hours). Some complaints were made of local pain after these injections. At 10 a.m. on the 17th there was slight urticaria, with a small lesion below the left eye and a larger one on the left flank. When seen again at noon, four more lesions had appeared on the extensor surface of the right forearm. One capsule (50 mg.) of "benadryl" was given t.i.d. for one day, and by the following morning the urticaria had entirely subsided and there was no recurrence. No untoward reactions were noted. The maximum temperature recorded during the attack was 99° F. (37.2° C.), and a blood count on Aug. 19 showed: W.B.C., 8,800 per c.mm. (polymorphs, 48.5%; lymphocytes, 44%; mononuclears, 4%; eosinophils, 3.5%).

Case II

Male aged 38, with a diagnosis of latent syphilis. This was discovered in August, 1945, when the cerebrospinal fluid was normal but the blood Wassermann was strongly positive and the quantitative Kahn 20 units. Since then, though antisyphilitic treatment had been continuous, at the time of admission the Wassermann was still strongly positive and the quantitative Kahn 2 units. There had been a previous attack of urticaria following an injection of antitetanic serum while in India in 1935. In September, 1945, he received

2,400,000 units of penicillin over 7½ days without ill effect. This was consolidated with two full courses of neoarsphenamine and bismuth, which were completed in July, 1946.

Present Attack.—Penicillin therapy was begun on July 26, 1946, and injections of 40,000 units were made every three hours. On Aug. 6, when 3,120,000 units had been administered, generalized urticaria developed involving the back, thighs, wrists, and knees. There was no pyrexia, and a blood count on this day showed the W.B.C. to number 8,800 per c.mm. (polymorphs, 52%; lymphocytes, 41%; mononuclears, 4.5%; eosinophils, 2%; basophils, 0.5%). One capsule (50 mg.) of "benadryl" was then administered orally. By the following day there was some improvement, and the dose was increased to one capsule t.d.s. By the 8th further improvement was evident, there remaining only a few scattered erythematous patches. Three more capsules were given, making a total dosage of 350 mg. given over 2½ days, and by the next day the skin was quite clear.

While the result was not dramatic, the improvement was steady and maintained. The usual duration of such a severe reaction before improvement is manifest is, in my experience, about 4 days.

Case III

Man aged 29, with a diagnosis of sero-positive primary syphilis. There was no history of allergy or of previous penicillin treatment.

Present Attack.—Between July 17 and 24, 1946, a total of 2,400,000 units of penicillin were administered in conjunction with 10 daily intravenous injections of 0.06 g. of mapharside. The arsenic injections were completed on the 28th, at which time a white cell count showed W.B.C., 8,000 per c.mm. (polymorphs, 61%; lymphocytes, 33.5%; mononuclears, 4.5%; basophils, 1%). On this day he developed severe generalized urticaria of left thigh, buttocks, and both legs. He was given two doses of adrenaline 10 min. (0.6 ml.) and tab. ephedrin. 1/2 gr. (32 mg.) t.i.d. On the 29th the urticaria was unchanged in severity, and one capsule of "benadryl" (50 mg.) was prescribed t.d.s. By the following morning four capsules (200 mg.) had been taken, but the urticaria was worse, and it was decided to give a further 10 minims of adrenaline in addition. This time the administration had rather alarming results. The patient at once became pallid, developed a rapid thready pulse, and collapsed. As he recovered, his temperature rose within an hour to 101° F. (38.3° C.). A blood count gave the following results: R.B.C., 5,030,000; Hb, 99%; W.B.C., 13,300 (polymorphs, 83.5%; lymphocytes, 13.5%; mononuclears, 2%; basophils, 1%). At this time it was thought that the severe reaction to the adrenaline might in some way be aggravated by the concurrent administration of "benadryl." Both drugs were therefore discontinued.

On the 31st the general condition was much improved, though intense pallor persisted. The urticarial lesions were still pronounced on the thighs and chest, and the temperature was 99° F. (37.2° C.). Ephedrine 1/2 gr. (32 mg.) t.i.d. was then renewed, and by the following day the lesions were subsiding, though the temperature remained at the same level. The patient continued with the ephedrine and by the 8th the skin was normal, but the temperature was still 99° F. He was discharged to duty on Aug. 14.

Case IV

A youth of 18½ with recurrent impetigo; the lesions were on the face and behind the ears. There was no history of previous allergy. In June, 1946, he had been admitted to hospital with impetigo of the face, and was treated with penicillin cream for two weeks. Two weeks after discharge the condition relapsed, and he was readmitted and treated with penicillin cream for a further week. After another week at his unit, a second relapse occurred, and he was admitted to hospital again on Aug. 3.

Present Attack.—He was treated locally for 4 days with penicillin cream, after which time intramuscular injections of penicillin were given. When he had received 8 three-hourly injections to a total of 320,000 units he developed a generalized urticaria and had a temperature of 101° F. (38.3° C.). Three capsules of "benadryl" (150 mg.) were given over 24 hours with entirely satisfactory results, the urticaria disappearing.

Case V

A 19-year-old youth, with impetigo (beard area), giving a history of penicillin sensitivity. He was admitted to hospital on July 22, 1946, having been treated elsewhere with penicillin cream for impetigo of the face. He thought this had made the condition worse. He was then treated with intramuscular penicillin for 26 three-hourly injections of 40,000 units up to a total dose of 1,040,000 units, and at the same time a gentian-violet lotion was applied to the face. The local condition showed considerable improvement, but on July 30 penicillin cream was again applied and the skin relapsed.

Present Attack.—On Aug. 11 it was decided to give him a further course of penicillin, but by the next day he had severe generalized urticaria with oedema of the eyelids, swelling of both wrists, and an effusion in both knee-joints. Three capsules of

"benadryl" (150 mg.) were given on that day, and on the 13th the urticaria had gone, though the oedema around the eyes and wrists persisted. This too had subsided by the next day, and the "benadryl" was continued until a total dose of 450 mg. had been given over 3 days with entirely satisfactory results. On the following day, however, there was a relapse, both of the oedema around the eyes and wrists and also of the urticaria. This time it was treated by ephedrine, and the condition subsided gradually over 5 days. The temperature was normal throughout.

Case VI

A youth aged 18. The diagnosis in this case was giant urticaria and drug sensitivity. There was no history of previous allergy or sulphonamide administration. The patient was a seborrhoeic subject and had some lesions of seborrhoeic dermatitis on the chest of some two months' duration.

He was admitted on July 19, 1946, with an acute oedema of his penis giving it a corkscrew appearance. He had always had phimosis. There was no evidence of subpreputial or urethral discharge, and his Wassermann and Kahn reactions later proved negative. He was given two divided doses of adrenaline μ viii (0.5 ml.) and ephedrine gr. 1/2 (32 mg.) t.i.d., and a course of sulphathiazole, 1 g. 4-hourly, was begun. Next day, there being little change, the treatment was repeated. By the 22nd, however, after receiving 15 g. of sulphathiazole, there appeared a generalized toxic erythema and the scrotum also became oedematous. This was ascribed to the sulphonamide, and the drug was discontinued. A blood count showed: W.B.C., 17,500 (polymorphs, 72%; lymphocytes, 25%; mononuclears, 2.5%; eosinophils, 0.5%). On the 23rd the skin in both groins was weeping. He was treated with calamine lotion and luminal gr. 1/2 thrice daily, and showed steady improvement, as the generalized erythema faded and the weeping areas dried and became inactive.

Present Attack.—On July 27, after receiving a total of 6 gr. (0.4 g.) of luminal, there was slight swelling of the dorsum of the left hand. On the 28th the dorsa of both hands had swelled and two bullae had appeared in the third and fourth finger clefts on the right side, and both thighs, moreover, showed large erythematous and urticarial patches. Treatment was started with "benadryl," a capsule (50 mg.) t.d.s., with very satisfactory results in so far as the urticaria and the oedema subsided within 24 hours. The bullae, however, noticeably increased in size, and four developed on the dorsum of the right hand and one at a similar site on the left. It was then decided to aspirate these as they interfered with flexion of the fingers: some 5 ml. of clear fluid was withdrawn from each. By the 30th no more urticaria had appeared, and the "benadryl" was discontinued after 450 mg. had been given; though the bullae had to be aspirated again on this date.

Improvement was then rapid, and, apart from peeling of some skin that had been affected by the bullae, by Aug. 2 there was no lesion requiring treatment. On the 5th another attack of swelling of the penis and an exacerbation of the seborrhoeic lesions in the groin occurred. As with the previous attacks there was no elevation of temperature, and a blood count showed the W.B.C. to number 10,500 (polymorphs, 63%; lymphocytes, 32%; mononuclears, 3.5%; eosinophils, 1%; basophils, 0.5%). This relapse was treated with "benadryl," one capsule (50 mg.) three times a day. There was great improvement within 24 hours, and by 48 hours the oedema had completely subsided. A total dose of 450 mg. was given for the relapse.

Summary

An account is given of 6 cases of urticaria treated with "benadryl," of which 5 were associated with intramuscular penicillin therapy.

The doses ranged from 150 to 450 mg. in each case.

A reaction was noted in one patient who received concurrent adrenaline.

The results obtained showed success in five cases and failure in one (Case III). Two of the successes relapsed (Cases V and VI), one of which was again treated with the drug with a satisfactory result.

I am grateful to Major B. Schwartz, R.A.M.C., and Major L. Sefton, R.A.M.C., for their help, and to Messrs. Parke, Davis and Co. for kindly supplying me with the "benadryl."

In a White Paper entitled *Organization of the Colonial Service*, recently issued by the Colonial Office, the need for large reinforcements is stressed. Government policy aims at progressive self-government by the peoples in the Colonies, and it is from them that many of the recruits must be drawn. The potentialities and abilities of these peoples have been neglected in the past; they lack the opportunities for education available to candidates in the United Kingdom and Dominions; so the creation of educational facilities will be immediately undertaken by the Government, and the sum of £1,000,000 has already been allocated over the next ten years to enable selected Colonial candidates to receive higher education.