dosage of the drug is reduced, smaller doses being tolerated (Tedder, Cases 2 and 3). (3) Eruptions due to a combined effect of sulphanimide and light. In the first two groups the rash is more or less generalized; in the third it occurs mainly or wholly on surfaces exposed to light. Our case falls into the last group, since the rash was almost entirely limited to exposed parts and was quite sharply demarcated at the collar and elbow. The patient had been working in the open, but the weather had been dull and changeable, with little direct sunshine. This is possibly a point of some importance.

It is not definitely known exactly what part is played by light in cases belonging to the third group. Schölzke (1938) recorded a series of cases in which the patients were given uleron and exposed to ultra-violet light. No change in light-sensitivity could be demonstrated. A similar series, also with negative results, was mentioned by Eidinow (1939), who used sulphanimide instead of uleron. From this it is clear that an increase in sensitivity to light is at any rate not a constant sequel to sulphanimide medication. On the other hand, Newman and Sharlit (1937) and Brunsting (Tedder, 1939) have been able to produce a spread of an already existing rash to unaffected parts by exposing them to ultra-violet light.

As Tedder points out, this may be due to a non-specific effect of the light, producing a slight degree of irritation which determines the site of the rash. This phenomenon is well known to occur in rashes of widely different types, in which irritation due to light seems to produce a *locus minoris resistentiae*. This might have happened in the case mentioned by Hallam, but in our case exposure to light was so trivial—and this on parts habitually exposed—that even the slightest degree of irritation cannot be presumed. We are therefore bound to assume that light-sensitivity was present. This may have arisen in two ways, as suggested by Newman and Sharlit (1939): either there is a direct light-sensitization caused by the drug, as is produced by fluorescent compounds such as eosin, or sensitization is indirectly due to the drug by the production of porphyrins. The first hypothesis is made unlikely by the experiments of Schölzke and of Eidinow, since if sulphanimide had this effect it should be regularly observed. Light-sensitization by porphyrins remains and appears to fit the facts; the production of porphyrins is known to occur when sulphanimide is given, and their quantity to vary considerably in different cases. Unfortunately in neither Hallam's nor our case were examinations made for these substances. Brunsting, however, observed two cases of this type of eruption in which urinary porphyrins were much above normal. It may be remarked that the presence of cyanosis due to porphyrinaemia does not always go hand in hand with light-sensitivity. This is probably due to the fact that different porphyrins have different sensitizing powers when present in the blood stream. The present evidence points, therefore, to porphyrinaemia as the cause of light-sensitization following sulphanimide medication.

It is of further interest to note that in *hydroa aestivale* a bullous eruption following exposure to light is associated with haematoporphyrinaemia.

We are indebted to Dr. E. Colston Williams, medical officer of health for Glamorgan, for permission to publish this case.

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OBSERVATIONS ON THE AGGLUTINATION TEST FOR WEIL'S DISEASE

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Although in principle this test is essentially similar to a bacterial agglutination test, difficulties have been met with which would mask or invalidate the results in the hands of an inexperienced observer. In the first place, though all the strains of the organism which we have used have been isolated from patients in England whose sera have reacted strongly to the standard London human strain of *Leptospira icterohaemorrhagiae*, only certain of these strains are suitable for the agglutination test. To take a typical example, five human strains of *L. icterohaemorrhagiae* were subcultivated in Fletcher's broth until the growth in each of the cultures was sufficiently vigorous to be apparently suitable for the agglutination test. The cultures were then formalized to exactly 0.2 per cent. One serum was put up against these five cultures, using Schüffner's technique, in dilutions ranging from 1 in 10 to 1 in 30,000. The result of this was as follows: one strain showed no agglutination; one was positive up to a serum dilution of 1 in 100; one was positive up to 1 in 300; and two were positive up to 1 in 1,000. The technique employed in this case was twenty-four hours' interaction at room temperature. The results were read with a microscope, 2/3-inch objective and $\times 10$ ocular with dark-ground illumination, no cover-slip being used. This serum consistently gave a titre of 1 in 3,000 with our standard formalized culture. By "standard" culture we do not mean that it has been standardized after the manner in which the Oxford bacterial cultures are standardized, but merely that for the last five years it has been known to give consistent and repeatable results.

We have some reason to believe that cultures which have been quite recently formalized are not agglutinated to so high a titre as those formalized for forty-eight hours or more. The question of formalization of the cultures has not presented any difficulty, and we have not met with the acid agglutination referred to by Professor Schüffner. We have always used analytical reagent formalin, and have not added more than 0.2 per cent.

From time to time a macroscopic agglutination technique has been advocated, and there is no doubt that when a suitable antigen can be obtained a florid serum will give a positive result after one hour's incubation. Pot (1936) advocates a macroscopic test, and claims that out of twenty-six known positive sera twenty-five gave a positive reaction with his method. In our experience the macroscopic method is not nearly so sensitive as the microscopical, and we are of opinion that certain sera of low titre, such as those met with shortly after the sixth day of disease, may be missed if the macroscopic test is employed. Using the microscopical procedure the titres obtained by Brown (1935) approximated very closely to those obtained by Professor Schüffner when a series of sera were examined by both observers.

Technique of the Test

When examining a serum it is necessary to put up a known positive serum in all dilutions at the same time. This will indicate any change in agglutinability of the

antigen. We have known formolized antigens which have been perfectly satisfactory for six months to have suddenly lost their agglutinability. Occasionally sera are met with which, when examined under the dark-ground microscope, give the appearance of a definitely positive reaction. On critical examination of the white aggregations standing out against a dark background, they are seen to be composed not of leptospira but of minute somewhat spherical particles. If they had been composed of leptospira the fibrillar composition of the aggregations would have been seen and the background would have shown absence of the organism. The inexperienced observer can easily make a mistake under these circumstances. If there is still any doubt about the matter a cover-slip should be applied and the preparation examined with a 1/12-inch objective and dark-field illumination. In two of the sera which have given this reaction false positive Wassermann reactions were obtained.

We are strongly of opinion that, until some method of standardizing cultures of leptospira is employed the serological diagnosis of Weil's disease should only be undertaken at laboratories where the idiosyncrasies of the antigens are well known.

We should like to thank our assistant, Mr. R. J. Reed, for his skill and care in looking after the cultures of leptospira during the last five years.

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Clinical Memoranda

Pneumococcal Peritonitis with Bilateral Pneumococcal Empyemata

Treatment with M & B 693: Recovery

The high mortality rate in cases of pneumococcal peritonitis is largely due to the early association of pneumococcal septicaemia, and it is felt that M & B 693 was of great value in the case here recorded. As Professor Fleming (1938a, 1938b) has pointed out, one cannot claim or hope to give such doses as would kill off the organisms in such a severe case; one can merely restrain growth, so that the natural defences of the body may succeed in overcoming the infection.

CASE REPORT

On November 10, 1938, a girl aged 10 was admitted to the General Infirmary at Leeds. Two days previously she first became ill with vomiting and diarrhoea. She complained of abdominal pain around the umbilicus. On examination the child was flushed, the tongue was furred and dry, and her abdomen was distended and generally tender. Temperature 100.5°, pulse 132, respirations 32. Progress and treatment were as follows.

November 10.—Laparotomy performed by Mr. Michael Oldfield. On opening the peritoneum greenish-yellow fluid was evacuated. Swab taken for bacteriological examination. Appendix inspected; found to be normal and left. Abdomen closed with pelvic drainage. A diagnosis of pneumococcal peritonitis was made, and the same day a course of M & B therapy was started. (Dosage: first dose 1 gramme, then 1/2 gramme four-hourly for three days, then six-hourly for four days. Stopped.) Felton's serum, three doses of 10,000 units at three-hour intervals; subsequently 10,000 units daily for eight days.

November 12.—Report on swab taken from abdomen at operation showed profuse growth of pneumococci. T. 98.2°; P. 138; R. 36.

November 17.—Radiograph of chest showed an opacity at right base suggesting effusion. T. 98.4°; P. 128; R. 33.

November 19.—Blood culture positive for pneumococci Type I. T. 100°; P. 156; R. 41.

November 20.—M & B 693, one tablet six-hourly. T. normal; P. 140; R. 36.

November 21.—Signs of pneumonic condition of right middle lobe. T. normal; P. 160; R. 36. Blood transfusion: 3/4 pint by vacoliter drip method.

November 22.—Bilateral aspiration of chest—thick green pus obtained. Mr. Allison operated on both empyemata, using rubber catheters and closed drainage. Abdominal wound still draining. Report on pus from chest: pneumococci Type I. T. normal; P. 134; R. 34.

November 24.—Patient still very ill. Treated in oxygen tent for next three days. Improvement. Catheters draining well. T. 100.2°; P. 144; R. 30.

November 26.—Decided to increase dose of M & B 693 considerably. (Dosage: first dose 2 grammes, then 1 gramme four-hourly for three doses, 1 gramme six-hourly for four doses, 1/2 gramme four-hourly for three days. Stopped.) T. 101°; P. 150; R. 36. With this treatment the patient improved. Occasional vomiting, some cyanosis and restlessness.

December 1.—Radiograph showed catheters *in situ*; no fluid, but empyema cavities extending down to level of twelfth rib behind (lipiodol). T. normal; P. 140; R. 40.

December 3.—Blood culture report: no growth after thirty-six hours. T. 100°; P. 144; R. 40. Patient continues to improve; takes nourishment well and is gaining in strength.

December 10.—Blood culture report: sterile. T. 100.5°; P. 136; R. 42. 1/2 gramme M & B 693 thrice daily for one week.

December 19.—Bilateral rib resection carried out by Mr. Allison to drain cavities below level of insertion of catheters. Improvement soon noticeable, and patient had no further pain; drainage ceased after a few days. T. normal; P. 126; R. 36.

December 31.—Radiograph with lipiodol showed no cavities. Drainage tube removed. Wounds granulating from base. T. normal; P. 132; R. 34.

January 3.—Patient's condition very satisfactory; she feels well, eats well, and has no pain. Sent to convalescent home. T. normal; P. 120; R. 28.

February 5.—All wounds dry. Chest expansion good. No abdominal pain or tenderness.

SUMMARY

A case of pneumococcal peritonitis with recovery is described. The points I wish to stress are:

1. The advisability of giving serum together with M & B 693 to enhance its effect.
2. The fact that fairly large doses of M & B 693 were given without any serious toxic effects.
3. When the child's condition was most critical on November 26 the dosage of M & B 693 was considerably increased. From this time her condition gradually improved, and it was thought that M & B 693 was the main factor in this crisis which turned the scales in her favour.

I wish to thank Mr. L. R. Braithwaite for permission to publish this case, and Mr. Michael Oldfield and Mr. P. R. Allison for their help and advice in compiling this report.

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