the optimum dose must be minute. I originally used a 1 in 1,000 solution for testing purposes, but I now use a 1 in 100,000, or even 1 in 1,000,000, for the preliminary test. Cases treated recently have given better results than the earlier ones, and I attribute this to the reduction of the therapeutic dose. The results of skin tests in normal persons and patients suffering from the skin diseases under discussion show very striking differences, for while only 16 per cent. of normal persons gave positive reactions to their own proteoses, 67 per cent. of the skin cases responded in this way.

With regard to the statements of Barber and Oriol, my results tend to show that the amount of proteose excreted is not of very great significance, for the difference between that excreted in health and in various skin diseases was not great. More, however, was excreted from patients suffering from skin diseases, and in one case of angio-neurotic oedema more was excreted during an attack than in a quiescent interval. I have also confirmed the statement that exacerbations of the skin condition may follow relatively large doses of proteose. My clinical findings agree very closely with those of Eichenlaub, and I agree with his conclusion that the method should be more widely used in order that its full value may be determined.

SUMMARY

1. Treatment with proteose prepared from the patient's urine has given satisfactory results in cases of chronic eczema and urticaria. Less striking results were obtained in cases of psoriasis and Besnier's prurigo, but benefit seemed to be derived from the treatment in some cases.

2. Sixteen per cent. of normal persons and 67 per cent. of patients suffering from various skin diseases gave positive reactions to their own proteoses. Slightly more proteose was excreted by the latter than by the former.

3. All the cases relieved by this treatment gave positive skin reactions to their own proteoses before treatment, while, after treatment and cure, all those tested gave negative skin reactions.

REFERENCES

- ¹ Barber and Oriol: *Lancet*, 1928, ii, 1064.
- ² Idem: *Ibid.*, 1930, ii, 231.
- ³ Oriol: *Proc. Roy. Soc. Med.*, 1931, xxiv, 55.
- ⁴ Barber: *British Medical Journal*, 1931, ii, 1060.
- ⁵ Freeman: *Ibid.*, 1931, ii, 1011.
- ⁶ Burgess: *Ibid.*, 1932, i, 37.
- ⁷ Lyon, Percival, and Stewart: *Ibid.*, 1932, i, 136.
- ⁸ Eichenlaub: *Arch. Dermat. and Syph.*, 1933, xxvii, 316.

CALCIUM THIOSULPHATE IN THE TREATMENT OF THE COMPLICATIONS OF "914" AND BISMUTH ADMINISTRATION IN SYPHILIS

PRELIMINARY COMMUNICATION

BY

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Schamberg and Brown (1930) introduced calcium thiosulphate into the therapy of the post-arsenobenzol complications, and in 1932 Schamberg and Wright quote Cannon as having employed the preparation in a series of cases of arsphenamine dermatitis with excellent results. It was particularly effective in drying up surface exudation. The dose recommended was 5 c.cm. of a 10 per cent. solution daily for three days, and subsequently two or three times a week. Schoch (1931) commented: "A new drug brought out for the treatment of arsphenamine dermatitis is calcium thiosulphate. The highly rational combination of calcium with the detoxifying action of the thiosulphate radical may prove to be an excellent prophylaxis for treatment reactions from arsphenamines other than arsphenamine dermatitis." The value of the sodium salt of thiosulphate, introduced by Ravaut (1920)

for the treatment of arsenical dermatitis, has been shown by McBride and Dennie (1923, 1924) and by many subsequent observers, while the value of calcium chloride in the prevention of certain cutaneous inflammations has been shown by Wright (1896), Chiari and Januschke (1911), and Blum (1921). On theoretical grounds, therefore, the combination of calcium and thiosulphate should be advantageous, especially in that group of cases which fails to react to sodium thiosulphate or which fails to clear up completely under its administration.

CASE RECORDS

Recently the following series of cases of intolerance to "914" or bismuth has been treated with calcium thiosulphate.

1. *Early Arsenical Dermatitis*.—Male, aged 31. Sero-negative primary syphilis. Developed arsenical erythematous dermatitis three weeks after completion of first course of "914" and bismuth. Calcium thiosulphate, 0.6 gram intravenously, daily for three days, then at three-day intervals. Skin lesions completely clear on the thirteenth day.

2. *Post-arsenical Dermatitis*.—Male, aged 50. Persistent sero-positive syphilis. Developed exfoliative dermatitis, which was treated over a period of several months with sodium thiosulphate. Condition became stationary, with scattered areas of scaly, fissured, infiltrated skin over flexures of arms, legs, and trunk. After twenty-two injections of calcium thiosulphate, at three-day intervals, the skin was completely clear.

3. *Jaundice*.—Male, aged 49. Persistent sero-positive syphilis. Had post-arsenical jaundice in April, 1932, which yielded after one month's treatment with sodium thiosulphate. Four months later administration of "914" was recommenced. Developed jaundice December, 1932, while under dual therapy. Calcium thiosulphate, 0.6 gram intravenously, the first two doses on successive days, then at two-day intervals. Icterus completely clear after the fifth dose.

4. *Immediate Reaction (Vomiting) after "914"*.—Male, aged 40. Persistent sero-positive syphilis. Vomited after each injection of "914." No other signs of intolerance over a long period of treatment. Vomiting controlled by admixture of sodium thiosulphate; equally well controlled by calcium thiosulphate. Other factors—bulk of injection, rate of administration, etc.—were kept as far as possible unchanged.

5. *Bismuth Dermatitis*.—Male, aged 49. Persistent sero-positive syphilis. Developed arsenical erythema while under dual therapy. This yielded rapidly to sodium thiosulphate. Bismuth administration recommenced two months later. After a course of 3 grams metallic bismuth in ten weeks he reported with a scattered papulo-squamous erythematous rash on the trunk, with moist, fissured, eczematous lesions of scrotum. The skin lesions partly cleared under the administration of sodium thiosulphate, but those of the scrotum remained unaltered after bi-weekly treatment for one month. Calcium thiosulphate was then commenced, 0.6 gram bi-weekly; the scrotal lesions and the residua on the skin cleared up completely after five injections. That bismuth was an aetiological factor in the production of this dermatitis, in a skin previously damaged by an arsenical erythema, was proved by the recurrence of a similar rash on the re-exhibition of bismuth.

6. *Dermatitis, probably due to Bismuth*.—Male, aged 27. Sero-negative syphilis. Treated originally with "914" and mercury, then with "914" and bismuth. No "914" for three and a half months, during the last ten weeks of which he received 3 grams metallic bismuth. In the eighth week of the bismuth therapy he reported a papulo-squamous erythematous dermatitis, which was aggravated by the subsequent injections. There had been no intolerance while under dual therapy, a total of 13.35 grams "914" and 8.7 grams bismuth having been administered. The dermatitis was considered to be due to bismuth, and treatment with calcium thiosulphate was instituted. After the seventh injection (0.6 gram bi-weekly) the skin had completely cleared.

In one case of bismuth stomatitis the pain and discomfort were relieved by the administration of calcium thiosulphate, although clinically there was no improvement in the condition of the mouth. One case of seborrhoeic dermatitis, which showed a tendency to flare up during the administration of bismuth, was markedly improved.

Apart from the feeling of intense heat in the skin, which comes on during or immediately after the injection, and persists only a few moments, the intravenous injection of calcium thiosulphate has been uneventful. Where it was possible 0.6 gram was administered daily for three days, then bi-weekly injections were given. Where sodium thiosulphate was given the first injection was 0.6 gram, and subsequent injections 1 gram.

CONCLUSIONS

The results of the calcium thiosulphate treatment of six cases of intolerance to "914" or bismuth are reported; in these cases calcium thiosulphate appeared to exert a definite curative influence. The total number of cases treated is, however, small, and more widely extended observations are necessary before any final conclusions can be reached as to the place of this drug in the control of the sequelae of arsenicals and bismuth.

BIBLIOGRAPHY

- Blum, L.: *C. R. Soc. de Biol.*, December 18th, 1921, p. 1156.
Chiari and Januschke: *Arch. f. Exp. Path. u. Pharmacol.*, 1911, lxx, 120.
McBride, W. L., and Dennie, C. C.: *Arch. Derm. and Syph.*, 1923, vii, 63; *Journ. Amer. Med. Assoc.*, 1924, lxxxiii, 2082.
Ravaut: *Presse Méd.*, 1920, xxviii, 73.
Schamberg, J. F., and Brown: *Proc. Eighth Internat. Congress Derm. and Syph.*, Copenhagen, 1930.
Schamberg, J. F., and Wright, C. S.: *Syphilis*, 1932, 252, 286.
Schoch, A. G.: *Internat. Clin.*, 1931, ii, 227.
Wright, A. E.: *Lancet*, 1896, i, 153.

A NOTE ON MONILIA INFECTION OF THE RESPIRATORY TRACT

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In Jersey during 1932 568 patients had their sputa examined both by direct and by cultural methods. As a result, they can be classified as follows: T.B. + = 103, monilia + = 294; negative to T.B. and monilia = 171.

When the sputa from a patient are repeatedly examined over a long period, direct and cultural examination shows varying flora; the only organism which on culture is persistently present is monilia. Apart from the fact that monilia is frequently associated with pyogenic organisms, its action in the respiratory tract will here be discussed from two points of view—the mechanical and the allergic. When incubated at blood heat and in suitable fluid media, monilias can be divided into three groups, according to their method of growth:

1. Those which grow round the glass of the test tube in what is known as "collar" formation.
2. Those which grow over the surface of a medium in a continuous sheet.
3. Those which, starting as "islets" on the surface, grow into a sheet as under 2.

Monilias stain with all ordinary stains, and are practically all Gram-positive. When stained by the Ziehl-Nielsen method they are found to contain acid-fast granules. In the human being the ordinary condition of "thrush" (monilia) is to be seen on the mucous membrane of the mouth, and consists of the well-known whitish patches, which on removal frequently show ulceration of the underlying mucous membrane.

Mechanical and Allergic Manifestations

It should not be difficult to appreciate what is likely to occur when monilias infect the air passages. If we compare the bronchi and the bronchioles to test tubes we can visualize monilia growing in the air passages either in "collar" or in "surface" growth formation. Monilia growing on the mucous membrane of a bronchus would

give rise to a patch, and would tend to spread round the bronchus in "collar" formation. Ulceration is likely to occur, and haemorrhage will result, giving rise to blood-stained or pinkish sputum; the irritation of the condition sets up a cough, and results in a weakening of the bronchial wall and consequent dilatation. Where the condition has existed for a considerable time irregular thickening and dilatation of the bronchial tree occurs. This bronchiectatic condition is well seen on x-ray examination, and is referred mostly to the bases. In these cases the brunt of the infection falls on the bronchial tree. A second type of case can be referred to Groups 2 and 3 above, where, in the smaller bronchioles, the growth produces occlusion and collapse of the alveoli at the distal end, with consequent cavitation. Such cases show "fluffing" of lung tissue on x-ray examination. The above conditions are frequently found in combination.

The allergic manifestations connected with moniliasis are similar to those connected with other diseases of the lungs and of the respiratory tract where allergy is found to be present—hay fever, asthma and bronchiectasis, and tuberculosis. Allergy is due to the sensitization of the body to a foreign protein, and for the purposes of this paper it is not necessary to discuss whether the foreign protein concerned is of vegetable or of animal origin. Is it possible that there may be a common factor, a foreign protein, which gives rise to allergic manifestations? To attempt to prove this one must take each disease separately. In hay fever the chief pollen held responsible for the condition is that of Timothy grass. This grass has a well-known acid-fast bacillus associated with its name. Turning to asthma, Storm van Leeuwen has shown that many asthmatics give a positive von Pirquet—that is, they are allergic to tuberculin. True spasmodic bronchial asthma is recognized as not due to tubercle infection, yet these cases are sensitive to tuberculin, which contains acid-fast substance. As regards tuberculosis, the von Pirquet and the Mantoux reactions are recognized as pathognomonic of tubercle infection. Now, both in asthma and in bronchiectasis monilias are present, and, as recorded above, monilias on staining by the Ziehl-Nielsen method are found to contain acid-fast granules. The amount varies according to the strain of monilia and according to the medium on which it is grown. Cultures on agar give a far greater acid-fast granule content than do cultures grown on Sabouraud's medium. Cases of these monilia infections give rise to cuti-reactions when tested with monilia vaccine.

One common factor in these diseases, then, is that the organisms connected with them are recognizable by the presence of acid-fast substance, and it is suggested that the "foreign protein" which is common to all is this acid-fast protein, and that allergic manifestations are due to it.

CONCLUSIONS

The presence of monilia in chronic lung infections gives rise to pus formation. Apart from this, monilias have a mechanical action. This mechanical action is due to the local growth of monilia on the mucous membrane, similar to the growth of monilia ("thrush") in the mouth. Two types may be recognized, one affecting the bronchial tree and resulting in a bronchiectatic condition of the air passages, the other occurring as the result of occlusion of the bronchioles and collapse of the lung alveoli, the brunt of the infection falling on the lungs. Monilia infection gives rise to allergic cuti-reactions. Such reactions are known to occur also in hay fever, asthma, non-tuberculous broncho-pulmonary lesions, and in tuberculosis. A common factor in all these diseases is the presence of acid-fast substance in their respective causal organisms. It is suggested that the foreign protein which is responsible for allergy is this acid-fast substance.