in the first series of cases treated by a succinate compound without aspirin.

The calcium double salt of benzoic acid and succinic acid benzyl ester has also been used for the treatment of rheumatic fever by Wégria *et al.* (1948). They conclude that neither the natural course of the disease nor its signs and symptoms were modified by succinate therapy.

The group treated with heparin was very little different from the salicylate group when the duration of joint pains, of increased pyrexia, and of increased blood sedimentation rate is considered, although it does seem that the duration of pyrexia was less in the cases given heparin. The presence of carditis on follow-up was found in 62% of the cases given heparin, but in only 40% of the cases given salicylates. Practically all of the cases in the heparin-treated group had carditis on admission, before treatment with heparin had begun, but they had been given salicylates outside by their own doctors before coming under observation. As in the case of the succinates, therefore, not much importance can be attached to this finding.

It would seem from these studies that we have not yet found anything which represents an advance in therapy in the treatment of rheumatic fever. Nevertheless, although succinates are certainly not effective, as are salicylates, in cutting short the pyrexia of an acute rheumatic episode, there has been offered no proof in this paper that they are not an adjuvant to salicylate therapy. Until some method of administering heparin is found which will maintain a constant blood level without the necessity for repeated intravenous injections, a really satisfying trial of this product cannot be made.

Conclusions

Succinate compounds given with ascorbic acid in the dosage recommended by Gubner and Szucs are ineffective in the treatment of acute rheumatism. Heparin, in a dosage of 1,000 T.U. three times daily, does not significantly reduce the duration of episodes of acute rheumatic fever treated with salicylates.

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REFERENCES

- Breusch, F. L. (1943). *Science*, **97**, 490.
 Glazebrook, A. J., and Cookson, B. (1947). *Edinb. med. J.*, **54**, 193.
 Gubner, R., and Szucs, M. (1945). *New Engl. J. Med.*, **233**, 652.
 Guerra, F. (1946). *Science*, **103**, 686.
 Heilbrunn, L. V. (1943). *An Outline of General Physiology*, 2nd ed. Saunders, London and Philadelphia.
 Krebs, H. A. (1943). *Advances in Enzymology*, **3**, 191.
 MacLagan, T. (1876). *Lancet*, **1**, 383.
 Muñoz, J. M., and Leloir, L. F. (1943). *J. biol. Chem.*, **147**, 355.
 Szucs, M. M. (1947). *Ohio St. med. J.*, **43**, 1035.
 Wassen, E., and Zander, G. (1946). *Svenska Läkartidn.*, **42**, 1768.
 Wégria, R., Fischel, E. E., and Wilson, P. E. (1948). *New Engl. J. Med.*, **239**, 117.
 Wrigley, F. (1948). West London Hospital, Department of Rheumatic Diseases: *Annual Report*, p. 28.

Dr. G. R. Wendt, chairman of the Psychology Department of the University of Rochester, U.S.A., is recently reported to have said that because a serious amount of charlatanism has developed in the U.S.A. it is essential that all groups concerned with the mental health movement should collaborate to protect the public through legislation (*New York Times*, September 11, 1949). Dr. Wendt considers that it is the primary responsibility of the medical profession to take the initiative in working for the protection of the public. He decried the almost complete lack of mental health legislation in the U.S.A. despite the great need for it. Only in Kentucky is there a law making it mandatory for each psychologist to get a licence before he can conduct private practice.

SUBACUTE POISONING BY THALLIUM TREATED WITH BAL

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In our paper on a fatal case of subacute thalliotoxicosis (Mazzei, Schaposnik, and Pedace, 1948a) we emphasized the basic clinical characters of acute, subacute, and chronic poisoning by thallium, together with the micropathology of each. The present paper deals with another case of poisoning by thallium—a suicidal attempt—which was successfully treated with BAL.

Though there does not seem to be any clinical experience with this drug in this type of poisoning, we decided to try it. Afterwards, Furmanski (1948) explained the beneficial action of BAL in poisoning by thallium. He used the drug with favourable results in severe peripheral neuropathies which had proved intractable to large doses of vitamins and crude liver extract. He based the treatment on the accepted view that such neuropathies are caused by the inactivation of the enzymatic systems of the nerve cells by toxins or toxic metabolites. He thought that BAL acted in these cases in a similar way to that in metal poisoning—i.e., by combining itself with the toxic metabolites after setting free those enzymes vitally related to cell respiration.

With these facts in mind, we thought that in human cases of poisoning by thallium BAL could be of use by displacing and then eliminating the metal already combined with protein enzymes of the nervous cells.

Dosage and Toxic Disorders

In the light of Eagle's wide experience, the Council of Pharmacy and Chemistry of the American Medical Association suggests the following outline of dosage in arsenical poisoning; this outline can be extended to poisoning by other metals.

In severe arsenical reactions.—First and second day, six daily injections of the drug, each of 3 mg. per kg. of body weight. Third day, four injections of the same dose. During the following 10 days or until full recovery is attained, two daily injections.

In reactions of medium severity.—Each injection should consist of 2.5 mg. per kg. of body weight. During the first two days four doses should be given, two on the third day, and one during the following 10 days or until full recovery.

In our case we used approximately the medium-severity doses, the total amount of drug injected being 3.1 g.

The administration of BAL may give rise to some unpleasant though transient effects. In view of its affinity for heavy metals, some of the toxic disorders following the use of high doses can be attributed to its combination with the metals which form part of the molecule of certain enzymes (copper, zinc, iron, and manganese). The removal of the heavy metals renders inactive the corresponding enzymes by depriving them of their protein groups (Furmanski, 1948). This theory seems to be supported by the drop in the magnesium content of the blood and disruption of the calcium/magnesium balance seen in patients receiving BAL, thus giving rise to the characteristic

symptoms of tetany. However, the enzymatic inhibition is rapidly reversible, so the accident does not seem to have undue importance.

The most common toxic symptoms are excessive salivation, vomiting, lacrimation, sweating, generalized myalgias, headaches, severe fleeting pains at the site of the injection, tachycardia, increased blood pressure, dyspnoea, and precordial constriction.

We must call attention to the high levels of the blood pressure in our patient. Though thalliotoxicosis is often accompanied by high blood pressure—especially the diastolic—the rise was evidently coincident with the course of BAL; it must therefore be attributed, partly at least, to the action of the drug.

Case Report

The patient, an Argentine girl aged 16, was a student at a secondary school, and lived in La Plata, province of Buenos Aires. During the three days September 16–18, 1948, she swallowed approximately 34 g. of the rat-poison paste "zelio," which contains 2% of thallium sulphate. On September 20 she began to feel skin hyperaesthesia and pains in the muscles of her lower limbs. On the following day her temperature rose to 38° C. (100.4° F.) and the myalgias had become very severe. The mere touch of the bedclothes caused violent pains, and she became progressively unable to use her legs.

On September 20 one of us was called in to see her. The temperature was 40° C. (104° F.). She was restless, with facies dolorosa, of asthenic habitus, and was lying on her back because of severe pain in her feet and legs, which was greatly intensified by the slightest touch or movement. She was undernourished, with small amount of subcutaneous fat. Her skin was hot and dry. The shape and reflexes of the pupils were normal. Her pulse was rhythmic, 84 a minute; blood pressure 170/120 mm. Hg. On palpation the whole of the abdomen was tender. The liver and spleen were within normal limits; the renal areas were painful. She was completely unable to move her lower limbs, and passive mobilization caused intense pain, particularly in the feet. The severe hyperalgesia made it impossible to carry out a thorough examination. The Achilles-tendon, patellar, and abductor reflexes were increased.

A psychiatric examination was performed by Dr. Alejandro Resis, who reported: "Her mental picture is prior to her attempt at poisoning, and must be the determining factor of the same. The symptoms correspond to the development of a constitutional and atypical exacerbation, which is due to the overlapping of the emotional psychasthenic and schizoid components (hypermotivity, erythrophobia, exaggerated psychomotor reactions; varied neurotic tendencies, phobias, and certain obsessions; a tendency to introversion and isolation, ideo-affective disassociation of personality)."

Laboratory Tests.—Blood count: red cells, 4,789,000; Hb, 95%; platelets, 240,000; white cells, 6,400 (neutrophils 60%, eosinophils 0.66%, monocytes 13%). Coagulation time: five minutes; bleeding time: two minutes. Sedimentation rate: first hour, 15 mm.; second hour, 38 mm. Blood urea, 30 mg. per 100 ml.; blood sugar, 96 mg. per 100 ml.; blood cholesterol, 180 mg. per 100 ml.; alkali reserve, 50 vols. %; chloride in cells, 1.56 mg. per 100 ml.; chloride in plasma, 264 mg. per 100 ml.; blood proteins, 8.28 g. per 100 ml. (serum albumin, 4.82 g.; serum globulin, 3.46 g.). Urine: turbid; acid reaction; slight sedimentation; specific gravity 1009; ammonia 0.47 g., urea 13.1 g., chlorides 2.2 g., phosphates 1.3 g., albumin 1.5 g. per litre; no sugar, acetone, or bile pigment. The sediment showed granular and hyaline casts, some red cells, and a large number of desquamation cells.

Treatment and Progress

On September 23 treatment was started with sedatives, analgesics, 25% glucose solution intravenously, vitamin B complex, and 15% magnesium sulphate with 0.05 g. of papaverine intramuscularly. Two days later the first phials of BAL from an English firm were obtained. During the first two days

300 mg. was injected daily. After this the treatment was continued with the same product, but of American origin (10% solution). A total of 3.1 g. was given (see Chart).

Throughout the administration of the drug the patient developed a morbilliform exanthema of varying degrees in the upper limbs, neck, and chest. Each injection of BAL gave rise to intense headaches and greatly increased the pains in the lower limbs; opiates were partially successful in alleviating these conditions. Weekly estimations of the urine showed considerable fluctuations in the albumin content (between 0.2 and 1.5 g.); albumin, together with renal elements, finally disappeared in February, 1949.

A few days after treatment was suspended the pains in the lower limbs began to decrease, and by December, 1948, the patient was free from them. The muscles of the thighs and legs gradually recovered their original tone and size with the help of massage. The hair on the head began to fall on October 5, and within a few days only a few patches of short hair remained.

For three months the patient was treated in a private mental institution. Insulin shock brought about a definite improvement in her psychic manifestations; moreover, her weight increased by 7 kg. (15 lb. 7 oz.). During this period massage was continued until total recovery. The last examination (April, 1949) showed that she had completely recovered.

Summary

A case of subacute thalliotoxicosis caused by swallowing 45 g. of a rat-killer paste containing 2% thallium sulphate is described. A total of 2.85 g. of BAL was given in the course of 13 days. The patient fully recovered.

The pharmacology of the drug is described, together with the reasons for using it in poisoning by thallium.

REFERENCES

- Furmanski, A. R. (1948). *Arch. Neurol. Psychiat., Chicago*, **60**, 270.
Mazzei, E. S., Schaposnik, F., and Pedace, E. A. (1948a). *Prensa méd. argent.*, **35**, 1119.
— (1948b). *An. Cated. clin. Méd.*, **2**, 29.

The need for new legislation for the prevention of smoke was the principal theme discussed on September 29 at the conference of the National Smoke Abatement Society in Harrogate. Reports of the limited success and difficulties of several local authorities in administering new local Acts of Parliament emphasized the form that new laws must take if they are to be effective in preventing, rather than just abating, smoke. Strong criticism of the opposition of "big industry" to a new Parliamentary Act obtained by the city of Birmingham, which had led to a serious weakening of its smoke clauses, was made by Dr. W. R. Martine, Senior Assistant Medical Officer of Health. In contrast, an officer of the Smoke Control District of Los Angeles, who was present as a visitor to the conference, described the effective and far more stringent regulations imposed in California and many American cities. Dr. Metcalfe Brown, hon. secretary of the Manchester and District Regional Smoke Abatement Committee, reported on an investigation in the Carrington area, near Manchester, where one of the country's biggest power stations is being erected, and other industries are causing concern. Local authorities around the area are co-operating in running a network of instruments, extending over 36 square miles, to measure the pollution of the air for comparison with conditions when the power station is operating. In conjunction with this a survey on the effects of smoke and fumes on plant life—an important matter for farmers—is being conducted jointly by the Smoke Abatement Committee, the Department of Botany of Manchester University, and the Agricultural Research Council.