means "a teacher," although in this country it has also come to have the more special meaning of "healer." One of the functions of doctors is to contribute of their knowledge and experience to the development of a healthier and happier state and to the education not only of the people but of the people's leaders. I would urge that your science and your humanism must come to serve the State in fuller measure than the science and humanism of the older generations have done.

Will you accept, therefore, that you are going out into the world in a few years' time not only to cure and palliate disease but—true to your title of doctors—to teach health and the causes of health and the necessary provisions for health, remembering always that this teaching must first find a firm basis in the science of health? Towards all this your present studies provide an important introductory discipline—but only a partial one, for the emphasis of teaching is often in the wrong place, and the co-ordination of your many subjects is not yet what it might be. In much the same way it may be urged that our existing medical services often apply the emphasis in the wrong place and lack the co-ordination we would one day like to give to them. And so will you in your generation also help us in ours to bring health or wholeness to our educational systems and to those collaborations of social and individual medicine with which it will one day be your privilege and responsibility to serve the people of this and other countries?

Last of all, for I have not yet mentioned your very proper duty to yourselves, remember that the doctor who has poor opportunities or a scant regard for his personal health—which above all other blessings should bring balance to his life and judgment to his work—can scarcely become the most respected and effective teacher.

TREATMENT OF SUPERFICIAL TUBERCULOUS LESIONS BY LOCAL APPLICATION OF PROMIN*

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The results obtained by Feldman, Hinshaw, and Moses (1940, 1941, 1942) in the treatment of experimental tuberculosis in guinea-pigs by promin (sodium salt of *p,p'*-diaminodiphenylsulphone - N, N'-di - [dextrose sulphonate]) have aroused great interest both in America and in this country. Not only did the drug, given daily by mouth, prevent or limit the development of disease, in animals inoculated with a virulent bacillary strain, when treatment was begun on the day of infection, but even when it was delayed for six weeks thereafter the effect was pronounced, and in some animals no tuberculous lesions were found at necropsy 192 days after inoculation. Feldman, Mann, and Hinshaw (1942) have now repeated the experiments, but have proved by biopsy the presence of microscopic tuberculous lesions in the livers of the animals when treatment was started, six weeks after infection; and again several treated animals showed no lesions at necropsy, at 224 days. While some factors involved in these results require further discussion, they appear to be the most impressive yet reported in the chemotherapy of tuberculosis in the guinea-pig.

* The drug has been developed by Messrs. Parke, Davis and Co. Ltd. in America, where the name "promin" was given to it; but in this country, owing to difficulties in registration, it will be known as "promanide." It will, however, be referred to in the article as "promin."

The guinea-pig tolerates a daily dosage, by mouth, of 300 to 400 mg. over long periods. In man, unfortunately, much lower dosage relative to weight may soon produce toxic effects, particularly haemolytic anaemia. Trial treatment of pulmonary tuberculosis has been fairly extensive, though published results are yet scanty. But, from wide informal discussion, it appears that outstanding success has not been attained with any dosage which is well tolerated.

One of us (W. H. T.) has had in hand for some seven months a guinea-pig experiment similar to those of Feldman, Hinshaw, and Moses, with comparable results, so far as they are yet apparent. The very evident effect of the drug in this experiment suggested that it might be exploited in the treatment of accessible non-pulmonary lesions, to which effective concentrations might be applied locally without producing a toxic blood level. After treatment of this type had begun, we learned that in America promin has been applied locally by spray or inhalation in some cases of laryngeal or tracheo-bronchial tuberculosis, with good results. More recently we have heard, by personal communication, that Dr. G. T. Allerton of Torquay has been applying the drug to superficial lesions with much success.

Method

The high solubility and rapid absorption of promin indicated that the maintenance of an effective concentration in the lesion might require frequent application of strong solutions unless the drug were incorporated in a medium which would limit diffusion. The medium first tried was tragacanth, which at relatively low concentrations gives a stiff insoluble jelly; and this medium has proved so satisfactory that no extensive trial has been made of others. One preparation of promin and tragacanth in glycerin was made, in the hope that the gum, by absorbing water in the lesion, might produce a stiffer gel than could be injected, but the preparation in itself proved difficult to handle and to inject. The use of tragacanth, however, makes sterilization difficult. Promin in 40% solution may be autoclaved at 120° C., and if cooled slowly remains in solution, particularly if 5% glucose has been added. If the solution is cooled rapidly, or with weaker solutions in any case, precipitation occurs, though solutions of 1% or less only become hazy. But, owing to the insoluble nature of the tragacanth gel, and to the stiffness required, it is not practicable to sterilize the gel separately and then add the necessary promin in sterile form. For the lesions so far treated, therefore, we have not attempted sterilization, but have relied on the bacteriostatic effect of the drug, which is considerable at the strength used. For injection into closed serous or similar cavities, however, it would be desirable to develop some method of sterilization which would exclude the presence of viable spores, particularly those of *Cl. tetani*.

In the preparation of a smooth jelly the most important step is the rapid dispersion of the tragacanth powder throughout the aqueous solution, before swelling and lump formation occur. The promin solution, in a beaker, is stirred mechanically by a rapidly rotating propeller blade, and the tragacanth is dusted in directly over the blade. The jelly is then smoothed out by sucking in and expelling through the bare nozzle of a large syringe, and finally by expelling through an attached needle (18 S.W.G.). Two different batches of tragacanth have given satisfactory gels at 3.5% and 3.0% respectively, the stiffness being such that considerable pressure is required to force it through the needle. In use the jelly is either sucked into the syringe through the bare nozzle, or may be filled into the open barrel, and injected either through the needle or, for sinuses, through a fine catheter tied to the nozzle. The first jelly contained 5% promin, which caused no irritation, and was increased to 10% and then 20%. The latter caused increase of exudation, and though the end-results were good we have now gone back to 5% as giving equally satisfactory results.

At the time of writing 10 cases have been treated in Glan Ely Hospital, Cardiff, of which notes are given below. So far, only such lesions have been selected as were easily accessible either to aspiration and injection or to instillation into open sinuses.

Case Notes: Closed Abscesses

Case 1.—Man aged 25. June 13, 1942: Admitted Glan Ely Hospital. Pulmonary tuberculosis, caries dorsal spine. Abscess pointing in lumbar region; 170 c.cm. pus aspirated; 5 c.cm.

promin (5%) in glycerin injected. Repeated nine times to July 17; about 40 c.cm. pus each time. Aug. 4: 140 c.cm. pus aspirated; 5 c.cm. P. jelly (10%) injected. Sept. 18: 42 c.cm. pus aspirated; 8 c.cm. P. jelly (20%) injected. No further aspiration necessary. *Laboratory Report*.—May 12, 1942: Pus; acid-fast bacilli found after concentration. Culture yields growth of human type T.B. No other organisms in film or blood-plate culture.

Case 2.—Man aged 37. June, 1941: Admitted Glan Ely Hospital. Advanced pulmonary tuberculosis. Fair progress to June, 1942, when red swelling appeared in midline above sternum, and another in right axilla, both fluctuant. June 23: Neck abscess; 4 c.cm. pus aspirated; 2 c.cm. P. jelly (5%) injected. June 25: Repeated. June 28: Abscess broke down, and healed completely in a few days. July 2: Axillary abscess; 14 c.cm. pus aspirated; 4 c.cm. P. jelly (5%) injected. July 6: 22 c.cm. pus; 4 c.cm. P. jelly (5%) injected. Abscess did not refill. Sept.: Abscess formed over middle of sternum. Aspirated three times at three-day intervals; each time 3 c.cm. pus; 2 c.cm. P. jelly (10%) injected. A few days later the abscess broke down, and then healed rapidly. Nov.: General condition improved; no further abscesses. *Laboratory Report*.—June 23, 1942: Pus; acid-fast bacilli in film. Culture yields growth of human type T.B. No other organisms in film or blood-plate culture.

Case 3.—Man aged 33. Sept., 1941: Pain in back. April, 1942: Dorsal swelling; pus aspirated in hospital. July 7: Admitted Glan Ely Hospital. Radiograph showed caries D.V. 12 and L.V. 1. Large abscess lower dorsal region; aspirated. July 20: 3 c.cm. P. jelly (5%) injected. July 23: 3 c.cm. (5%). Aug. 26: 14 c.cm. (20%). Aug. 30: 9 c.cm. (10%). Sept. 3: 8 c.cm. (10%). Sept. 8: 5 c.cm. (10%). Sept. 18: 5 c.cm. (10%). Nov.: Abscess remains flat since last treatment.

Case 4.—Man aged 34. 1931: Tuberculous left testicle removed. Discharging sinus from right testicle for four or five years. Dec., 1938: Pain in back. Aug., 1939: Radiograph showed caries D.V. 11. Sent home on plaster bed. July 2, 1942: Readmitted Glan Ely Hospital for observation. Nervous disturbance, diagnosed functional. Aug.: Up. Sept. 5: Abscess lumbar region; aspirated, no pus obtained; 2 c.cm. P. jelly (20%) injected. Sept. 11: Fluctuant, 4 c.cm. thick pus aspirated; 3 c.cm. P. jelly (20%) injected; abscess gradually became non-fluctuant. Nov.: Only small hard area remains. *Laboratory Report*.—Aug. 11, 1942: Urine—pus, but no acid-fast bacilli in film. Culture yields growth of human type T.B.

Case 5.—Man aged 41. June 11, 1942: Admitted Glan Ely Hospital. Suspected tuberculous spine. Diagnosed probable new growth, belied by steady clinical improvement. Oct. 16: Abscess lumbar region; 35 c.cm. creamy pus aspirated; 5 c.cm. P. jelly (5%) injected. Abscess disappeared fairly rapidly. No further aspiration necessary or possible. *Laboratory Report*.—Oct. 16, 1942: Pus; no acid-fast bacilli after concentration. Culture for T.B. negative so far (21 days). Film shows cocci. Blood-plate culture gives pure growth *Staph. aureus*.

Open Sinuses

Case 6.—Man aged 31. Nov., 1940: Injury to back; pain ever since. July, 1941: Lumbar abscess. Nov. 15: Admitted Glan Ely Hospital. Caries lumbar spine, sinus lumbar region, persistent to July, 1942. July 7: 1 c.cm. P. jelly (5%) instilled by catheter; continued daily to Sept. 1, when sinus was too small to retain jelly. Nov.: Still a superficial remnant; small discharge. *Laboratory Report*.—July 11, 1941: Pus; acid-fast bacilli in film. Culture yields growth of human type T.B. No other organisms in film or blood-plate culture.

Case 7.—Man aged 28. Jan., 1941: Abdominal pain; fever. Feb. 28: Laparotomy; tuberculous peritonitis. Aug. 10: Persistent sinus in laparotomy wound, no progress. Feb. 2, 1942: Admitted Glan Ely Hospital. Faecal fistula, which closed but left persistent sinus. July 17: No fistula; sinus remains; 1 c.cm. P. jelly (5%) instilled by catheter daily to Sept. 1, when sinus was dry. Nov.: Healed scar, firm and healthy.

Case 8.—Man aged 31. June, 1941: Swelling left loin. July: Opened in hospital. Nov.: Radiograph showed caries of lumbar spine. Feb. 19, 1942: Admitted Glan Ely Hospital. Sinus discharging thick foul pus, continuing to July. July 17: 5 c.cm. P. (5%) in glycerin instilled to bottom of sinus; continued daily. P. jelly (20%) used for three weeks, continued to present; now using 5%. Discharge at first increased and thinner; later decreased. Nov., 1942: Sinus still open, but much shallower, with little discharge. *Laboratory Report*.—July, 1941: History states pus reported sterile.

Case 9.—Man aged 22. Treated in Glan Ely Hospital, Oct. 15, 1936, to July 7, 1937, for caries of lumbar spine. Dis-

charged quiescent. Worked to Jan., 1942, when he fell and injured back. May 25: Readmitted Glan Ely Hospital; abscess pointing in right groin; repeated aspirations. Aug.: Sinus formed. Aug. 30: 5 c.cm. P. jelly (5%) instilled to bottom of sinus; since then, 3 or 4 c.cm. 20% every four days. Nov.: Sinus very shallow; no pus. Treatment continues. *Laboratory Report*.—May 28, 1942: Pus; acid-fast bacilli after concentration. Culture yields growth of human type T.B. Film shows some Gram-negative bacilli, but blood-plate culture sterile.

Case 10.—Man aged 23. April, 1941: Doubtful history of pain in back. Nov.: Swelling left groin, opened in hospital. May 21, 1942: Admitted Glan Ely Hospital; discharging sinus; radiograph showed caries L.V. 4 and 5. Sept. 8: Abscess pointing over right ilium; aspirated every three or four days, and 5 c.cm. P. jelly (20%) injected. Sept. 29: Abscess broke down; catheter passed into sinus 16 in. deep; 5 c.cm. P. jelly (5%) instilled to bottom, continued daily to present. Nov.: Discharge less, and thinner. Sinus about 6 in. deep. The first injections into closed abscess did not reach beyond superficial part of the large cavity.

Three other cases of cervical adenitis with abscess formation were treated, but as the lesions were opened and scraped shortly afterwards the results are without significance.

Discussion

With the exception of Case 5 all the lesions treated were considered on clinical grounds as undoubtedly tuberculous. In 4 cases tubercle bacilli were demonstrated by film and culture, and in a further case, No. 4, in culture from the urine. All cultures were human type. In the two closed abscesses, and in one of the two sinuses, in which tubercle bacilli were demonstrated, there was no secondary infection at the time of examination. In the other sinus Gram-negative bacilli were seen in film but did not grow in culture.

While the results were somewhat irregular the clinical opinion is that the improvement in all was greater or more rapid than would have been expected by orthodox methods applicable. In Case 2 the results were spectacular, in that three different abscesses each healed completely within two weeks of starting treatment, leaving only small fibrous residues.

In two cases, each on one occasion, there was a rise of temperature on the day after treatment, probably depending on disturbance of large abscesses. Apart from these isolated events nothing that could be interpreted as a toxic effect was seen.

It is thought that these results justify a more extensive trial of the drug by local application to suitable lesions, and possibly to more deep-seated lesions which can be injected. At present we are turning our attention particularly to cervical glands in which softening has occurred. These lesions can be treated by injection in the dispensaries, and it is hoped in this way to obviate the need for operative measures, often involving a long wait for admission to hospital, with prejudice to the patient and the occupation of valuable bed-space when admitted.

We wish to express our gratitude to the manufacturers for liberal supplies of the drug, and to their medical representative, Dr. J. Stanley White, for much assistance and information. We also acknowledge gratefully our obligation to Dr. A. Brownlee, medical superintendent of Glan Ely Hospital, for permission to carry out the investigation in that hospital.

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Those who claim that they derive valuable information about the heart from the quality of its sounds may find some graphic support in the vibrocardiograms of Kountz and Smith (*Southern med. J.*, 1942, **35**, 713). Using a special microphone actuating a cathode ray, they record all sound vibrations between 1 and 500 cycles per second generated by the heart. Certain features of the graph so produced appear to change in quality in patients with "myocardial disease." It is impossible to evaluate the results because clinical details are entirely lacking. However, the method deserves attention, for the quality of the heart sounds and its relation to disease is still a vexed question, and if it can be settled by graphic means it will be helpful.