CHEMOTHERAPY IN GONORRHOEA

A PRELIMINARY REPORT ON THE USE OF 2-(*p*-AMINO BENZENESULPHON- AMIDO)PYRIDINE, M. & B. 693

BY

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"One of the most intriguing characteristics of medical research work lies in the possibility that overnight a remedy of unbelievable therapeutic potency may be produced and that the millennium of gonorrhoea control may be close at hand." Thus writes Parran (1937) in respect of what may emerge from sulphanilamide in the control of gonorrhoea.

The introduction of 2-(*p*-aminobenzenesulphonamido)-pyridine, M. and B. 693, is an event which bids fair to produce a notable advance in the attack on the gonococcus. Reference has already been made to some of its results in experimental work in mice by Whitby (1938), in pneumonia by Telling and Oliver (1938) and Evans and Gaisford (1938a, 1938b), and in the treatment of gonorrhoea by Lloyd, Erskine, and Johnson (1938). The following report, essentially of a preliminary character, supports the findings, published at a similar stage of experimental treatment, by Lloyd *et al.*, and is of considerable interest in its clinical bearings.

Analysis of Cases Treated

Through the courtesy of Messrs. May and Baker, Ltd., who are kindly maintaining a supply of M. and B. 693, it is now possible to give some details of thirty-one cases of gonorrhoea treated orally by the drug, thirty being male patients and one a female case of gonococcal ophthalmia neonatorum. Of the thirty male cases twenty-seven were of acute anterior urethritis and three of urethritis and prostatitis: twenty-three of the anterior and one of the prostatic types were fresh untreated cases, the other four and two respectively having resisted previous treatment by urethral lavage, benzyl-sulphanilamide and/or sulphanilamide, and in one case by gonococcus antitoxin.

Taking the fresh cases first (twenty-three of acute urethritis and one of additional prostatitis) the results were as follows: six cases were gonococcus-negative in one day, ten in two days, six in three days, one in eight days. One patient showed gonococci up to the seventeenth day, but in his case there was reason to believe that he was not taking his M. and B. 693 regularly. Of the six previously treated (four of urethritis and two of prostatitis) five were gonococcus-negative in two days and one in three days. Thus of thirty cases six were negative in one day, fifteen in two days, seven in three days, one in eight days, and one in seventeen days. (These figures err, if anything, in favour of the gonococcus, if such an expression may be used, as the seven cases given as being negative in three days were not seen till that period of treatment had elapsed, and may have been negative before, but for purposes of these notes are given as three-day results.) The cases were controlled by direct staining and/or culture of pus and urethral secretion at or up to the periods stated. If such pus or secretion was not available, as occurred in a number of cases very rapidly, a centrifuged urinary deposit was investigated by similar methods. "Gonococcus-negative" means the absence of gonococci by any of these methods of examination.

While these negative results were observed, and while most patients when asked would answer that their discharge had disappeared in one day or two days, varying degrees of muco-pus or mucus from the urethra and threads in the urine were noted for periods differing from three to even eighteen days, and showing pus cells up to that time. In most cases, however, it was with difficulty that any urethral discharge or secretion could be found after a week. Though final tests of cure have not yet been applied, none of the thirty cases has shown either clinical or bacteriological signs of relapse in the two to four weeks during which they have been under observation since cessation of treatment. It is worthy of note that so far as could be ascertained not one of the anterior cases has developed any invasion of the posterior urethra. The prostatic cases likewise did not result in further complications.

The Dosage Used

The dosage of M. and B. 693 in twenty-three patients was 3 grammes daily for four to seven days, then 1.5 grammes daily for a similar period in most cases. At first a few were treated for a longer period, probably quite unnecessarily. A trial of 1.5 grammes daily from the commencement of treatment was made in seven cases. Of these, five were gonococcus-negative in two days, one in eight days, and one not till the seventeenth day. The total dosage varied actually from 42 to 14 grammes. The average amount necessary is yet undecided, but it would appear that anything from 15 to 25 grammes suffices, and the suggestion is made that the initial dose should not be less than 3 grammes daily. The following dosage is to be tried in uncomplicated cases of urethritis: first day, 4 grammes; second and third days, 3 grammes per day; fourth to seventh day inclusive, 1.5 grammes daily. Urethral lavage (potassium permanganate, 1 in 8,000) was given to twenty-four cases, mainly for psychological reasons, but of six patients who did not have anything other than M. and B. 693 five were gonococcus-negative in two days and one in three days. The duration of infection—which varied from thirteen weeks to one day—prior to treatment did not seem to have any influence on the result of M. and B. 693.

Toxic results were noted in seven of the thirty patients: nausea in two, dizziness in two, headache and lassitude in one, drowsiness in one, and breathlessness in one. All were slight. The last-mentioned showed some methaemoglobinaemia, and in this patient only was it deemed advisable to withdraw the drug, when his breathlessness promptly ceased. By this time, however, the desired effect upon his infection had been accomplished. Cyanosis was not seen in any case.

A Case of Gonococcal Ophthalmia Neonatorum

A case of gonococcal ophthalmia neonatorum remains to be mentioned, and for permission to include it thanks are due to Dr. Michie, senior resident medical officer at the City Hospital, Aberdeen. A female infant, infected in one eye, had been treated actively with boric lavage and silver nitrate, and had also received protosil. At the end of seventeen days the notes read, "Making very slow progress . . . needs intensive treatment." She was then given 0.25 gramme M. and B. 693 thrice daily for three days. The notes then read, "Sudden, almost dramatic, improvement. . . . Conjunctiva clear and only minimal pus." This occurred in forty-eight hours. A culture and smear examined one day after the cessation

of treatment were free from gonococci and from pus cells. The child was discharged three days later.

Comment

It is not intended to make any comment meantime other than that, of three preparations—benzyl-sulphanilamide, sulphanilamide, and M. and B. 693, the first and second having been tried extensively in the Aberdeen clinic—the last is the swiftest in action. So far it would appear to be a highly efficient and comparatively safe drug in the doses which apparently suffice to deal with the gonococcus. But out of this very efficiency there may arise the necessity, for obvious reasons, of strict control in the sale and distribution of such a preparation. It is hoped that at some future date a more detailed report may be made on the use of M. and B. 693 in the treatment of gonorrhoea.

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X-RAY PELVIMETRY

A SIMPLE METHOD FOR MEASURING THE PELVIC BRIM

BY

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External pelvimetry is still practised by obstetricians and general practitioners, but probably more as a matter of routine than from the conviction that an accurate knowledge of the internal pelvic measurements will be gained. Even internal pelvimetry is unreliable. Besides, it is not easy to apply, and it is often painful or disagreeable to the patient.

In a recent article on the true conjugate and pelvimetry J. Howkins (1938) arrives at the conclusion that the clinical measurement of the true conjugate is either impossible in practice or inaccurate when measured in all but cases of severe pelvic contraction; that a genuine attempt to measure it in a primipara demands a full anaesthetic; that the location of the sacral promontory requires practice and skill, and is valueless, unless performed by one familiar with pelvic examination; and that the measurement, when truthfully obtained, is open to considerable experimental error, in addition to errors due to the particular anatomy of a given patient, such as the depth and inclination of the symphysis pubis.

It is mainly for the above reasons that radiologists have striven since the early days of the x-ray era to make use of radiography for measuring the pelvic brim. The first radiography of the pelvis (of a corpse) was performed in 1896 by Varnier and Chappuis, and required an exposure of three hours. In 1897, at the twelfth International Congress of Medicine in Moscow, Professor Budin showed an excellent radiograph of an oblique pelvis of Naegele: this required an exposure of three-quarters of an hour. At the same congress Professors Pinard and Varnier reported results of the radiological investigations of the female pelvis. "It is possible," they said, "accurately to diagnose in doubtful cases the symmetry or asymmetry of the pelvis, the site and degree

of the asymmetry, the presence or absence of atrophy of the sacrum or of sacro-iliac ankylosis." They estimated the various diameters of the pelvic brim by comparing the obtained radiograph with standard radiographs of dried pelves.

Since then the evolution of x-ray pelvimetry has followed a very devious and complicated path (Orley, 1933). Most ingenious devices and methods for measuring the pelvic brim have been invented, and then discarded because they were too complicated, too expensive, or unreliable. This paper deals with one method of x-ray pelvimetry only—namely, that which was originally suggested in 1897 by Albert, was rediscovered thirty years later by R. E. Roberts (1927) of Liverpool, and simplified by H. Thoms.

Description of Method

The technique described later differs somewhat from that suggested by Thoms. The principle, however, is the same. Briefly speaking, the method consists in placing the patient on the radiographic couch in such a way as to bring the plane of the pelvic brim parallel to the plane of the radiographic film. For this purpose the tip of the fourth lumbar spine is marked on the skin with a dermographic pencil or by a strip of adhesive plaster. The patient is then seated on the x-ray couch in a semi-reclining position, so adjusted that the tip of the spine of the fourth lumbar vertebra is at the same horizontal level as the upper border of the symphysis pubis. This is carried out in the following way: one leg of a pair of callipers is placed on the top of the x-ray couch in front of the symphysis pubis between the patient's thighs, and the callipers are spread until the tip of the other leg of the calliper is at the level of the upper border of the symphysis pubis. The inclination of the patient's spine is then so adjusted that the distance between the top of the couch and the skin mark corresponding to the tip of the fourth lumbar spine is equal to the spread of the callipers.

FIG. 1.—Diagram showing that when the tip of the spine of the fourth lumbar vertebra is at the same horizontal level as the upper border of the symphysis pubis the line which joins the two passes through the promontory.

Some workers dispense altogether with the marking of the tip of the fourth lumbar spine, and instead measure only the distance of the upper border of the symphysis pubis to the top of the table, placing the patient in such a way that her spine forms an angle of 57 degrees with the plane of the x-ray couch. The pelvic brim