recorded as "not improved." Those who had responded, and also the doubtful cases, remained under treatment for a further three months. The intermediate assessment was made on the grounds that effective treatment should not be withheld from the "not improved" cases. The continuation of treatment was primarily to ascertain if tolerance for the drug developed. No signs of drug tolerance were observed at the clinical evaluation stage and none have been observed since.

The final stage of the trial could be carried out in one of two ways. The essential requirement is that neither the clinician nor the patient shall know whether the tablets are active or inert. Selection of the patients for the subgroups to be given active or inert tablets may be made at random or by design. It was felt that selection should be by design in order to keep the subgroups as evenly matched as possible. The opinions of pharmacologists and other research workers were sought on this question, and it was generally agreed that selection should be by design.

At the final stage of the trial the assessment differed in seven instances from that which would have been expected if the recorded improvement had been entirely due to the use of the new drug. Analysis of these cases is of interest. Of the five patients who were "no worse" on the inert tablets, four had been classed at clinical evaluation as "worth while" and one as "good." In common with the other patients in the subgroup given inert tablets these five were returned to treatment with B.S. 5930 at the end of the two-weeks period. The four "worth-while" patients showed no appreciable difference in their condition at the next follow-up clinic. The "good" patient, after returning to the active tablets, not only stated that she felt better but also showed some objective improvement. Examination of the forms and notes of these patients suggests that the unexpected association at the final stage was due to taking too much account of the subjective phenomena at the clinical evaluation level in the case of the four "worth-while" patients and at the final assessment in the other. Both the patients who were assessed as "worse," although they had received active tablets, had been classed as "good" at the clinical evaluation. It is now felt that they should have been classed as "worth-while."

Modification of the clinical evaluation in the light of the final stage of the trial gives: from the group who had responded to previous treatment: 15 excellent, 13 good, 5 worth while, and 17 not improved; from the group who had not responded to previous treatment: 1 excellent, 2 good, 3 worth-while, and 11 not improved.

Finally, at the risk of stating the obvious, we would like to make two personal comments. Firstly, we feel that this investigation emphasizes the need for close collaboration between the clinician and the scientist, and for careful experimental design to meet particular circumstances. Secondly, we believe that clinical evaluation is still of great importance in the trial of new drugs, and that, although highly important in these trials, statistical analysis is not a substitute for clinical experience.

Summary

A new compound, B.S. 5930, has been tried in the treatment of 67 patients suffering from Parkinsonism. A clinical improvement was noted in 39 cases. The results were considered to be good or excellent in 31 cases, or 46%.

A new method of carrying out clinical trials of this type is described and its advantages are discussed.

We would like to thank Professor A. M. Boyd for permission for one of us (A. H. R.) to take part in this investigation; all those who have given valuable and helpful criticism during the course of the investigation; and Dr. C. J. Van Bortel, of Messrs. Brocades-Stheeman, for supplying the B.S. 5930 ("disipal") and inert tablets.

OPERATIVE TREATMENT OF VARICOCELE

BY

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For the treatment of varicocele Samuel Cooper, in 1828, advocated support with a suspensory bandage, the use of cold and alum lotions, and also that the blood be repeatedly taken away by means of leeches. He considered that radical cure could seldom be effected. In more recent years Everidge (1943) stated that, although the risks of operation for varicocele were almost negligible, the end-results often left much to be desired—an opinion which reflects the general feeling of dissatisfaction with the results of the operation as commonly practised to-day. Indeed, attention has been drawn to the inadvisability of operative treatment (Douglas, 1921; Campbell, 1928; Page, 1954).

The classical operation, in which a segment of the pampiniform plexus is excised between ligatures through an upper scrotal incision, has fallen into disrepute because of the common occurrence of post-operative complications. Tearing of thin-walled dilated veins often results in the formation of a haematoma, which may become infected, with consequent prolonged sepsis and delayed convalescence. Faulty estimation of the amount of venous plexus to be removed leads to the development of a hydrocele if too many veins are tied, whereas inadequate removal is followed by a recurrence of the varicocele. Because of the difficulty in identifying small arteries in the spermatic cord, the arterial blood supply of the testis may be damaged, with consequent testicular atrophy. "I think it is impossible to remove a varicocele of any size without damaging the spermatic artery" (Page, 1954).

In an attempt to avoid such complications, operations have been devised in which the spermatic veins are divided in the inguinal canal or at the internal inguinal ring. Such procedures are particularly applicable to cases in which there is a coincident inguinal hernia, but they still carry the risk of damage to the arterial blood supply and to the collateral venous return of the testis and epididymis.

The operation described in this paper is that of division of the spermatic veins, at a level 2 in. (5 cm.) above the internal inguinal ring, where the veins lie on the posterior abdominal wall. At this site impairment of testicular blood supply can be avoided.

Venous Drainage and Arterial Blood Supply of Testis and Epididymis

Venous Drainage.—The veins of the testis and epididymis form an anastomosing plexus—the pampiniform plexus—which lies in the spermatic cord. As the veins pass upwards to the internal inguinal ring they become reduced in number, and, on the posterior abdominal wall, form one or two veins which drain into the renal vein on the left side and into the inferior vena cava on the right side. In addition to this main route of drainage, secondary venous channels pass along the vas deferens to the internal iliac veins, and communications are present between the pampiniform plexus and the pudendal and circumflex systems of veins. The presence of these subsidiary routes of drainage has been confirmed in this unit by anatomical dissections and also by radiography after injection of diodone into the

pampiniform plexus. During the classical operation for varicocele the destruction of these anastomosing channels is responsible for some of its adverse results.

Arterial Blood Supply.—In the past different anatomical descriptions of the arterial blood supply of the testis and epididymis have given rise to confusion, but within recent years the position has been clarified by the work of Harrison (1949), who has demonstrated by arteriography the distribution of the vasal and cremasteric arteries and their anastomoses with the testicular artery. From his work it is apparent that in a number of cases division of the testicular artery alone might not impair nutrition of the testis, but in the classical operation for varicocele there is a considerable risk of damage not only to the testicular artery but also to the vasal and cremasteric vessels. Harrison has pointed out that the operative procedure is much safer if the testicular veins are ligated at a site where the testicular artery is large enough to be seen and avoided.

Operation

The operative procedure which has been used in this unit during the past three years is a modification of that described by Palomo (1949).

The operation is carried out under general anaesthesia. A 4-cm. incision is made 3 cm. above and parallel to the inguinal ligament, the midpoint of the incision being above the internal inguinal ring. The aponeurosis of the external oblique muscle is divided in the line of the incision, and the fibres of internal oblique and transversus muscles are separated as in a gridiron incision. Extraperitoneal fat and peritoneum are swept upwards and the testicular vessels exposed as they lie on the posterior abdominal wall, lateral to the external iliac artery, which serves as a useful guide. The vein or veins are isolated and divided between ligatures. The wound is closed in layers without drainage. The patient is allowed out of bed on the following day and is discharged home in four days. A scrotal support should be worn for one to two weeks after operation.

Post-Operative Course.—Following operation a marked diminution in the size of the varicocele occurs over a period of weeks, and eventually only residual thickening in the pampiniform plexus can be felt. The testis returns to a more normal level and the scrotum is no longer pendulous and relaxed.

Material

Thirty-five patients, all of whom were referred from the male subfertility clinic, have been submitted to operation. In five of these patients the varicocele was bilateral, thus making a total of 40 operations. The size of the varicocele varied considerably, in some cases being very large. In most of the patients there was associated softness of the testis. In the first 20 cases the Palomo technique of division of the testicular artery as well as of the veins was carried out, but in the light of Harrison's work on testicular arterial blood supply it was considered inadvisable to divide the testicular artery, damage to which may impair testicular nutrition if the collateral blood supply is inadequate. In the last 20 cases only the veins were divided.

Results

In one case no improvement occurred. This patient was submitted to a further operation, and it was found that the inferior epigastric veins had been divided instead of the spermatic veins. This error probably occurred because the incision had been carried too far medially.

In approximately one-third of the cases in this series slight oedema of the scrotum was noted for a few days. No other post-operative complications have occurred.

Despite the fact that the testicular artery, as well as the veins, was divided in the first 20 cases, there has been no case of testicular atrophy. The consistence of the testis has been noted to improve over a period of months.

The results of post-operative seminal analysis are reported in Mr. Selby Tulloch's article in this issue.

Summary

The unpopularity of the classical operation for varicocele is due to the high incidence of post-operative complications.

The operation of high division of the spermatic veins is described. This operation fulfils the obligation that any operation for varicocele should safeguard testicular arterial blood supply and preserve collateral venous return from the testis and epididymis.

The results of this operation in a series of 40 cases have proved very satisfactory.

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VARICOCELE IN SUBFERTILITY RESULTS OF TREATMENT

BY

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During recent years considerable interest has been directed to the subject of fertility in the male. It is becoming more fully appreciated that in the barren marriage the male should be examined, and that such an examination should precede the examination of the female.

When a subfertile state is found, attention is focused on the aetiology and the treatment. Recognized aetiological factors are inflammatory conditions of the urethra, prostate, seminal vesicles, and epididymis; endocrine disturbances; the failure of testicular development; traumatic and other conditions. Much has been written about methods of treatment: vitamins, hormonal therapy, operative intervention for mechanical obstruction have all been recommended. These methods have their supporters and opponents, and there is considerable variation of opinion regarding the value of treatment.

During examination of subfertile males, and in some cases sterile males, it has been found that the incidence of varicocele is very high. The term "varicocele" may be defined as elongation, dilatation, and tortuosity of the veins of the pampiniform plexus. It was observed in the physical examination of males who had a varicocele—far more common on the left side than the right—that the testis was sometimes smaller than normal and showed evidence of softening in varying degree. Often the testis on the opposite side showed a tendency towards softening. In many cases seminal analysis of the male who had a varicocele demonstrated variation from moderate degrees of subfertility to gross depression of the quality of the seminal fluid, even in some cases to azoospermia.

Dr. J. K. Russell (1954), in a careful study of the relationship of varicocele to subfertility in the male, has no doubt that the incidence of varicocele is higher in men with poor-quality seminal fluid. He concludes: "The purpose of this paper is not to plead for more active treatment (indeed, attention has been drawn to the dangers of active surgical treatment), but rather to challenge the traditional attitude that varicocele is an innocuous condition and to stress the need for more