so seriously in females as in males. There is then a period until puberty when sexuality is disregarded and discouraged. At puberty there is an outpouring of androgenic and oestrogenic hormones. We believe that the sex hormone tends to activate the sexual conditioning which accords with it—that is, androgenic hormones activate only male conditioning. If the individual has been conditioned so that its psychical sexuality accords with its somatic sexuality it excretes the oestrogenic hormone harmlessly, but, if not, the oestrogenic hormone activates the female conditioning in the male, producing the homosexuality so often seen at puberty. Once having reached heterosexual maturity the individual remains heterosexual (unless deprived of its proper sex object). At involution the endocrine instability may produce a similar result to puberty with similarly increased homosexuality.

Relation to the Psychoses

Pavlov has shown that neurosis in the dog (and presumably psychosis in the human) can result from conflict between different forms of conditioning. A great conflict in humans appears to be homosexual *versus* heterosexual conditioning. It is at those periods following puberty and the menopause that we have endocrine instability causing an accentuation of homosexual changes, and presumably these partly cause schizophrenia and involutional psychoses. The accentuation of the homosexual patterns produces terrific conflict with the heterosexual ones, and no doubt results in the cerebral disorganization we know as psychosis. Not every case, of course, shows such clear-cut homosexual-heterosexual conflicts as this present one, and some psychoses must be due to other conflicts.

The importance of the present case and of our work to treatment is that it points the way to a subtractive therapy, whereas previously (except in the thyroid) only supplementary therapy has been in use. We feel that where there is proved endocrine abnormality similar to that observed in this case the surgeon may be more successful than the physician.

We have to thank Lord Wakefield, without whose generous grants this research work would not have been possible; and also Dr. R. D. Gillespie for so kindly placing his case in our hands and allowing us access to his notes.

Nineteen representatives of local authorities and other organizations co-operating with the Department of Scientific and Industrial Research in investigations into the nature and extent of atmospheric pollution met on June 6 in half-yearly conference at the offices of the Department. The conference learned with interest of measurements which had been made in Scunthorpe by Dr. W. H. Hartston (the medical officer of health) of the amounts of zinc and lead in the matter deposited from the air. Other members who had had previous experience of measurements of zinc, lead, and other metals in the atmospheres of steel-manufacturing and other towns also took part in the discussion. The conference expressed its satisfaction at the welcome which had been given to the Public Health (Coal Mine Refuse) Bill in its recent passage through the House of Commons. Dr. G. M. B. Dobson, F.R.S. (chairman of the Atmospheric Pollution Research Committee) presented a report on the progress of the investigations carried out under the committee. He said that the special survey of atmospheric pollution in and around the City of Leicester had now entered upon its third year, during which special attention would be paid to problems which the previous work of the survey had shown to be important. This had required the establishment of three new observing stations, for the measurement of dust in the air, near the city. Special work on these problems would also be carried on in the laboratory during the year.

SPINAL ANAESTHESIA

A REVIEW OF THE TIME-DIFFUSION METHOD

BY

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It is many years since the first drug was introduced into the human spinal theca with the intention of producing an extensive regional anaesthesia, and, although the prophecy that the old inhalation anaesthesia would soon be entirely replaced by the new method has not been fulfilled, there is no doubt that this spinal anaesthesia has come to occupy a valuable place in the armamentarium of both surgeon and anaesthetist. A great number of drugs and methods for their administration have been tried, but the latter, in this country, have mainly been limited to three: that of Howard Jones, in which the height of anaesthesia depends on dosage; that of Etherington Wilson, depending upon the upward diffusion of a hypobaric solution for varying times; and a technique recently described by Lake, where the hypobaric solution is allowed to flow upwards to a required point determined by correct posturing of the patient. The following account is based on a series of observations in which one drug and one technique were used throughout. The drug was percaïne (Ciba) 1 in 1,500 solution in 0.5 per cent. saline, having a specific gravity of 1.0038 at 15.5° C. and generally known in this country as light percaïne; and the technique was based upon that of Etherington Wilson, with some modification. It cannot be claimed for this time-diffusion method that absolute accuracy is always obtained, and a small proportion of cases occur in which anaesthesia is unsatisfactory; but it can be claimed that it involves the minimum amount of manipulation of the patient, it is rapid, the technique is simple, it is safe so far as can be judged, and it is attended by the minimum of complications.

Technique

The only apparatus required over and above that necessary for the administration of any spinal anaesthetic is a watch with an easily visible seconds hand. It is important that the fit between the syringe and the lumbar puncture needle should be watertight, and the finer the needle the better.

As light percaïne is sensitive to slight changes in pH, the instruments used should be dry. A few cubic centimetres of the solution are drawn into a 20-c.cm. syringe, which is swilled out with it, emptied into a receiver, and then refilled with the remainder of the ampoule. The patient is now placed in a sitting position on the operating table, with his arms on his knees—not sitting sideways with his legs dangling over the edge. The skin is cleaned in the usual way and a small wheal raised at the proposed site of injection with the percaïne solution, which acts to some extent as a local anaesthetic. This can be done with a hypodermic needle fitted on to the 20-c.cm. syringe. The lumbar puncture needle is then introduced until its point is just inside the spinal canal, a position easily found by withdrawing the needle slowly until the flow of cerebrospinal fluid stops, and then reinserting it a short way. About 5 c.cm. of cerebrospinal fluid is allowed to escape. Without disturbing the lumbar puncture needle the syringe is attached to it, and the percaïne injected at the rate of 1 c.cm. per second, so as to avoid turbulence in the spinal canal so far as is possible. Solution at theatre temperature is used; presumably with this slow rate of injection it is at body heat by the time the intrathecal space is reached. Timing is begun when the injection is completed, the needle and syringe being held in the same position for the

whole period; when the required number of seconds have elapsed both are removed simultaneously. It is important to avoid leakage at any stage of the procedure. The patient is immediately placed on his back on the operating table, and the head tilted downwards to an angle of about 20 degrees. By the time the site of operation has been prepared and isolated by towels anaesthesia will be complete and the operation may be begun.

The dose used is 12 c.cm. for adults, down to 7 c.cm. for children of 12, if spinal anaesthesia is thought desirable in such young patients. Using this technique, a larger dose is unnecessary, and a smaller dose gives a higher proportion of unsatisfactory anaesthesia. It is, in fact, possible to perform operations on the upper abdomen and chest with as little as 3 c.cm. by means of a mid-dorsal injection and posturing, but apart from some interesting observations on blood pressure there appears to be no advantage in using these very small doses. The lumbar interspaces used are those between the second and third and the third and fourth vertebrae, and the time between fifteen and thirty seconds.

Results

For some reason an injection between the second and third lumbar vertebrae will not necessarily anaesthetize the sacral and lower lumbar nerves, so for any operation involving their area of distribution the third to fourth lumbar interspace must be used. On the other hand it is, as a rule, impossible with this dose to obtain anaesthesia above the sixth thoracic nerve using an injection between L. 3 and 4, so that for upper abdominal operations the percaïne should be administered between L. 2 and 3. A further observation is that the maximum height of anaesthesia appears to be obtained after thirty seconds: patients have been sat up as long as sixty seconds without any increase in its level. Thus, using the maximum dose of 12 c.cm., there seems to be little foundation in fact for one of the criticisms levelled at Wilson's method—that of the danger of diaphragmatic paralysis and medullary involvement.

The following table shows the level of anaesthesia which should be expected with different sites of injection and timing. In this series of cases the level was tested with a towel clip in the mid-axillary line, the figure in column 4 corresponding to the highest insensitive intercostal space. A certain amount of variation appears in individual patients, where anaesthesia may be somewhat higher than intended, except in the case of upper abdominal operations. The timing in column 3 is the number of seconds during which the patient sits up after receiving the full dose.

Dose	Interspace	Time	Level
12 c.cm.	2-3 lumbar	15 seconds	10 thoracic
"	" "	20 "	8 "
"	" "	30 "	4 "
"	3-4 "	20 "	11 "
"	" "	25 "	8 "
"	" "	30 "	6 "

The maximum obtainable anaesthesia appears to be to the fourth thoracic. Two cases only in this series went higher; in both of these the second and third thoracic were also involved.

A few cases requiring subsequent spinal anaesthetics for various reasons after a lapse of a few days did not react in the same way, and an additional five seconds was necessary to give the same level of anaesthesia as before.

Supplementary Medication

At the beginning of this series premedication consisting of morphine was given half an hour before the operation; but this did not appear to be sufficient, and in more recent cases omnopon and scopolamine have been used. It is true that in a certain number of cases their effect is small, but in the majority this more extensive premedication has been quite satisfactory and has never given rise to anxiety, many patients falling asleep shortly after receiving the anaesthetic. Before coming into the operating theatre the patient's eyes are covered with a light bandage, and the ears may also advantageously be lightly plugged with cotton-wool. Absence of noise in the theatre makes it easier for the patient to sleep, and it may not be out of place here to mention that it is quite unnecessary to rouse the patient at intervals to ask him if it hurts. If it does it will be quite obvious. Fall of blood pressure is inevitable in a successful spinal anaesthesia; it can be partly remedied by the injection of ephedrine, which is given as a routine at or just before the time of anaesthesia. It has never caused any alarm, and the mere fact that the blood pressure has fallen is in itself no indication for the suspension of the operation.

Supplementary general anaesthesia may be necessary in cases where the spinal method is unsatisfactory (*vide infra*), or it may be desirable in the case of some patients. If this is so, sufficient anaesthetic to make the patient drowsy is, as a rule, all that is necessary, and for this purpose a few minims of chloroform, very slowly given, have proved eminently satisfactory.

Sources of Error

Although the technique is simple it is well worth while paying attention to details, as it is only by so doing that the best regulation of anaesthesia can be obtained. There are four common sources of error. (1) Leakage of fluid at any stage of the proceedings. (2) Failure to keep the vertebral column vertical during the injection and subsequent timing. (Wilson's experiments with coloured fluids in a glass tube demonstrate effectively what happens when the tube is tilted, and this is borne out by clinical observation.) (3) Delay in placing the patient on his back after the lumbar puncture needle and syringe have been removed. (4) Injection in the wrong lumbar interspace: this is not so absurd as it sounds in dealing with stout patients, when the surgeon is confronted with a back innocent of palpable bony points.

It may be of some value here to analyse briefly the various types of unsatisfactory anaesthesia encountered from time to time. In this series of cases failures have been recorded when supplementary general anaesthesia, however light, has been necessary for the successful execution of the operation. These consisted of 4 per cent. of the whole series, the proportion diminishing with increasing experience. They may be divided into three groups.

1. Those where the level of anaesthesia was not high enough and which occurred exclusively in operations on the upper abdomen. This group, which needs no further explanation, comprised 1 per cent. of the cases.

2. Cases in which relaxation is complete but in which the sense of touch is acutely present. A finger on the abdomen is construed as a painful stimulus by these patients. It may be significant that this type of failure is the one in which premedication has had little effect. A few drops of chloroform, sufficient to make the patient drowsy, are the most effective remedy; in many cases it may be discontinued after a few

minutes, the patient remaining asleep during the rest of the operation. This group accounted for $2\frac{1}{2}$ per cent. of the cases, or, if the upper abdomen be excluded, 3 per cent.

3. There is a small proportion of cases—0.5 per cent.—in which, in spite of apparently perfect technique, a spinal anaesthetic has no effect whatever: full sensation is present, there is no relaxation and no fall in blood pressure. In the absence of technical faults one is forced to fall back on the rather unsatisfying explanation of a "rachi-resistant" patient. This small number of cases comprised the only complete failures, and are ones that require supplementary full general anaesthesia.

Complications

The only complication to give any trouble during the performance of the subsequent operation was retching, occurring occasionally in upper abdominal operations, but very rarely otherwise. This phenomenon is most often observed in those patients in whom premedication has had little effect, and may occur at any time during the operation: it is fortunately temporary, and passes off spontaneously in a few moments.

There has been no mortality due to anaesthesia in this series of cases and, barring headache, no other complications that at various times have been attributed to spinal anaesthesia. Headache must not be regarded as the bogey of spinal anaesthesia; it occurs in about 7 per cent. of cases, is not of the intractable variety, and rarely lasts more than twenty-four hours. The incidence of this complication appears to be decreased by allowing cerebrospinal fluid to escape before injecting the percaine.

Summary

The results of observation on a series of cases of spinal anaesthesia administered by the time-diffusion technique are recorded. The series consisted of a total number, up to the time of writing, of 907 cases, in 551 of which dosage, timing, level of anaesthesia, etc., were carefully observed and correlated, and a further 356 cases administered as routine, which were not specially observed but which proved satisfactory.

The drug used throughout was light percaine, with the maximum dose of 12 c.cm. Presumably the results obtained would not hold good for other solutions.

The method appears to have a considerable margin of safety, is rapid, reasonably accurate, and has proved most satisfactory in practice.

The 551 cases were administered over a period of some seventeen months at the Anlaby Road Hospital, Hull, and for permission to publish them I wish to express my thanks to Dr. N. Gebbie, medical officer of health for Hull, to Dr. Tod, superintendent of the hospital, and to Mr. C. H. Corbett, consulting surgeon to the hospital. The remainder of the cases were administered at the Royal Infirmary, Sheffield, and for permission to publish these I wish to express my thanks to Mr. R. St. Leger Brockman, surgeon to the infirmary.

A circular letter from the Ministry of Health to medical officers in charge of venereal disease treatment centres states that under the arrangements being made for the examination and calling up of men liable for service under the Military Training Act, 1939, it may well happen that patients receiving treatment at the centres are affected. As it is most desirable that the treatment should not be interrupted, information regarding each case should be available to the Medical Board undertaking the examination; also details of previous treatment should be made known to the medical officer at the depot where the patient is called up. Each patient affected should therefore be supplied with Form V.15 setting out particulars of his case, and should be instructed to hand it to the medical officer concerned.

PREGNANEDIOL EXCRETION IN THE MENSTRUAL CYCLE

BY

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The absence of a satisfactory method of determining the functional activity of the human ovary has been a serious obstacle to gynaecologists in the treatment of disorders of the menstrual cycle and of sterility. The difficulty of detecting the small amounts of gonadotrophic hormone and of oestrin excreted in the cycle renders such estimations of little value. In 1936 Venning and Browne isolated from human pregnancy urine the glucuronide of pregnanediol, and showed that its excretion during pregnancy and the menstrual cycle is directly related to corpus luteum hormone secretion in the body. The amount of pregnanediol recovered in the urine was found to be equal to 40 to 45 per cent. of the amount of corpus luteum hormone being secreted, on the basis of the quantity of pregnanediol recovered after injection of progesterone, the corpus luteum hormone. In a study of the excretion of pregnanediol by about twenty healthy women Venning and Browne (1937a, 1937b) found a considerable variation in the output, the range being from 3 to 60 mg.; they also found that variations existed in the excretion in different cycles of the same individual. As a general observation it was noted that where the amount of pregnanediol excreted was low—for example, less than 20 mg. in six days—and where the luteal phase was short, there was a history of functional sterility. No pregnanediol was found during the follicular phase—that is, the proliferative phase in the endometrium—but only during the luteal phase of the cycle—that is, from about two days after ovulation until one to two days before menstruation, covering a period roughly from the twelfth to the twenty-seventh day of the cycle, or a total excretion period of eleven to sixteen days. During the luteal phase, when pregnanediol occurs in the urine, the endometrium is no longer proliferative but secretory. It is thus possible to determine the existence of a functional corpus luteum in two ways: (a) by histological examination of endometrial scrapings, and (b) by estimation of the excretion of pregnanediol in the urine. In the present investigation the two methods were employed, and the result of each was given independently of the other and without knowledge of the finding obtained or information as to the stage of the cycle.

Methods and Results

The five patients mentioned in this report were suffering from sterility, and it was deemed advisable to estimate the activity of their ovarian luteal tissue as well as to examine the reaction of the uterine endometrium. Estimations of the excretion of pregnanediol will reveal, it is hoped, those cases of sterility and other abnormalities in which progesterone therapy is specifically indicated.

Pregnanediol.—The improved method of extraction of sodium pregnanediol glucuronide published by Venning in 1938 was used, and the weights of the glucuronide converted into pregnanediol by the approved formula.