CLINICAL EXPERIENCES WITH PERCAIN,
A NEW LOCAL ANAESTHETIC.

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LOCAL anaesthesia—a term used in this article to cover tissue infiltrations, nerve trunk and splanchnic blocks, and spinal anaesthesia, whether for the production of “anaesthesia” or “analgesia”—has not been, and possibly never will be, as popular in this country as on the Continent and in certain parts of the United States. This is probably largely owing to the traditional ideas established in the minds of the public, which make them less likely to co-operate willingly with the surgeon, and create a bias in favour of complete unconsciousness. It must be pointed out that the technique of local anaesthesia demands much more than the somewhat perfunctory attention usually paid to it; moreover, the special care that must be given to certain details in the performance of operations under local anaesthesia of necessity restricts the surgeon's freedom of action, and this may at times be considered a sufficiently grave inconvenience to outweigh any advantages the method might offer. The last point in its turn will depend upon the type of operation and the temperament of the surgeon.

Other things being equal, however, the disadvantages would be minimized if the local anaesthetic could conform with the following desiderata.

1. Practical non-toxicity in relatively large doses and the absence of idiosyncrasy.
2. Rapidity of action in order that the injection itself may be painless and that complete anaesthetization of the area may be induced within a reasonable period of time.
3. Good powers of diffusion and penetration.
4. A duration of anaesthesia sufficient to enable the most extensive operation to be performed without reinjection.
5. An ideal quality would be a prolonged period of dulled sensibility after the anaesthetization proper had passed away.
6. There should be no impairment of tissue vitality or retardation of healing—a fatal defect of quinine and urea hydrochloride, a substance that exhibits the previously mentioned quality to a pronounced degree.
7. The substance should be readily eliminated.

In addition to these physiological properties the local anaesthetic should have the following physical characteristics.

1. It should be stable both in the solid and in the dissolved condition.
2. It should be unaffected by exposure to air, or by exposure to heat, for the purpose of sterilization; or by admixture with saline, adrenaline, and such substances as may reach it from the walls of vessels, instruments, and syringes.
3. For spinal injection it would be advantageous for the solution to be effective in such low concentration that the specific gravity could, if necessary, be made lower than that of the cerebro-spinal fluid—that is, about 1006. Inexpensiveness would, of course, be an added attraction.

The anaesthetic group in use at the present time (the novocain group) possesses many of these characteristics and gives on the whole considerable satisfaction. Among the chief disadvantages, however, are the following: the anaesthesia, even in conjunction with adrenaline, is not sufficiently long for the performance of some major operations, so that reinjection is sometimes necessary; there is no post-operative anaesthesia, indeed sometimes there is abnormal post-operative pain (it must be admitted that this is due usually either to defective haemostasis, which must be meti-

culous when adrenaline is used, or to the employment of heterotonic solutions); it is liable to destruction by oxidation, is none too stable on heating, and is very labile in the presence of even traces of alkalis. In contrast with cocaine, its action on intact mucous and other surfaces, such as the conjunctiva, nasal mucosa, and urethra, is lamentably inferior. Its mild vaso-dilator action is readily counteracted by the use of adrenaline.

We have recently tried in a considerable number of cases of all types a new local anaesthetic, percaïn, made by Ciba of Basle, and handled in this country by the Clayton Aniline Company. Percain is a quinoline derivative, being the hydrochloride of diethyl-ethylene diamide of alpha-butyl oxyquinolinic acid, with the structural formula

It forms colourless crystals soluble in water; the solution may be sterilized without deterioration by boiling. In the preparation of such solutions, however, care must be taken that no alkali comes into contact with them lest precipitation should occur, a particularly serious event where the concentration is so low. Glass free from alkali should be used, and the saline prepared with doubly distilled water, containing no trace of sodium carbonate or bicarbonate; accidental contamination by these may be countered, however, by the addition of a minute quantity of dilute hydrochloric acid—for example, two or three drops per litre. Percain is miscible with adrenaline. The specific gravity of effective dilute solutions in water may be as low as 1002, and, therefore, by the use of varying degrees of tonicity of saline, solutions of any specific gravity likely to be desired can be produced. This, it should be realized, is the first time that a watery solution of anaesthetic having a specific gravity either equal to or even appreciably less than that of the cerebro-spinal fluid has been available. This fact promises to revolutionize the whole technique of spinal anaesthesia, since it enables anaesthesias to predetermined levels to be obtained with reasonable certainty. The special methods adopted to obtain high-level anaesthesia with percaïn are at present being standardized by Dr. Howard Jones, senior anaesthetist to Charing Cross Hospital.

The following are the outstanding physiological qualities that attracted attention. (1) The extreme degrees of dilution in which the drug is capable of producing efficient anaesthesia. (2) The prolonged period of action. With regard to the former, its effective concentration on the cornea of the rabbit is 1 in 120,000, compared with 1 in 15,000 for cocaine; weight for weight, therefore, it is easily the most powerful local anaesthetic known. Against this it must be admitted that percaïn is far from being non-toxic, a subcutaneous dose of 0.01 gram per kilo being lethal to the rabbit, giving rise to excitement, dyspnoea, and cramps, with death from respiratory paralysis; rapid intravenous injection is fatal in a dose of 0.0045 gram per kilo. This may be compared with the following figures for other local anaesthetics: cocaine, injected slowly intravenously in the rabbit, 0.019 gram per kilo; cocaine hypodermically in dogs, 0.025 per kilo; novocain intravenously in rabbits, 0.06 per kilo. The British Medical Association Committee's scale of relative toxicities is as follows: cocaine 1.0; stovaine 0.625; novocain 0.49; beta-eucaine 0.414. (Allen, however, gives the toxicity of novocain as being six to seven times less than that of cocaine.) On this scale, therefore, percaïn would stand at about 4.0.

Percain shows inhibition of bacterial growth, but in the concentrations employed is not definitely bactericidal. Hofer states that its minimal effective concentration in the rabbit subcutaneously is 1 in 140,000, and that “there seems to be a particular sensitivity of the splanchnic system to the preparation, these vessels being enormously swollen in the killed animal.” Owing, however, to the extreme intensity of its action there would appear to be not the slightest likelihood of anything approaching the lethal dose being needed for operative procedures. There is, further, as far as can be ascertained, no record of

such personal idiosyncrasy as is notorious in the case of cocaine.

With regard to the second quality—namely, prolonged period of action—percaïn is surpassed only, though easily, by quinine and urea hydrochloride; this last substance, however, has two almost insuperable contraindications—its painful induction and sometimes disastrous local toxic effects. With percaïn a duration of anaesthesia of between two and six hours, according to the concentration, is alleged to be obtained.

Personal Tests.

We have tested the anaesthetic properties of percaïn upon ourselves, with the following results. The intradermal injection (1 in 2,000 without adrenaline) produced immediate and complete insensitivity lasting about two and a half hours. Subcutaneous infiltration (without massage or kneading, which we have found to accelerate induction) was followed by anaesthesia in about five minutes, lasting over three and a half hours. In neither case was there subsequent hyperaesthesia or dermal change (for example, desquamation). In the intradermic, and to a less extent in the subcutaneous injections, there was an immediate severe hyperaemia coterminous with the anaesthesia. In the infiltration of a small subcutaneous nerve (perineural infiltration with the same concentration) there was anaesthesia in about twelve minutes, lasting over five hours.

Clinical Experiences.

Our experience, which now extends over four months, would appear to support the claims made. The substance has been employed in local infiltration (of the Schleich type), nerve blocks, paravertebral anaesthesia, splanchnic blocks, and spinal anaesthesia. The concentrations used have been 1 in 1,000 to 1 in 2,000. It is usually recommended that ten minims of adrenaline (1 in 1,000) to each ounce of local anaesthetic solution is the appropriate dose; we find that this may be doubled or even trebled with no deleterious effect, but with greatly enhanced convenience as regards speed and intensity of action. The addition of adrenaline is essential, as without it percaïn seems to have a much greater local vaso-dilator action than novocain. In the above concentrations we have frequently employed three or four ounces of solution; in one instance seven and a half ounces were used (this was a partial gastrectomy with parietal and splanchnic infiltrations; the concentration was 1 in 1,500, and the total quantity, therefore, about 2 grains).

In the considerable number of cases now dealt with we have observed no evidence of toxic effect, either general or local; there has been no undue tissue reaction and no impairment of healing after any local infiltration. Thiersch grafts removed under subcutaneous infiltration (1 in 2,000) take in a perfectly normal manner. There has been no evidence of neuritis or impaired conduction after any nerve block.

When due attention is paid to the special points to be observed in all operations under local anaesthesia—for example, avoidance of traction on structures attached outside the infiltrated field—the procedures could be carried through without giving pain to the patient. Phenomena of sensory dissociation are quite frequent, painful sensation always being lost, but that of pressure and touch sometimes being retained. This, of course, is commonly observed in all forms of local anaesthesia, although never to the same startling extent as with small spinal injections. Post-operative anaesthesia was uniformly seen, varying from three to six hours. This admittedly falls short of the ideal, which would have a duration of several days; but nevertheless it is sufficient to confer a very distinct advantage.

A detailed list of the cases in which percaïn has been used would be tedious and unnecessary; the following summary will, however, indicate the practically unrestricted scope of the preparation. Finger operations (infiltration of root); Dupuytren's contracture (wrist infiltration and ulnar and median block); simple subcutaneous tumours; diagnostic removal of glands; oral anaesthesia for radium (lingual and dental nerve blocks); scalp anaesthesias,

Thiersch grafts, sympathectomy, herniorrhaphies, varicocele and hydrocele operations, anal operations, simple mastectomy, ventriculography, colostomy. Among the more extensive procedures are: gastro-enterostomy, gastrectomy, appendicectomy, cholecystectomy (with a localized splanchnic block in addition), gastrectomies, thyroidectomies, pituitrectomies. In these, general hypnotics have, in addition, been administered—hyoscine or morphine.

Surface Anaesthesia.

We have no experience of percaïn in its application to the conjunctiva and to the nasal mucosa. It has been repeatedly employed in a 1 in 1,500 concentration to the urethral mucosa for the performance of cystoscopy—but has not seemed quite equal in intensity to the usual cocaine-chloreton combination.

Spinal Anaesthesia.

While percaïn can be claimed to show a distinct advance on previous local anaesthetics in its application to infiltration and nerve-blocking anaesthesia, there can be no doubt that its greatest attraction lies in the special advantages it confers in spinal anaesthesia. These are the duration of action and the low specific gravity of effective solutions. The latter characteristic has made necessary and possible some important modifications of the usual technique of administration; these, as has already been stated, are still in process of standardization, and will therefore not be dealt with fully in this article. Our experience of some hundred cases, however, enables us to make certain positive statements. The anaesthesia takes somewhat longer to develop than that with novocain, but the rate varies, of course, with the concentration employed. It may last anywhere up to six hours, again depending on dose and concentration. As an indication of the extent of action it may be stated that complete anaesthetization of the abdomen, including the splanchnic nerves, may be obtained by the injection of 12 to 16 c.cm. of a 1 in 2,000 solution at the first or second lumbar interspace. The most prolonged abdominal operation may therefore be performed under intrathecal injection alone. The anaesthesia has persisted several hours after the completion of resection for gastro-jejunal ulceration, the abdomino-perineal removal of the rectum, and operations of like severity.

The fall of blood pressure produced by splanchnic paralysis is probably less severe than with novocain, though, of course, it lasts much longer; it can to a large extent be overcome by administration of ephedrine, but particular care must be taken of the posturing of the patient for many hours after the operation is completed. It may be emphatically stated, however, that in this long series of cases no instance of serious vasomotor collapse has been met with such as to give rise to the least anxiety or to call for any special treatment. The early sickness which is so common with novocain injections is relatively infrequent with percaïn, as are also post-operative headaches.

Sensory and motor dissociations have been observed apparently in a greater proportion of cases than with other intrathecal agents, possibly in part owing to the very low specific gravity of the solution. No irritant effects on nerve roots or cord have been observed. The upper level of action has been sufficiently high in some cases to cause numbness and tingling of the hands; the need for caution with regard to the avoidance of phrenic paralysis when using a drug with a four hours' action is obvious. So far, at any rate, the trouble has not arisen.

Conclusions.

Weight for weight, percaïn is less expensive than novocain, and when the dilution is taken into account (0.075 to 0.05 per cent. as compared with 0.5 per cent.), it is very much cheaper. Contrasted with ether and gas and oxygen the cost per patient is infinitesimal.

As a result of our experience we are led to conclude that percaïn marks a definite advance over existing local anaesthetic substances, and particularly we believe that it promises to mark a very considerable advance in spinal anaesthesia.