done in order to enable a large final dose to be given and at the same time to avoid the inconvenience which would have been caused to the patients had it been decided to work up to the maximum dose by an increased number of injections. Very few of those inoculated developed a general reaction; in such cases intermediate doses were administered with only a 50 per cent. increase over the previous dose. A very small percentage required the full number of five doses. In the few cases in which a reaction occurred, there was already existing some degree of mild, acute, or chronic catarrh. By paying careful attention to the importance of already existing catarrh, it should be possible to avoid general reactions.

Persons subject to "colds" and influenza are to a large extent the "carriers" of the coryza epidemics. The micro-organisms which they pass on have often an increased virulence. They are the most susceptible to infection, and have the lowest resistance. In our efforts to reduce epidemics, these cases must be immunized against their own micro-organisms, and, for a few years, should be prophylactically immunized against the prevailing coryzal infection.

The result of this inoculation on absenteeism for catarrhal conditions was as follows. The percentage of inoculated persons who lost time owing to catarrhal affections was 35.294; while the corresponding percentage of uninoculated persons was 51.625. There is little doubt that the beneficial effect of inoculation would be much more obvious were it not for the efficacy of the treatment applied to the uninoculated who subsequently became infected.

TREATMENT OF CATARRHAL CONDITIONS

Patients reporting sick were divided roughly into two classes:

1. Those in whom severe symptoms had developed. These cases were subdivided into: (a) those where the onset of symptoms occurred less than thirty-six hours before the patient reported sick; (b) those where the onset of symptoms occurred more than thirty-six hours before the patient reported sick, and where he had neglected to seek medical advice in the early stages of the infection.

2. Those presenting only mild symptoms.

The cases classified as severe were those with a temperature of over 100°, pulse over 120, headache and severe coryza, or physical signs of involvement of the lungs or bronchi. The mild cases were given simple symptomatic treatment—for example, quinine, aspirin, expectorants, etc.

The treatment for cases classified as severe was determined by the duration of the symptoms. Patients who gave a history of thirty-six hours or less were given 1 c.cm. of S.U.P. 36 intramuscularly. Injections were made at first into the upper border of the trapezius muscle, but later into the deltoid, as injections at this site produced less discomfort.

Cases which were of more than thirty-six hours' duration were given 2 c.cm. hypodermically of a polyvalent antibody. The preparation which gave the most satisfactory results is that sold under the name of "antibacsyn." This injection was repeated daily in a number of patients who were able to continue at work, but who still presented some symptoms.

It is to be noted that the patients treated with S.U.P. and antibacsyn were such as, in the ordinary course of events, might be expected to be disabled from one to three or more weeks. In a few instances in which the patient "did not believe in injections," the refusal of treatment was followed by absence from work of from two to six weeks, and many of these cases were certified as acute bronchitis, lobular and lobar pneumonia.

The absenteeism among the severe cases so treated was 3.958 days, while the absenteeism among the mild cases amounted to 3.536 days. In other words, the severe

cases so treated lost less than half a day more than the very mild cases which were given simple symptomatic treatment. One may conclude, therefore, that in S.U.P. 36 for early cases, and in antibacsyn for later cases, two valuable agents are available for combating the enormous loss of efficiency which catarrhal conditions impose on the community.

CONCLUSIONS

Prophylactic inoculation showed a definite reduction in the incidence and severity of catarrhal illnesses. This reduction is to some degree obscured by the successful use of S.U.P. 36 and antibacsyn in the treatment of the uninoculated—S.U.P. administered within thirty-six hours of the onset of the symptoms and antibacsyn administered after this period—which very substantially reduced the absenteeism from acute catarrhal conditions.

I must express my thanks to Dr. Brady for his invaluable advice and for his assistance in the preparation of the vaccines.

THE PHARMACOLOGY OF PERCAINE

BY

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While considerable clinical experience of percaïne has been reported in this country, in the *British Medical Journal* and elsewhere, both as a local anaesthetic (Lake and Marshall,¹ Walker,² Popper³) and for spinal anaesthesia (Howard Jones⁴), no report of the pharmacology of this drug has, to our knowledge, appeared from a British laboratory. In view of the discrepant findings of Continental workers (Uhlmann,⁵ Lipschitz and Laubender⁶), and of the increasing use of local and regional anaesthesia in surgery, a further investigation of percaïne, and a comparison of it with the more established members of the group, seemed desirable.

Percaïne is a quinoline derivation—the hydrochloride of the diethylethylenediamide of α -butyloxycinchonic acid.

It is manufactured at Basle, and the first publication of its properties was made in June, 1929, by Uhlmann.⁵ It is available in crystalline form, and is colourless, odourless, and easily soluble in water or normal saline, but is readily precipitated by alkali. The makers' claims—that it can be heat-sterilized without loss of strength, and that it can be combined with adrenaline—have been confirmed. Sterile solutions are stable, retaining full activity for several months at least. We have had some evidence that solutions which have not been kept under aseptic conditions lose their activity in a relatively short time.

The following experimental investigations have been carried out, in the hope that the value of the new drug might be fairly assessed.

Intradermal Wheal Test on the Human Subject

Solutions of various strengths in 0.9 per cent. NaCl were injected intradermally, always using 0.5 c.cm. for a test. The sensation of pain was tested by the application to the skin of a pin-point suitably mounted. Tests were directed to determine (a) the minimal concentration required for anaesthesia as compared with novocain, and (b) the duration of the anaesthesia afforded by any given

concentration. The results are given in tabular form, showing (1) the drugs used by themselves, and (2) with adrenaline as an adjuvant. It will be seen (1) that the minimal effective concentration of percaine is about one-fortieth of that of novocain; (2) that 0.05 per cent. percaine produces anaesthesia for longer than 1 per cent.

TABLE I

Drug	Concentration (per cent.)	Duration of Anaesthesia in Minutes	
		(1) Without adrenaline	(2) With addition of adrenaline, 0.002 per cent.
Percaine ...	0.008	0	(60)
	0.012	0	100
	0.016	0	240
	0.025	35	280
	0.05	70	320
Novocain ...	0.12	0	(60)
	0.25	0	160
	0.50	6	220
	1.00	25	270

Note.—Adrenaline alone is probably responsible for the anaesthesia shown in parenthesis.

novocain; (3) that when both are mixed with adrenaline 0.002 per cent., 0.05 per cent. percaine and 1 per cent. novocain produce anaesthesia of equal duration in the skin—nearly five hours.

Blocking of the Nervous Impulse in the Frog's Nerve-Muscle Preparation

This test is mainly of academic interest, being valuable for the comparison of the ability of anaesthetics to block impulses in motor nerve fibres. About 1 cm. of the nerve of the ordinary sciatic-gastrocnemius preparation is immersed in a solution of the anaesthetic, and the duration of immersion in which conduction is just suspended is determined. The two hind limbs of the frog yield two similar preparations, so that two drugs can be fairly accurately compared for their activity. By this test percaine is about seven times as efficacious as cocaine.

Anaesthesia of the Rabbit's Cornea

This test is of importance for its application to ophthalmological practice in particular, and the anaesthesia of mucous membranes in general. The method prescribed by Sollman⁸ was used. The conjunctival sac

TABLE II.—Anaesthesia of the Rabbit's Cornea

Percaine						
Dilution (per cent.) ...	0.002	0.005	0.010	0.017	0.025	0.05
Duration (minutes) ...	0	0	10-15	45-60	90-120	over 180
Cocaine						
Dilution (per cent.) ...	0.2	0.5	1.0	2.0		
Duration (minutes) ...	0	7-10	15-20	30-40		

is flooded with the solution under test for one minute, and the corneal reflex is stimulated at intervals until it returns. The durations of anaesthesia thus obtained for various concentrations of percaine and cocaine are given in Table II.

It will be evident that percaine is efficacious in about one-fiftieth of the concentration of cocaine which abolishes the reflex. No adrenaline was added to the solutions in any of these experiments.

Experimental Spinal Block in the Cat

In two of three experiments in which novocain and percaine were alternately introduced by lumbar puncture into the spinal theca of a chloralosed cat, it was found that percaine abolished active reflexes, such as the knee-jerk, in a dosage of about one-fortieth of that of novocain, and the anaesthesia, as tested by the abolition of these reflexes, lasted three or four times as long—for example, two hours with 0.5 mg. of percaine, as against half an hour with 20 mg. novocain. This is quite in accordance with the claims made for percaine by Howard Jones.⁴

Toxicity of Percaine

This is obviously a matter of great importance, for percaine, like other local anaesthetics, falls short of the ideal in being a distinctly toxic drug. We have carried out estimates of relative toxicities by the lethal dose following (1) subcutaneous injection into guinea-pigs, and (2) intravenous injection into cats, using paralysis of respiration as an end-point. The details of this second method, which we have elaborated in order to get a more accurate measurement of relative toxicity—two drugs being compared on a single animal—will be published elsewhere.⁹

The results of the guinea-pig method indicate that percaine is about twenty-five times as toxic as novocain and three times as toxic as cocaine; by the cat method the corresponding figures are fifteen and two respectively, and in the authors' opinion the latter figures are the more reliable. Taking these figures we can form, as in Table III, an estimate of the relative efficiencies of the three drugs.

TABLE III.—Relative Efficiency

Relative Efficiency	Percaine	Cocaine	Novocain
(a) In intradermal wheal ...	10	1	6
(b) In rabbit's cornea ...	25	1	1/3 or less
(c) As spinal anaesthetic ...	3	—	1

The efficiency of a local anaesthetic for any purpose is determined by the ratio of the active or adequate dose to the toxic dose.

DISCUSSION

The figures of Table III suggest that percaine and novocain are of the same order of efficiency when used for subcutaneous anaesthesia, and the difference in favour of percaine for spinal anaesthesia is probably not as great as it appears to be, for the action of novocain intrathecally can be limited and intensified and prolonged by giving it in a viscous solution. On the other hand, for local application to mucous membranes percaine is quite the most efficient local anaesthetic we have so far investigated. As far as can be seen, no injurious results follow from continued application of the drug to mucous membranes—even to a membrane as delicate as the conjunctiva. Thus 0.05 per cent. percaine was applied once a day for fourteen days to the eye of a rabbit without any noticeable ill effects. The fact, noted by Uhlmann,⁵ that much higher concentrations may cause corneal opacities is of toxicological rather than of ordinary practical interest.

From these experiments we conclude that for infiltration anaesthesia, in view of its considerably greater toxicity, no great advantage can be claimed for percaine as a substitute for the novocain-adrenaline combination to which the surgeon is well accustomed. Occasionally, where adrenaline action is to be avoided, percaine would supply an adequate duration of anaesthesia without interfering significantly with the local circulation; and percaine is a cheap substitute for novocain, especially since it is

effective in considerable dilution. For mucous membranes, on the other hand, we agree with Popper³ that percaïne is a most promising addition to the surgeon's pharmacopœia, and may well pave the way to the abandonment of cocaine.

REFERENCES

- ¹ Lake and Marshall: *British Medical Journal*, 1930, i, 488.
- ² Walker, K.: *Brit. Journ. Urol.*, 1930, ii, 129.
- ³ Popper, O.: *British Medical Journal*, 1930, i, 669.
- ⁴ Jones, W. Howard: *Brit. Journ. Anaes.*, 1930, vii, 99 and 146.
- ⁵ Uhlmann, T.: *Narkose und Anaesthesie*, 1929, vi, 168.
- ⁶ Lipschitz, W., and Laubender, W.: *Klin. Woch.*, 1929, viii, 1438.
- ⁷ Idem: *Ibid.*, 1930, ix, 968.
- ⁸ Sollman, T.: *Journ. Pharm. and Exper. Therap.*, 1918, ii, 17.
- ⁹ Macdonald, A. D., and Israëls, M. C. G.: *Journ. Pharm. and Exper. Therap.* (in the press).

THE MECHANISM OF CEPHALIC PRESENTATIONS

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The main features of the mechanism which the head goes through, when in the pelvis, in cephalic presentations are easily understood; but the rotations which occur after the head is born are usually ill described. This is probably because these rotations are not very important in practice. A clear conception of them is nevertheless

mechanical conception of the movements is of assistance, since it tends to a clear understanding of the whole mechanism of cephalic presentations, provided that the limitations of such mathematical conceptions are realized.

The following generalizations are helpful in a consideration of the exact nature of the movements of the head after disengagement.

1. Restitution is equal in degree but opposite in direction to internal rotation.
2. Restitution plus external rotation together make a right angle.

When rotation of the head occurs in the pelvis, the shoulders as a rule do not undergo much rotation, and for the present purpose we shall consider that, apart from descending, they remain fixed and do not rotate. As soon as the head is born the twist on the neck is undone, and the head slips back to the position it occupied when engagement occurred. This movement is called restitution, since the head is restored to its normal position in relation to the shoulders. In anterior positions restitution is slight, occurs through one-eighth of a circle, and is difficult to observe. In posterior positions internal rotation of the occiput occupies three-eighths of a circle; according to our rules restitution ought to be a movement of corresponding extent, though of opposite direction; and external rotation, a small movement through one-eighth of a circle in the reverse direction to restitution, so as to bring the bisacromial diameter and the sagittal suture at right angles.

MECHANISM OF L.O.A. (Face Looks to Right).

The circle represents the pelvis seen from above. The dotted line is the bisacromial diameter. The arrow is the sagittal suture, and the dot at its tail the occiput.

MECHANISM OF R.O.P. (Face Looks to Left).

desirable, especially for the student. Two phases of mechanism of the head may be considered:

1. In the pelvis—consisting of engagement, descent with internal rotation,* and extension at the outlet, causing disengagement or birth of the head.
2. Outside the pelvis—consisting of restitution and external rotation.

These two movements of the head after it is born are commonly ascribed to untwisting of the neck and rotation of the shoulders respectively. Their exact extent is not usually described, and is, in fact, hard to determine. Observation is difficult, since the movements may occur rapidly. The exact extent of these rotations is not of great importance in practical midwifery, since the head is already born when they occur, and subsequent difficulty is relatively uncommon. Nevertheless, an accurate

Internal and external rotations are sometimes described as being in opposite directions in all cases. While it is true that the rotations of the head occurring in the pelvis and outside the pelvis are in opposite directions, it will be seen from the diagrams that in posterior positions it is the part of rotation outside the pelvis called restitution which is opposite in direction to internal rotation; and that the true external rotation—that is, that due to rotation of the shoulders—is actually in the same direction as internal rotation of the head, though only of small degree. The foetal neck is capable of considerable torsion, but the head and shoulders cannot, in posterior positions, be considered as independent of each other. Internal rotation of the head takes place when the foetus is low in the pelvis, by which time some rotation of the shoulders will also have begun. For the sake of clearness this need not upset our mechanical conception, and for teaching purposes it is simpler to

* The term "internal rotation" means rotation in the pelvis, and does not refer to the direction of rotation.