

old bogey of post-operative pyelitis has also been laid by Colonel Fraser, for in his own case it did not occur, and 11 years later the patient conceived and went to term.

Cases of inoperable vesico-vaginal fistula are among the most tragic known to gynæcologists, and I feel sure that every surgeon will welcome this contribution to our art, and particularly applaud the philosophy attending the last part of his paper, where he explains the necessity of two operations by telling his illiterate patients that "the urine is escaping from two holes, hence he can only close one hole at a time."

Pruritus ani.—There is no condition in the East which can give so much trouble as the above disease.

From a practical point of view, there are two main groups; the one having some definite local cause which gives rise to an abnormal amount of perianal moisture, such as prolapsing piles, sentinel piles, fissure, fistula, thread worms, etc., which can be cured by removing the excitant cause, or by simple lotions and potions.

The other group are those in which examination reveals no obvious cause whatever and all one sees is excoriation, or fissuring of the skin around the anus, although microscopic examination may demonstrate epiphytic or vegetative organisms beneath the artificial dermatitis produced by scratching.

For these cases x-rays are used, subcutaneous injections given, caustic paintings made, and even operations performed without permanent relief, the patient developing a pathetic state of mental distress. Recently, however, Gabriau has reported marked success following the use of an oily substance, known as Benacol or A. B. A. made by Allen and Hanbury; 2 to 4 c.c. are injected subcutaneously around and up to the anal margin, commencing under the area of maximum of irritation. The injection is repeated in 3 to 7 days going round the anus clock-wise; the treatment is painless and without reaction, as a rule 3 to 6 injections are necessary.

The dermatitis improves dramatically and does not recur.

CENTEPEDA ORBICULARIS.

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Botany.—*Centepeda orbicularis*, or sneezewort, is a well-known indigenous herb. It is best known by its Hindi name *nakchhikni*. It belongs to the natural order Compositæ, and is found in the plains of India and Ceylon. It grows wild in the uncultivated fields in the latter part of the cold season. It is a small plant with leaves only 3 mm. in length growing radially from a central root, the stems numbering 4 to 6 give out small

rootlets, the whole plant covering a space about 6 to 7 inches.

Alleged properties.—It has a wide range of use in indigenous medicine; it is used in powder form as a snuff in ozæna, headache, cold in the head. It is also applied as a paste in toothache, hemicrania, and joint pains. Internally it is given as a vermifuge and in various forms of paralysis. Infusion of the drug is used as an eyewash in all forms of ophthalmia.

It was by accident that we started to work out the pharmacology of this herb. While searching for diuretics in the indigenous medicine we mistook *Centepeda orbicularis* for *Dregea volubilis* which is alleged to be a diuretic. Thinking that probably its alleged diuretic effect might be through the circulation, a crude experiment with a watery extract was tried on a frog's heart. After a few preliminary failures we found that its watery extract had a distinct stimulating action on a frog's failing heart. At this stage we found out our mistake that the drug we were experimenting with was not *Dregea volubilis* but *Centepeda orbicularis*, but finding that it had a stimulating action on the heart we decided to continue to work out its pharmacological action.

We could not find in what doses it was meant to be administered, and suspecting that the drug was more or less poisonous, we proceeded to determine its dose in the following manner:—

A crude tincture was prepared from the whole plant exactly on the same lines as given for the preparation of pharmacopœial tincture of digitalis from digitalis leaves. A volunteer was selected. His average blood-pressure and pulse rate were noted. Then he was given the tincture, starting from 1 m. three doses daily and steadily working up to 30 m. A rise of 5 mm. of blood-pressure was noted at this stage, accompanied with resulted griping, but without any purgative effect. We took this as a safe dose of the tincture we had prepared.

Chemistry.—Besides containing the ordinary plant constituents, *Centepeda orbicularis*, when subjected to chemical analysis, yielded sufficient evidence to indicate the presence of an alkaloid, a bitter principle of a glucosidal nature, a saponin, some resins, and colouring matter.

An alcoholic extract was made by macerating 10 gms. of the drug in 4 ozs. of rectified spirit, the whole dried and extracted with water. The watery solution gave practically no reduction with Fehling's solution, but on hydrolysis in 1 per cent. sulphuric acid for one hour it copiously reduced Fehling's solution, thus giving an indication of the presence of a glucoside.

A similar alcoholic extract was boiled in 1 per cent. sulphuric acid, and precipitated a copious resinous material as residue. The clear acid fluid was neutralized with ammonium hydroxide and extracted with ether. On evaporating the ether a mass was left, indicating the presence of an alkaloid.

Ten grammes of the drug was boiled in 500 c.c. of distilled water and kept for a time.

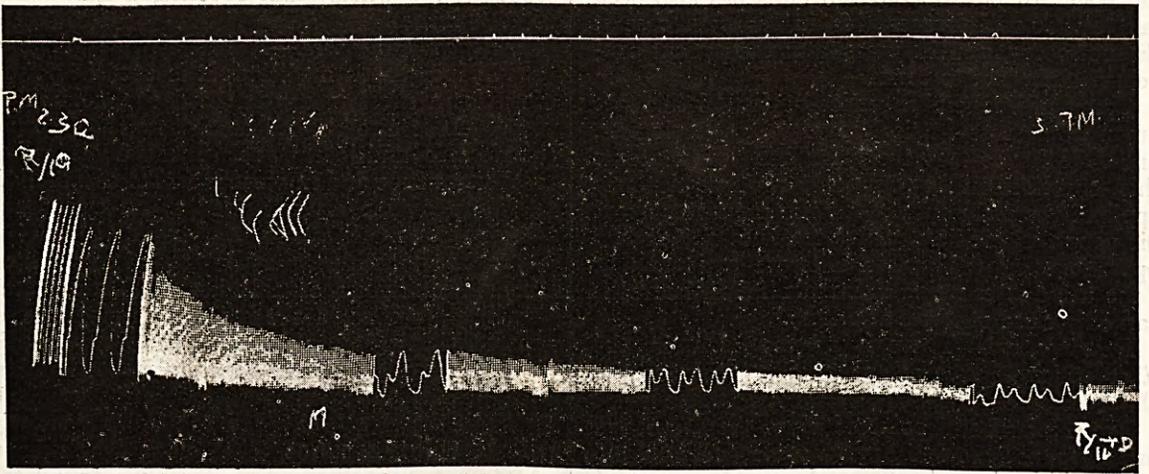


Fig. 1 A.

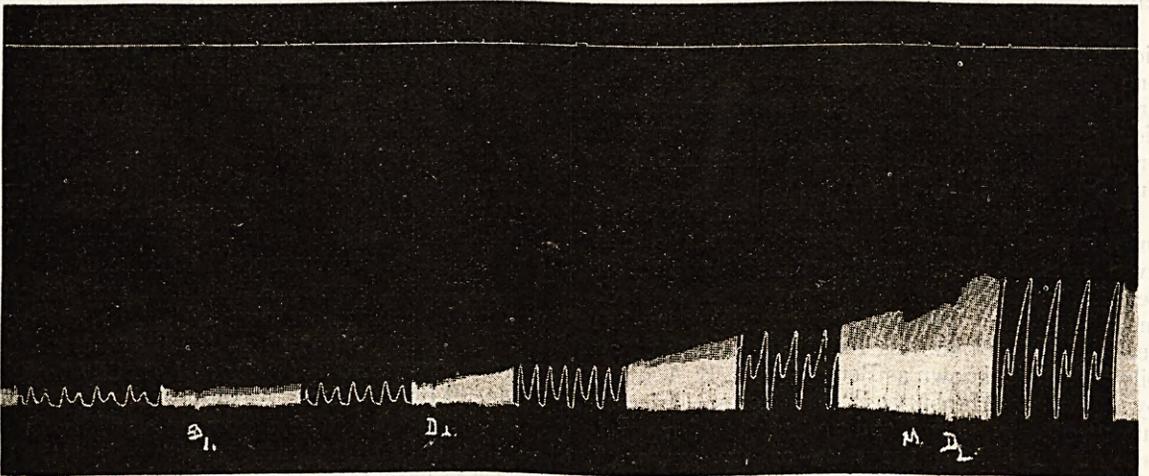


Fig. 1 B.

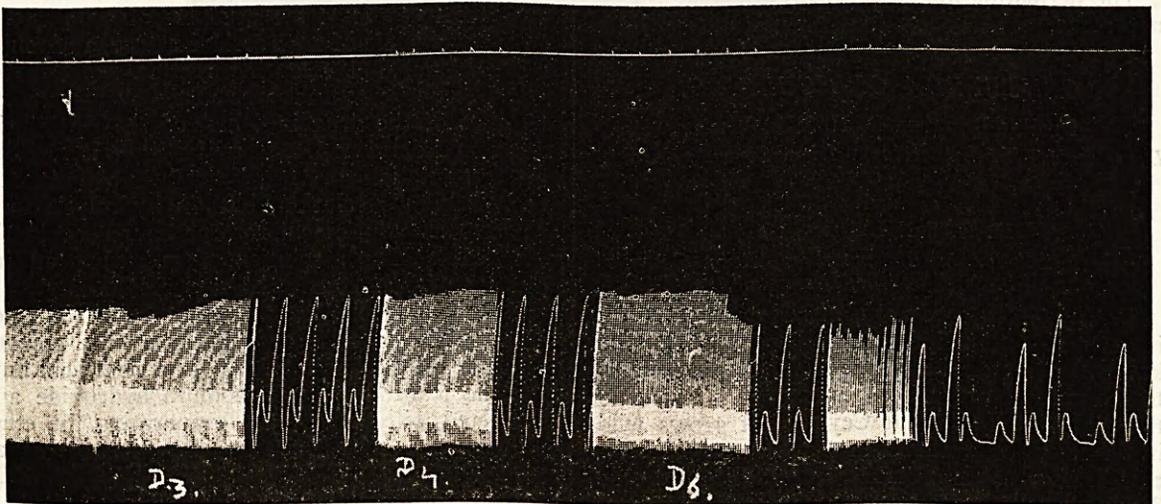


Fig. 1 C.

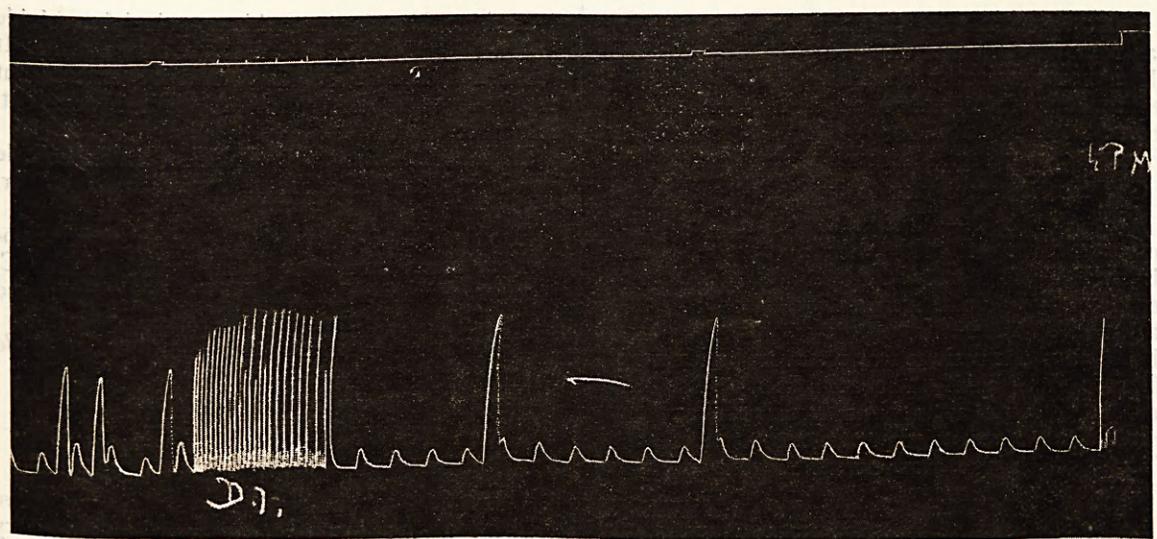


Fig. 1 D.

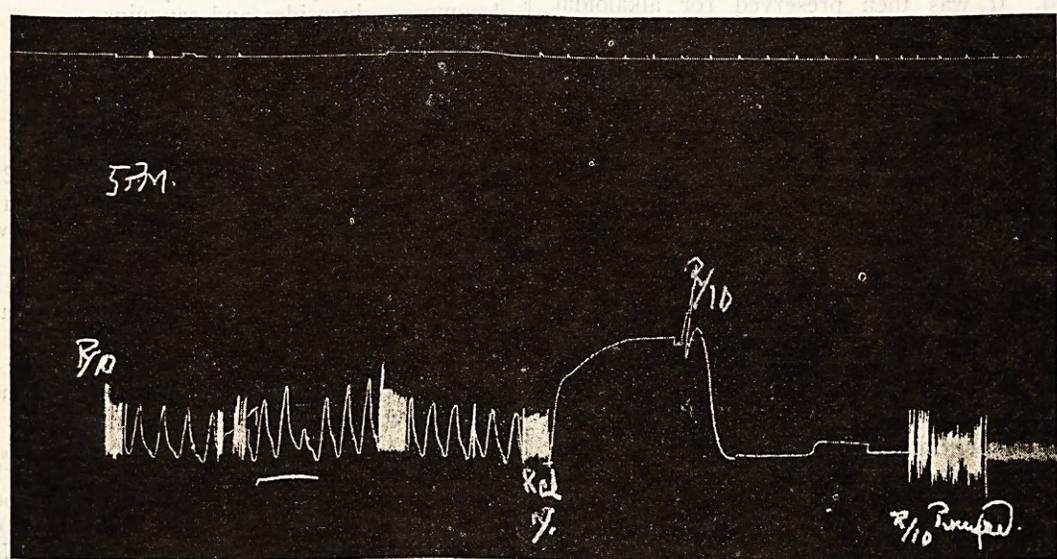


Fig. 1 E.

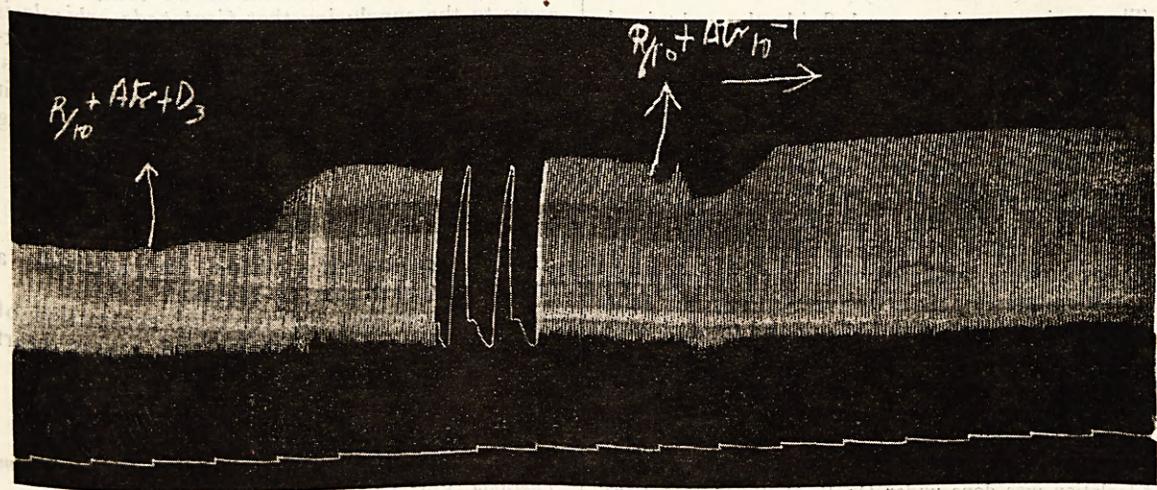


Fig. 1 F.

A gelatinous material deposited on the top. It was removed and filtered, giving a clear red fluid which became frothy on shaking, giving a suggestion of the presence of a saponin. After keeping the solution for 48 hours the solution decomposed giving a brownish precipitate.

Our next attempt was to isolate* the alkaloid.

Method No. 1.—Half a pound of powdered *nakchhikni* was treated with 1 per cent. sulphuric acid on a water bath for two hours and kept overnight with frequent agitation at intervals. The dilute acid extract was pressed and filtered, and the residue was exhausted with water till free from acid. The acid extract was now neutralized with ammonium hydroxide and the whole evaporated to dryness on a water bath. The dried residue was extracted with absolute alcohol and filtered. The filtrate was diluted with an equal volume of water (to precipitate the resins) and filtered. It was then evaporated, treated again with 1 per cent. sulphuric acid and filtered. It was then preserved for alkaloidal tests (*Fluid No. 1*).

Method No. 2.—Next we proceeded to deal with the watery extract which in our preliminary experiment showed a stimulating action on the frog's heart. Two pounds of powdered drug was boiled with water for six hours. The whole was pressed and strained. On cooling a layer of gelatinous substance collected at the top which was removed. The watery extract was red and produced a persistent froth when shaken. The whole of the watery extract was dried to a paste and extracted with rectified spirit, filtered and evaporated. This was now extracted with chloroform. The residue was a bitter principle, preserved for test (*Residue No. 1*). The solution of the extract was filtered and evaporated. Some of it was preserved for tests (*Residue No. 2*). It was then boiled in 1 per cent. sulphuric acid, which left a dark green resinous residue, and a clear solution above. It was filtered and both preserved for tests (*Residue No. 3*), and (*Fluid No. 2*).

The various residues and fluids thus obtained were then tested to determine whether they contained alkaloids, glucosides or resins.

Tests.—Fluids Nos. 1 and 2 gave a precipitate with mercury perchloride, picric acid, tannic acid, iodine solution, phosphomolybdic acid, phosphotungstic acid, mercury potassium iodide (Dragendrof's reagent). A control was kept with 1 per cent. sulphuric acid and with 1 in 1,000 of quinine sulphate, which gave corresponding precipitates. It also gave a Prussian blue reaction when fused with sodium and treated with ferrous sulphate and acidified with hydrochloric acid (test for nitrogen). It gave no colour reactions, probably due to impurities.

Residue No. 1 was a bitter principle, soluble in water and alcohol, less so in chloroform. It reduced Fehling's solution to some extent, but copiously so when hydrolysed with 1 per cent. sulphuric acid.

Residue No. 2 was insoluble in water, soluble in alcohol and chloroform, greenish in colour, and when tasted it gave a pricking sensation.

Residue No. 3 was a dark green resinous substance, colourless, and when heated to 100°C. it becomes semi-solid. It dissolves in alkalis and in alcohol, but is insoluble in water and acids.

It appears from the above tests that *Centepeda orbicularis* contains:—

- (1) An alkaloid.
- (2) A soluble glucoside.
- (3) Traces of saponin.

Of the above total contents probably the active element is the alkaloid, inasmuch as a watery solution kept for over three months was found pharmacologically active a period sufficient to decompose glucosides and saponins.

PHARMACOLOGY.

Heart.—A frog's heart was perfused with R|10 Ringer's solution (i.e., NaCl 0.6 per cent., KCl 0.03 per cent., calcium chloride 0.0025 per cent., *vide* Burridge, at 19°C. with the usual result of a diminution of contraction within half an hour.

Next at D₂ the watery extract in R|10 at pH 10 was perfused. A gradual rise in contraction followed, as shown in tracing 1B. The strength was successively increased with the result that the maximum contraction was attained at D₂. It was maintained at practically the same level till the strength was increased to D₆. At D₇ it began to show positive signs of heart block, ventricular contraction nearly disappeared, followed by complete stopping (Fig. 1D).

The heart was washed out with R|10. Normal rhythm was restored.

From the above observation we could not but come to the conclusion that *Centepeda orbicularis* has a distinct action on the frog's heart, stimulating it by increasing the force of the contractions, and prolonging its systole. In larger doses it has a poisonous action as shown by its causing final heart block.

SUMMARY.

- (1) *C. orbicularis* contains an alkaloid, a glucoside, and traces of saponin.
- (2) It increases the force of contraction of heart, prolongs the systole, and causes heart block in larger doses.

REFERENCES.

- Burridge. *Archives Internationales et Pharm. Therapie*, Vol. XXVII, p. 37.
 Burridge (1915). *Quarterly Journal of Medicine*, Vol. IX, p. 44.

* Isolation was done under Dr. S. M. Sane's directions (Department of Organic Chemistry, University of Lucknow).