

patients who are already stabilized on pentolinium tartrate alone, the dose on adding rauwolfia has usually been reduced to one-third and final adjustments made from that level.

A patient who has had no previous treatment is given rauwolfia for some weeks, as suggested by Smirk *et al.* (1954). Then pentolinium tartrate is added, starting with 20-mg. doses and increasing by increments of 20 mg. until satisfactory levels are obtained. We have found that a better control is achieved when the drug is given three times rather than twice daily.

The reduction in dosage reduces or abolishes the undesirable effects of the ganglionic blockade. Where formerly postural hypotension was a problem, this has been less evident on the combination. Rauwolfia has been shown to stimulate the intestine, and this, in addition to the smaller dose of pentolinium tartrate required, makes the control of the bowels easier. There is therefore less risk of cumulative effect through retention and subsequent absorption of pentolinium tartrate in the bowel.

Patients have been definite in expressing their views that they are much more comfortable, and have been willing to continue treatment, whereas formerly on pentolinium tartrate alone they were incapacitated by weakness, dry mouth, visual disturbances, constipation, and the variability of effect on the degree of hypotension this produced.

In most cases there is no urgency in the control of the hypertension, and gradual reductions of the blood pressure are better tolerated. The aim should be the maximum reduction which keeps the patient comfortable, since the symptoms and signs of hypertension will regress when the pressures have been reduced to levels which are still above the accepted normal.

It would seem also that, once the diagnosis of essential hypertension has been established, cases are better controlled with the patient living his normal life.

### Summary

The use of pentolinium tartrate in combination with rauwolfia alkaloids in the control of essential hypertension is compared with the use of the former drug alone.

The dosage necessary with the combined drugs is greatly reduced.

The undesirable effects of the ganglionic blockade have been much lessened and patients have found the treatment more acceptable.

### REFERENCES

- Smirk, F. H. (1953). *Lancet*, **1**, 457.  
 — Doyle, A. E., and McQueen, E. G. (1954). *Ibid.*, **2**, 159.  
 Vakil, R. J. (1949). *Brit. Heart J.*, **11**, 350.

The Medical Section of the Library Association held a week-end conference in Birmingham on March 25–28. Members were the guests at dinner of the Vice-chancellor (Professor ROBERT AITKEN), in whose absence Professor H. A. CRONNE presided, supported by Professor J. F. D. SHREWSBURY. In a symposium on medical libraries and literature in 1984 the chief topics discussed were the establishment of national editorial assessment boards and a consequent reduction in the number of medical periodicals, academic courses in medical librarianship, changes in the medical profession itself and their effect on library provision, national economic changes and their effects on medical libraries, and the potentialities of new technical methods in documentation. A visit was paid to the Birmingham Medical School, where the sub-dean, Professor C. F. V. SMOUT, announced plans for a new medical library building on a scale commensurate with the other splendidly equipped departments. Special exhibitions of rare medical books were on view, both at the School and at the Birmingham Medical Institute.

## INEFFECTIVENESS OF CHICKEN ANTI-ULCER FACTORS IN TREATMENT OF GASTRIC AND DUODENAL ULCER IN MAN

BY

K. BRØCHNER-MORTENSEN, M.D.

N. B. KRARUP, M.D.

E. MEULENGRACHT, M.D., LL.D.

AND

Aa. VIDEBÆK, M.D.

(From the University Hospital of Copenhagen, Medical Department A, and from Bispebjerg Hospital Medical Departments B and C)

The present study, carried out in collaboration with Professor H. Dam, is aimed at deciding whether materials acting prophylactically against gizzard ulcer in chicks have any curative effect in gastric and duodenal ulcer in man. Dam (1954) has set out the reason for undertaking this work.

The development and prevention of ulcers in the muscular stomach (gizzard) of the chick have been described by Dam (1934, 1946, 1951), Dam and Schönheyder (1934), Dam and Segal (1945), Dam, Noer, and Søndergaard (1950), Cheney (1938, 1940, 1942), and others. According to Dam and his associates young chicks reared on an artificial diet containing cod-liver oil develop ulcers which are often severe and may perforate. The disease may be prevented by including in the diet hog liver, calf's brain, or certain extracts therefrom. The prophylactic effect is associated with the lipid fraction as well as with the residue that remains after these organs have undergone extraction with fat solvents. A marked prophylactic effect is obtained by a combination of the lipid extract and an aqueous extract of calf's brain. The aqueous extract contains vitamin B<sub>12</sub> and may be replaced by this vitamin. In the lipid extract it is the highly unsaturated fraction of the fatty acids that carries protective activity. Arachidonic acid has shown such effect, while fatty acids from fish oils aggravated the symptom.

### Material

We studied 152 patients with gastric or duodenal ulcer. They were admitted to the medical departments B and C of Bispebjerg Hospital and the medical department A of the University Hospital of Copenhagen during the period July 1 to December 1, 1954. Of these patients, 82 were treated with anti-gizzard-ulcer factors and 70 were given placebos. Diagnosis was based on anamnesis, x-ray examination (niche deformation), and, if present, demonstrable haemorrhage. All patients showed typical ulcer symptoms.

The patients in the two groups were chosen at random. Each of the three hospital departments was divided into two halves. All patients with gastric or duodenal ulcer admitted to one half formed the experimental group; those with the same diseases admitted to the other half formed the control group. The groups did not differ significantly in sex, age, location of the ulcer, symptoms, or duration of the disease before admission to hospital (Table I).

### Treatment

Patients in the experimental group were given daily for four weeks 80 g. of "preparation A," a granulate consisting of ether extract of calf's brain mixed with three parts of

TABLE I.—Comparison of 82 Patients Treated with "Anti-gizzard-Ulcer Factors" (Experimental Group) and 70 Patients Treated with Placebos (Control Group)

		Experimental Group	Control Group
Sex distribution	Male/female	55/27=2.0	45/25=1.8
Age distribution	No. of Patients	No. of Patients	No. of Patients
	15-24 years .. .. .	4 (5%)	3 (4%)
	25-34 " .. .. .	12 (15%)	6 (9%)
	35-44 " .. .. .	19 (23%)	18 (26%)
	45-54 " .. .. .	18 (22%)	14 (20%)
	55-64 " .. .. .	17 (21%)	19 (27%)
65+ .. .. .	12 (15%)	10 (14%)	
Site of ulcer	Duodenum .. .. .	48 (59%)	40 (57%)
	Body of stomach .. .. .	12 (15%)	13 (19%)
	Juxtapyloric .. .. .	11 (13%)	8 (11%)
	Duodenum and body .. .. .	1 (1%)	1 (1%)
	Haemorrhage without demonstrable ulcer .. .. .	10 (12%)	8 (11%)
Reason for admittance	Pain .. .. .	53 (65%)	44 (63%)
	Haemorrhage .. .. .	29 (35%)	24 (34%)
	Other cause .. .. .	0	2 (3%)
Duration of disease before admittance	0-1 year .. .. .	21 (26%)	13 (19%)
	2-5 years .. .. .	30 (37%)	29 (41%)
	Over 5 years .. .. .	31 (38%)	28 (40%)
	Average .. .. .	6½ years	7½ years

sucrose. The amount of ether extract in the 80 g. corresponded to 300 g. of fresh brain. The preparation was swilled down with milk or water. In addition, these patients received three times a day one tablet containing 5 µg. of vitamin B<sub>12</sub> ("cycobemin") and intrinsic factor corresponding to 1.8 g. of fresh hog pyloric mucosa.

The patients in the control group were given corresponding amounts of "preparation B" (placebo), a granulate consisting of one part of powder of autoclaved milk (at 120° C. for one hour) mixed with three parts of sucrose. Instead of vitamin B<sub>12</sub> tablets they received placebo tablets consisting of lactose and potato starch. Patients and nurses did not know which of the preparations given contained the anti-gizzard-ulcer factors.

Both groups were subjected to the following regimen: light confinement to bed for three weeks, thereafter out of bed. All received a purée diet, and, daily, one tablet containing vitamin A, 5,000 I.U.; vitamin D<sub>3</sub>, 600 I.U.; vitamin B<sub>1</sub>, 3 mg.; vitamin B<sub>2</sub>, 3 mg.; vitamin C, 75 mg.; and nicotinamide, 20 mg. Tablets consisting of 0.15 mg. of atropine sulphate, 500 mg. of sodium bicarbonate, and 500 mg. of basic magnesium carbonate were given as required when cardialgia occurred. The number of tablets given daily was carefully recorded.

Preparations A and B were tested for anti-gizzard-ulcer activity in the Department of Biochemistry and Nutrition, Polytechnic Institute, by Mr. E. Søndergaard, as described by Dam, Noer, and Søndergaard (1950), using the mode of graduation of gizzard ulcers introduced by Cheney (1942). Preparation A together with vitamin B<sub>12</sub> showed the same

protective activity against gizzard ulcers as was found in earlier experiments (Dam, Noer, and Søndergaard, 1950) for ether extract of calf's brain given with vitamin B<sub>12</sub>. Preparation B showed no protective effect in the chicken test.

**Results**

Several criteria were used to evaluate the result of treatment: (1) complaint of pain, which was also estimated by the number of tablets of atropine and alkali consumed; (2) intensity and duration of visible or occult bleeding, measured by benzidine tests on each stool; and (3) comparison of x-ray pictures of the stomach taken just before, during, and after treatment.

**Pain.**—In the experimental group 50 patients had pain which continued after they had been confined to bed and given the purée diet; 11 had pain all through the experimental period. In the control group 53 patients had pain at the beginning of the treatment, and 10 of these still had pain after four weeks' treatment. Fig. 1 shows that the cardialgia disappeared equally fast in the two groups. After one week's treatment 75% of the experimental group had pain as compared with 78% of the controls; after two weeks 56% and 54% respectively still had pain; and after three weeks 35% and 28% had pain. Fig. 2 shows that the number of atropine and alkali tablets required was a little larger in the experimental group than in the control group.

**Haemorrhage.**—Fig. 3 expresses the intensity and duration of haemorrhage in the two groups as measured by the number of positive benzidine reactions. Melaena was given 4 points; in cases with occult bleeding an immediately positive benzidine reaction was given 3 points; a reaction which became positive within 30 seconds, 2 points; and a reaction which was positive after 30 to 60 seconds, 1 point. The sum of each day's points for the 82 experimental patients and for the 70 control patients was then calculated as if there were 100 patients in each group. Bleeding diminished at the same rate in the two groups. In the experimental group, 29 had melaena or haematemesis, against 25 in the control group. The average time required for cessation of bleeding in the two groups was 9½ and 10 days respectively. Evaluating the treatment by reduction or disappearance of pain and/or bleeding, as shown in Table II, indicates that the results obtained in the experimental and the control group were approximately equal.

TABLE II.—Clinical Evaluation of Result of Treatment in Experimental and Control Groups

	Experimental Group (82 Patients)	Control Group (70 Patients)
Unchanged .. .. .	17 (21%)	9 (13%)
Improved .. .. .	63 (77%)	60 (86%)
Aggravated .. .. .	1 (1%)	0
Questionable .. .. .	1 (1%)	1 (1%)

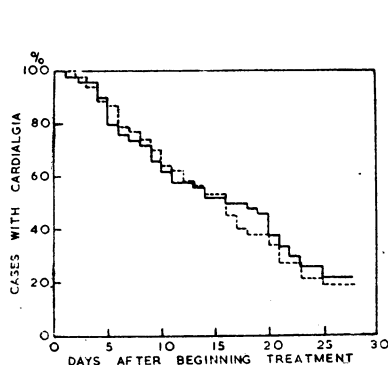


FIG. 1.—Diminution of cardialgia during four weeks' treatment. — Experimental group (50 patients). - - - Control group (53 patients).

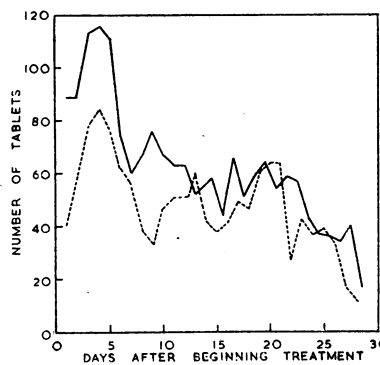


FIG. 2.—Number of tablets with atropine and alkali given daily per 100 patients. — Experimental group. - - - Control group.

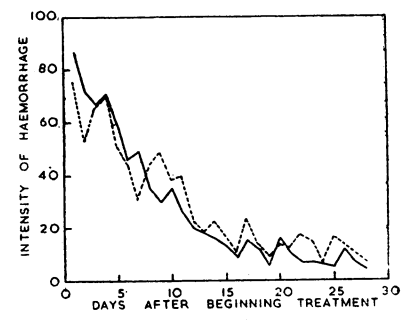


FIG. 3.—Intensity and duration of melaena or occult haemorrhage per 100 patients (see text). — Experimental group. - - - Control group.

TABLE III.—Radiological Evaluation of Result of Treatment in Experimental and Control Groups. Comparison of X-ray Pictures of Stomach and Duodenum Taken Immediately Before Treatment, After Two and Four Weeks of Treatment, and Again Two Weeks After Cessation of Treatment

	Experimental Group (82 Patients)	Control Group (70 Patients)
Unchanged .. ..	36 (44%)	30 (43%)
Improved .. ..	28 (34%)	27 (39%)
Aggravated .. ..	5 (6%)	3 (4%)
Questionable .. ..	13 (16%)	10 (14%)

*X-ray Examination.*—The evaluation of the results of the treatment from a radiological point of view is based on examinations immediately before treatment, after two and four weeks of treatment, and again two weeks after discontinuation of treatment. Only obvious differences have been taken into consideration, especially diminution of niche and marked change in the deformation of the duodenal bulb or the prepyloric canal. In cases of major haemorrhage the ulcer could not always be demonstrated, and thus the x-ray pictures from such patients could not contribute to the evaluation of the treatment. Table III shows the results of the x-ray examination. Also, no difference could be demonstrated radiologically between the experimental and the control group.

#### Summary and Conclusions

Eighty-two randomly chosen patients with gastric or duodenal ulcer have been treated with "anti-gizzard ulcer factors" (ether extract of calf's brain plus vitamin B<sub>12</sub>). Seventy similarly chosen control patients were subjected to the same regimen with placebos substituted for "anti-gizzard ulcer factors." After a preliminary short follow-up period the results of the treatment were evaluated. Diminished pain and bleeding and comparison of repeated x-ray examinations were used as criteria. The experimental and the control groups did not differ at all in their response to treatment. "Anti-gizzard ulcer factors" were thus of no value in the treatment of gastric and duodenal ulcer in man.

Thanks are due to A/S Orthana Kemisk Fabrik, Copenhagen, for generous assistance in preparing and furnishing the preparations used in this study.

#### REFERENCES

- Chency, G. (1938). *Amer. J. digest. Dis.*, 5, 104.  
 — (1940). *Proc. Soc. exp. Biol. (N.Y.)*, 45, 190.  
 — (1942). *Arch. intern. Med.*, 70, 532.  
 Dam, H. (1934). *Nature (Lond.)*, 133, 909.  
 — (1946). *Acta physiol. scand.*, 12, 189.  
 — (1951). *Ann. Rev. Biochem.*, 20, 289.  
 — (1954). *British Medical Journal*, 1, 1036.  
 Noer, B., and Søndergaard, E. (1950). *Acta physiol. scand.*, 21, 315.  
 — and Schönheyder, F. (1934). *Biochem. J.*, 28, 1355.  
 — and Segal, H. L. (1945). *Acta physiol. scand.*, 10, 295.

The Atomic Energy Authority has lent to the Science Museum at South Kensington a large working model of the "B.E.P.O." atomic pile, the larger of the two pioneer piles set up at Harwell. This pile went into operation in July, 1948. It is used for research purposes, and for "cooking" radioactive isotopes for use in medical research and treatment, in agricultural research, and in industry. The model goes through a complete cycle of operations in five minutes, and shows the working of the control and shut-down rods which govern the heat output of the pile, and the movement of the hoist for loading uranium rods into the pile. The uranium rods are the pile's fuel, and during its operation some of the uranium is "burnt up," and the rods become contaminated by the products of combustion. The rods then have to be removed and processed to remove the fission products.

## ERYTHRODERMIA WITH LIPOMELANIC RETICULUM-CELL HYPERPLASIA OF LYMPH NODES (DERMATOPATHIC LYMPHADENITIS)

BY

R. C. NAIRN, M.D., Ph.D.

Senior Lecturer in the Department of Pathology, University of Aberdeen

AND

T. E. ANDERSON, M.D.

Dermatologist, North-eastern Regional Hospital Board, Scotland

The association of an unusual type of hyperplasia of the superficial lymph nodes with certain pruritic skin disorders, first fully discussed by Pautrier and Woring (1937), has been amply confirmed by subsequent authors (Hurwitt, 1942; Soloff, 1942; Laipply, 1948; Obermayer and Fox, 1949; Laipply and White, 1951; Jarrétt and Kellett, 1951; Wilson, 1954). There is substantial agreement that the lymph-node change is merely reactive, though there is some doubt whether the condition always remains benign: occasionally it has been found in association with leukaemia (Laipply and White, 1951) or mycosis fungoides (Bluefarb and Webster, 1950).

This syndrome is not a rarity, but its significance is still not generally recognized. The present paper is a clinico-pathological account of 13 further cases, with follow-up of from one to four years, and reaffirms the essentially benign reactive nature of the condition.

The following case reports have been classified in four groups according to the clinical diagnosis.

#### (a) Generalized Exfoliative Erythrodermia

*Case 1.*—Female, aged 74 on admission, November, 1951. The eruption had been present for a few months and there was a generalized lymphadenopathy of moderate degree. She gave a history of a previous attack in 1947 which developed at the beginning of a course of gold injections for arthritis. Psychogenic factors were marked. Biopsy of a lymph node from the groin showed pronounced reticulum-cell proliferation to form large pale-staining sheets, though the general architecture of the rest of the gland was well preserved. Eosinophils were numerous; abundant melanin, almost entirely intracellular, was scattered throughout the medulla. There was no lipid or iron pigment. After a short course of A.C.T.H. the skin condition almost settled and the lymphadenopathy subsided. She was discharged in February, 1952, and her own doctor reports that the skin gave no further trouble. The patient died in the summer of 1952 of perforated appendicitis, peritonitis, and carcinoma of the ovary. At necropsy the skin was healed and there was no residual lymphadenopathy or evidence of reticulo-endothelial disease elsewhere.

*Case 2.*—Male, aged 51 on admission, August, 1952. The eruption, present for 11 months, had begun with pruritus and erythrodermia of the head and neck with rapid generalization. Exfoliation, beginning two months later, was associated with generalized alopecia. Psychogenic factors, profuse sweating, and a burning sensation in the skin were notable features. On admission there was moderate lymphadenopathy and the liver was enlarged 2 cm. below the costal margin. The peripheral blood picture was normal though the sternal marrow was very cellular (10% plasma cells). Biopsy of the skin showed a moderate infiltration of the