fluid toxoid in the last trimester of subsequent pregnancies.

An investigation is needed to determine whether, for primary immunization, alum-precipitated toxoid or aluminium hydroxide adsorbed toxoid might give better results than fluid toxoid, particularly in circumstances where only two injections are possible before delivery. There is a great need for a toxoid preparation containing an adjuvant which would enable primary immunization to be achieved with only one injection.

No reactions to the toxoid injections were noticed and, for the results achieved, the cost was not high. In countries where neonatal tetanus is common women can often be given inoculations during pregnancy although the medical services cannot yet provide them with domiciliary midwifery. It is thought that in such circumstances they have the best claim of any section of the civilian population to routine tetanus immunization.

We are grateful to Dr. J. Y. Hancock, Mr. D. R. Tucker, and Sister D. Rampton for assistance at Maprik; to Medical Orderly Taro for much work in the villages; to Dr. N. Ansari, of W.H.O., for his interest; and to Dr. R. F. R. Scragg, Director, Department of Public Health, Territory of Papua and New Guinea, for permission to publish.

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CHLORPROMAZINE IN TETANUS

BY

K. S. KOCHHAR, F.R.C.S.Ed.

*Assistant Professor of Surgery, Medical College,
Amritsar, India*

In recent years there have been many reports on the value of chlorpromazine in the management of tetanus. Most of them were based on trials conducted on a small number of patients, and one could not be certain that the conclusions reached were applicable to all cases. This study was undertaken to determine the response of a large series of tetanus patients to treatment with chlorpromazine.

The major prognostic criteria governing the ultimate outcome of tetanus are the length of the incubation period and the interval between the onset of trismus and generalized spasms. The results of any investigation are obviously influenced by the proportion of milder and graver forms of the disease included in the study. The incubation period was not thought to be a suitable standard from which the severity of the disease could be gauged, because the history of the injury might not be accurately given, the time of the injury might not

have been the time of infection, and there might even have been no history of injury at all. On the other hand, the interval between the onset of trismus and generalized spasms was regarded as a reliable index of the severity of the disease, as one could expect patients to be accurate about the actual time of onset of the disease.

Method and Material

The cases of tetanus admitted to the wards of the department of clinical surgery, Medical College, Amritsar, were divided at random into two groups without reference to the severity of the disease. The patients in group A were given paraldehyde (4–6 ml.) by intramuscular injection six-hourly, and the patients in group B were given chlorpromazine (50 mg.) in a similar manner. Neonatal cases were excluded from the investigation. All patients were also put on a standard treatment, which consisted of the following measures: (1) They were isolated in dark, quiet surroundings and given intramuscular injections of soluble phenobarbitone, 2–3 gr. (130–200 mg.), every six hours. (2) After a test dose, an intravenous injection of 100,000 units of antitetanic serum was given. (3) Injections of crystalline penicillin were administered, and those patients with pulmonary complications received streptomycin as well. (4) The portal of infection was treated surgically. (5) Nutrition was maintained on fluid diet, given by mouth or, if necessary, intravenously.

The results are shown in the accompanying table.

Table of Results

Interval Between Trismus and Generalized Spasms	No. Treated	Cured	
		No.	%
Group A (Paraldehyde Group)			
0-48 hours ..	58	30	51.7
More than 48 hours ..	31	26	83.9
Group B (Chlorpromazine Group)			
0-48 hours ..	54	28	51.9
More than 48 hours ..	27	23	85.2

Discussion

Chlorpromazine is a phenothiazine derivative which acts mainly on the formatio reticularis, abolishing excitement and lowering muscle tonus. At the same time it potentiates the action of other sedatives. Because of these properties chlorpromazine has been used by various workers in the management of tetanus.

In the present study, spasms were more rapidly controlled by chlorpromazine than by paraldehyde, and a good deal of muscle tonus remained in patients treated with the latter. Of the 89 cases in group A, 58 were of the severe type, and 30 (51.7%) of these patients survived. Among the 31 patients who had less severe tetanus, 26 (83.9%) survived. Group B contained 81 cases, 54 of them being of the severe type. Among these there were 28 (51.9%) survivors, compared with the 23 (85.2%) survivors among the 27 patients with a milder type of tetanus.

It is obvious that there is no significant difference in the ultimate results obtained in the two groups.

Summary

A clinical trial was conducted on 170 cases of tetanus in order to assess the comparative value of paraldehyde

and chlorpromazine in treatment. Chlorpromazine appeared to be the better drug for symptomatic relief, but had no statistically significant effect on the ultimate outcome.

I am grateful to Professor Yudhvir Sachdeva for permission to use the clinical material.

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FURTHER EXPERIENCES WITH HYPOPHYSECTOMY IN ADVANCED BREAST CANCER

BY

EVELYN BOESEN,* M.B., B.S.

E. J. RADLEY SMITH, M.S., F.R.C.S.

AND

D. N. BARON, M.D.

Royal Free Hospital, London

In 1958 a review of the effects of hypophysectomy in disseminated carcinoma of the breast at this hospital from January, 1955, to April, 1957, was published (Baron, Gurling, and Radley Smith, 1958). Since that time many other cases have undergone pituitary ablation, and patients have been observed for periods of up to 47 months after hypophysectomy.

Present Investigation

Clinical Material.—Over the past five and a half years up to July, 1960, 121 patients with disseminated malignant disease have been treated by pituitary ablation. Reports of three patients with malignant melanoma (Radley Smith, Gurling, and Baron, 1958) and 7 with disseminated carcinoma of the prostate (Radley Smith, Baron, and Gurling (1959) have been published. Only those 111 patients who have undergone pituitary ablation for disseminated carcinoma of the breast are considered here; they comprise seven patients who have undergone pituitary ablation by the implantation of either ^{198}Au or ^{90}Y seeds under stereotaxic x-ray control together with 104 who underwent surgical hypophysectomy. The only contraindication to pituitary ablation has been the presence of a tendency to bleed, secondary either to extensive hepatic metastases or to depression of platelet formation. Otherwise the patients are entirely unselected.

Pre-operative Assessment.—Patients are admitted a minimum of 10 days pre-operatively. A careful clinical assessment is made. Accessible lesions are measured and photographed. Pre-operative assessment of pituitary, thyroid, and adrenal function is essential (Baron and Gurling, 1960) in order that the functional

completeness, or otherwise, of hypophysectomy can be established for correlation with the clinical response.

Operative Technique

This has already been described in detail (Baron *et al.*, 1958).

The pituitary gland is approached by the right frontal route. After cutting the pituitary stalk and incising the diaphragma sellae it is sometimes possible to remove the pituitary gland in one piece. More often it is removed piecemeal. The anterior portion is carefully scraped away from under the clinoid processes. We continue to insert ^{198}Au seeds (5 seeds a total of 15 mc) into the pituitary fossa after complete removal of the pituitary. Only very small amounts of pituitary tissue remain in the fossa after surgical hypophysectomy. We believe that in these circumstances radioactive gold seeds, which are technically easier to insert into the fossa during our operative procedure than ^{90}Y , are adequate for the purpose of destroying any residual pituitary tissue.

Under stereotaxic x-ray control pituitary ablation has been attempted by the insertion of either ^{198}Au seeds or ^{90}Y rods into the pituitary fossa. The method has been described in detail elsewhere (Bennett, 1960). It is of particular value in patients with cerebral metastases in whom surgical removal of the pituitary is contraindicated. It has not been found possible to produce functionally complete pituitary ablation by the insertion of ^{198}Au seeds alone. The larger size of the ^{90}Y rods, when used in the stereotaxic procedure, probably produces considerable mechanical destruction of the pituitary, which, together with the β -particle activity emitted, results in pituitary ablation being functionally complete.

We continue to use hypothermia in anaesthesia in patients with extensive pulmonary metastases. In patients not requiring hypothermia, hyperventilation is used to increase the venous return and to reduce cerebral oedema.

Pre- and Post-operative Care

For patients undergoing surgical hypophysectomy, cortisone is administered during the pre-operative and operative period according to the schedule given below. This dosage has been modified in the past year from that previously used, since a marked fall in blood-pressure had occurred 12–24 hours post-operatively in a large number of patients. Although the total dosage over 24 hours is slightly less than that previously used, the cortisone is now given eight-hourly. It appears that eight-hourly administration of cortisone acetate, orally when possible but otherwise given intramuscularly, is essential in order to avoid an acute fall in post-operative blood-pressure. The revised schedule of cortisone administration is as follows:

24 hours pre-operatively:

Cortisone acetate 50 mg. I.M., morning and evening.

Day of operation:

Cortisone acetate 50 mg. I.M., morning.

Hydrocortisone hemisuccinate 50 mg. in 500 ml. 0.18% saline (1/5 isotonic) I.V. over operation.

Cortisone acetate 50 mg. orally (I.M. if not fit), 8-hourly, post-operatively.

Cortisone is reduced by 25 mg. every two days until a maintenance level of 25–50 mg. daily is reached.

For patients undergoing the stereotaxic procedure cortisone has been started and kept at the maintenance dosage of 25 mg. of cortisone acetate b.d. orally from the day of operation.

*Working under a whole-time grant from the British Empire Cancer Campaign.