As with reported studies on uropepsin, the plasma levels of pepsinogen in non-ulcer and duodenal ulcer patients have considerable overlap, though the great majority of the latter have readings over 160 units, while normal patients and those with functional dyspepsia or chronic gastric ulceration are below this arbitrary level (see Chart). In addition, the mean figure for the duodenal ulcer group is more than twice that of the normals and of the patients with functional dyspepsias or chronic gastric ulceration. That there is

Range and mean values of plasma pepsinogen in normal subjects (N), and patients with functional dyspepsia (F.D.), duodenal ulcer (D.U.), and gastric ulcer (G.U.). The dotted line indicates the mean figures.

such overlap is not surprising, as the digestive activity of the juice is only one component in ulcer formation: high levels of pepsinogen can only express a liability to the development of ulceration (Weiner *et al.*, 1957).

It is apparent that neither plasma nor uropepsin levels can be considered to be correlated directly with the amount and concentration of gastric pepsin, and that these assays are possibly better regarded as being related to the chief-

cell mass of the stomach rather than to chief-cell activity. This is suggested by both the lack of liability in these assays and the findings that gastro-enterostomy and vagotomy do not grossly influence plasma pepsinogen level, that two-thirds partial gastrectomy reduces it by approximately a half, and that total gastrectomy eliminates the enzyme entirely. Tongen (1950) contended on histological evidence that there is correlation between gastric acidity and parietal cell concentrations in human stomachs, and similar studies may be able to show a similar relationship between plasma pepsinogen and chief cells.

The plasma technique has the advantages of requiring a single blood sample and being unaffected by the common day-to-day stimuli. Even with its obvious limitations it probably has a useful place in the diagnosis of duodenal ulceration and of anastomotic ulcers. Further investigation is required to assess its helpfulness in differentiating haematemesis due to duodenal ulceration from that of portal hypertension. It may possibly serve as a guide to the amount of stomach resection to be undertaken for duodenal ulceration.

Summary

The plasma pepsinogen has been estimated in 246 patients.

The maximal and mean figures for patients with chronic duodenal ulceration are much higher than those found in normals and in patients who have gastric ulceration or functional dyspepsia.

It is suggested that a single plasma estimation reflects the gastric chief-cell mass; the consequent effect of a

partial gastrectomy is to reduce the pre-operative level by about a half.

It is suggested that a pre-operative level of plasma pepsinogen may give some indication of the amount of stomach to be resected for chronic peptic ulceration.

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RECOVERY FROM BUTHALITONE ANAESTHESIA

A METHOD OF ASSESSMENT

BY

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The ideal anaesthetic for use in an out-patient department is one which, among other things, permits a rapid return to normal consciousness. Buthalitone sodium has been claimed to possess this property as well as various other advantages over existing agents (Weese and Koss, 1954; Nobes, 1955a, 1955b; Ruddell, 1955). The present investigation was designed to compare buthalitone sodium with thiopentone sodium, using a new technique to measure the rate of recovery.

Method

Thirty-seven unselected out-patients attending for orthopaedic manipulation or minor surgery were given alternately thiopentone and buthalitone. The dosage was such that comparable anaesthesia was achieved with each drug: a 70-kg. man receiving 600 mg. of thiopentone or 1,250 mg. of buthalitone (8.6 mg./kg. or 17.85 mg./kg.). These figures agree closely with others that have been published (Orkin *et al.*, 1958; Henderson and Mackett, 1958). The patients either had pre-medication of atropine 1/100 gr. (0.6 mg.) or nothing.

When quietly resting before anaesthesia patients were each given a board and tracing paper. The purpose of

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the experiment was explained and the patients were asked to trace a straight line, sine wave, and circle already drawn on the board. Below these they were asked to sign their name and make a free drawing of a house (Fig. A). This procedure was repeated as soon as consciousness was regained, and again on two further occasions at approximately 30-minute intervals (Figs. B, C, and D); 37 sets of "drawings" were collected in this way. The drawings were assessed by an observer who did not know which anaesthetic agent was used for each patient (and who was indeed entirely unconnected with the hospital). The method was as follows. Each of the three post-anaesthetic drawings (the order of which was unknown to the assessor) was marked, using the pre-anaesthetic drawing as a baseline, 4 marks being allotted to each of the five items. Thus, if the patient's drawing was as good after the anaesthetic as before it he received a mark of 20 for that drawing.

When the marks were compared with the times (recorded from the beginning of the anaesthetic) it was seen that they reflected a steady return to normal consciousness; there was no instance of a lower mark following a higher one. This in itself provided evidence of the objectivity of the method.

Analysis of Results

For each patient we had a set of three markings varying from 0 to 20, relating to three periods of time following the anaesthetic. These times were not the same for each patient. The first drawing was made only when the patient was sufficiently recovered; and even after that no strict time-table was practicable. To simplify the analysis, therefore, we calculated for each patient the score at 30 minutes and 60 minutes, using linear interpolation (and rounding to the nearest whole number). For example, a patient scoring 12 marks at 15 minutes and 16 at 35 minutes was given an estimated score of 15 at 30 minutes. Patients who had not recovered consciousness scored zero.

The Table gives the distribution of markings at 30 and 60 minutes, together with the medians (calculation of the means might be misleading owing to the relatively large number of zero marks). At 30 minutes the

Numbers of Patients With Various Scores at 30 and 60 Minutes

Score	30 Minutes		60 Minutes	
	Thiopentone	Buthalitone	Thiopentone	Buthalitone
0	7	6	3	1
1	—	—	—	—
2	—	1	—	—
3-6	—	—	—	—
7	—	—	—	1
8	—	—	—	1
9	2	—	—	—
10	1	—	—	1
11	1	1	1	1
12	—	1	1	—
13	—	2	2	—
14	1	2	2	2
15	1	1	—	1
16	2	1	2	2
17	—	3	1	1
18	3	1	5	5
19	—	—	1	2
20	—	—	—	1
Total	18	19	18	19
Median*	9.8	13.1	15.2	16.4

* Based on exact scores.

Note: Though inspection of the table makes it clear that there is no statistically significant difference between the two sets of scores, the appropriate test is not obvious. Edwards (1958) suggests a simple method for use in such cases. The table is converted into a 2×2 table in such a way as to minimize the sum of the reciprocals of the class frequencies and a χ^2 test applied. Taking the figures for 30 minutes this rule divides the table between the score of 9 and 10, leading to a value of χ^2 (uncorrected) = 0.63 ($P > 0.25$).

advantage lay slightly with the buthalitone patients, the median being 13.1 compared with 9.8. However, this difference is one that might easily be due to chance, as can be seen from the similarity of the distributions.* By 60 minutes there was even less difference between the two groups of patients.

The slightly better early results with buthalitone may be expressed in a different way by comparing the times at which the first drawings were made in the two groups of patients. In the thiopentone group the average time was 35 minutes (standard error, 5.6) compared with 29 minutes (standard error, 4.6), and again the difference is one that might easily be due to chance.

Discussion

Buthalitone sodium was first described by Miller *et al.* (1936). In recent years there have been many claims

*See footnote to Table.

Drawings by woman aged 55 (weight 116 lb. (52.6 kg.), buthalitone 1.4 g.): A, when resting before anaesthesia; B, as soon as consciousness was regained; C, at 38 minutes; D, at 63 minutes.

that its properties made it highly suitable for out-patient anaesthesia (Weese and Koss, 1954; Nobes, 1955a, 1955b; Ruddell, 1955; McColl, 1955; Young, 1956; Henderson and Mackett, 1957). On the other hand, its brevity of action (compared with thiopentone) has been disputed by some workers, who have also reported unfavourable side-effects and sequelae (O'Mullane, 1957; Simmons and Blanshard, 1957; Henderson and Mackett, 1958).

An earlier comparison between buthalitone and thiopentone (Simmons and Blanshard, 1957) showed no significant difference between them; the criteria of recovery were the patient's ability to obey verbal commands and to rise unaided to the sitting position. But such a method hardly measures *complete* recovery to normal consciousness. Various ways of doing this have been tried, such as the flicker-fusion frequency of a light source (Nilsson, 1953), and have proved impracticable.

The present method was conceived as a form of intelligence test which might be suitable for use in a busy out-patient department. We have shown that it is in fact practicable and that it combines simplicity with objectivity. It is suitable for almost all patients, making no great demands on their co-operation and inducing no fatigue. Should the experiment be repeated it would probably be wise to specify exact times at which the tests should be made. This would simplify the analysis and obviate the risk of a subjective judgment being used to determine when the first test should be given.

Summary and Conclusion

A new method is described of comparing the rate of recovery from barbiturate anaesthesia. The method is simple and assesses recovery to very near normal consciousness. This method was used in a small trial, and there was found to be no statistically significant difference between buthalitone sodium and thiopentone sodium; it is unlikely, therefore, that there is any great advantage, in respect of rate of recovery, to be gained by using buthalitone rather than the well-established thiopentone.

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"In connexion with forms being prepared by the National Road Safety Council for the reporting of traffic accidents, the Public Health Committee recommended that provision be made on these forms for the recording of information whether the driver at the time of the accident was likely to be under the influence of any therapeutic substance the nature of which should also be specified. This recommendation was made in view of the widespread habit of self-medication and the hazards associated with the use of certain tranquillizing and other drugs freely used by the public." (*Health*, Journal of the Commonwealth Department of Health, Australia, September, 1959.)

LONG-TERM FOLLOW-UP OF 32 PATIENTS IRRADIATED FOR THYMIC ENLARGEMENT IN INFANCY

BY

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Irradiation of the thymus gland in infancy was often practised in the thirties for the treatment of a variety of symptoms thought to be associated with thymic enlargement. Prominent among these symptoms were stridor and attacks of cyanosis, dyspnoea, and syncope. X-ray or radium therapy was often employed in such cases, even when radiological evidence for enlargement of the thymus was uncertain. In America, "prophylactic" irradiation was even given to symptom-free infants shortly after birth at one time (Conti and Patton, 1948).

Thymic irradiation went out of fashion in many centres after about 15 years, when it had become apparent that the symptoms ascribed to enlargement of the gland usually cleared as quickly without irradiation. This was fortunate, as it was not realized until some years later that there might be an association between such treatment and the development of thyroid cancer and leukaemia.

Attempts to assess the degree of correlation have been made either by investigating the radiation histories of patients who developed thyroid cancer and leukaemia in childhood (Duffy and Fitzgerald, 1950; Clark, 1955; Stewart *et al.*, 1958; Polhemus and Koch, 1959; and others) or, as in a notable series reported by Simpson *et al.* (1955), by tracing children who had received thymic irradiation in infancy.

In view of the findings an attempt was made to follow up infants who had received irradiation for thymic enlargement at the Middlesex Hospital and at the Hospital for Sick Children, Great Ormond Street. While it is recognized that statistically valid conclusions must be based on larger numbers, this follow-up is presented for its interest and in the hope that it will be possible to combine results from other centres.

It is probable that the subsequent history of such patients sheds little light on the effects of thymic enlargement *per se*, as it is now recognized that true enlargement occurs rarely, and that the thymuses commonly reported as enlarged were probably normal.

A total of 32 infants were found to have received thymic irradiation by deep x rays or radium between 1932 and 1950. In all, 27 patients have been traced to the present time and are alive: one has been traced to 1946, and three have died. Only one has remained untraced since treatment was given and has not been notified as having died.

Sex.—Of 31 infants traced, 20 were male. This preponderance of male infants has been observed previously.

Age at which irradiated (Table I).—Of the traced patients, 16 had been treated at the age of 3 months or less. The age at irradiation may well be important, as it will influence the percentage area of body surface irradiated and as there may be an increased sensitivity to radiation at this time.

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