maternal care, and early exposure to foreign proteins. However, whatever the factor involved, it can only be expected to account for a minority of the cases of ulcerative colitis.

From a wider viewpoint, there is the interesting possibility that artificial feeding in the first few weeks of life may influence the liability to a number of diseases which occur in adult life. The ideal way to determine this would be to carry out a prospective study, but it is self-evident that the results would not be available for some decades. In the meantime the simple type of inquiry employed in the present study may be worthy of application to conditions other than ulcerative colitis.

Summary

The history of infant-feeding has been studied in 152 patients with classical ulcerative colitis and in an equal number of patients with other conditions matched for age and sex attending the Nuffield Department of Medicine during the same period. All the patients were asked a standard series of questions by the same interviewer. In 74% of the patients first-hand evidence was obtained from a witness (usually the mother) by means of a postal questionnaire.

It was found that breast-feeding had not been established in 30.3% of the ulcerative colitis patients and 14.7% of the controls, a difference which might occur by chance less than once in 500 times. However, when the groups were compared in terms of the proportions weaned by one month, no significant difference was apparent. When the ulcerative colitis group was compared with the control group in terms of year of birth, social class, residence at interview, and family rank a consistently higher proportion of patients who had been weaned within the first two weeks of life was found in the ulcerative colitis group.

These findings can be explained in a number of different ways, but the most likely interpretation is that early artificial feeding increases the liability to ulcerative colitis later in life. The theoretical and practical implications of this are briefly discussed.

We are indebted to Mrs. B. Hainge for matching the patients, classifying the answers to the postal questionnaire, and keeping the records of the study.

REFERENCES

- Annual Report of the Medical Officer of Health at the City of Oxford, 1954.
 Douglas, J. W. B. (1950). *J. Obstet. Gynaec. Brit. Emp.*, **57**, 335.
Maternity in Great Britain (1948). A Survey of Social and Economic Aspects of Pregnancy and Childbirth undertaken by a Joint Committee of the Royal College of Obstetricians and Gynaecologists and the Population Investigations Committee, Cumberlege, London.
 Registrar-General (1950). *Classification of Occupations*. H.M.S.O., London.
 Robinson, M. (1939). *Arch. Dis. Childh.*, **14**, 259.
 Truelove, S. C. (1961). *Brit. med. J.*, **1**, 154.

ASSESSMENT OF THE RADIOTRIOLEIN TEST IN STEATORRHOEA

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In the investigation of steatorrhea the fat-balance is generally regarded as the best means of assessing the severity and progress of the condition. However, there is general agreement that the fat-balance is a difficult test to conduct, and therefore alternative methods of obtaining the same information with less trouble have been proposed. One of these is the radio-iodinated triolein (RIT) test, which has received wide support in the last ten years.

Although differences in procedure are adopted by different workers, the principle employed is essentially that of a tracer test. A known dose of RIT is given by mouth, its excretion in the faeces is measured, and the result is expressed as a percentage of the dose. While quantitative agreement with the faecal chemical fat excretion is not claimed, many workers state that normal subjects excrete a low percentage of the dose, whereas patients with steatorrhea excrete a high percentage (Ruffin *et al.*, 1956, and others). Furthermore, it is claimed that the dividing line between faecal RIT excretion in normal subjects and in patients with steatorrhea is sharp enough to be of diagnostic value. The advantages of the RIT test are that it is easily performed, a standardized material is used, and faecal homogenization is unnecessary. Its obvious disadvantage is the possible danger inherent in the use of radioactive isotopes.

Further elaborations of the use of radio-iodinated lipids have been reported. The measurement of plasma levels of absorbed radioactivity (Berkowitz *et al.*, 1959) and the urinary excretion of ¹³¹I (Walker *et al.*, 1960) have been advocated as useful parameters of intestinal function. Again, it is claimed that steatorrhea of digestive origin can be distinguished from one of absorptive origin by comparing the absorption of RIT with that of radio-iodinated oleic acid (Reemtsma *et al.*, 1957). Finally, other workers have used these materials as a means of investigating generalized atherosclerosis (Hall *et al.*, 1959), congestive cardiac failure (Mäkelä *et al.*, 1960), diabetes mellitus (Sandberg *et al.*, 1960), cirrhosis (Fast *et al.*, 1959), the nephrotic syndrome, and other hyperlipaemic states (Stanley and Thannhauser, 1949).

Despite widespread acceptance of the method, a search of the literature reveals a paucity of critical investigations designed to assess the reliability of the RIT test in the diagnosis of steatorrhea. Fierst *et al.* (1958) have found a correlation between the vitamin A absorption test and the RIT test. An alternative approach to this aspect of the subject is to compare the results of the RIT test with those of the standard fat balance. Although there have been many reports relating to the use of RIT, few have included this comparison (Grossman and Jordan, 1958; Lubran and Pearson, 1958; Playoust *et al.*, 1959; Pimparkar *et al.*, 1960; Vaughan Jones, 1960). This paper is a report of a further series of cases in which concurrent faecal chemical fat and faecal RIT excretion determinations were made.

The Central Council for Health Education has issued a booklet, *Helping the Elderly to Live at Home*, which is intended to serve as an introduction to some of the problems involved for relatives who care for old people at home. In addition to what may be called "clinical notes," the booklet has useful sections on making use of the social services, a list of information leaflets, references, and a list of local organizations likely to be needed by relatives, with space left for addresses and telephone numbers. (C.C.H.E., Tavistock House North, Tavistock Square, London W.C.1, price 2s.)

Materials and Methods

Clinical Material.—100 medical and surgical patients were studied by means of a combined test in which simultaneous measurements of faecal chemical fat and faecal RIT excretion were made.

Preparation of Patient.—For two days prior to the administration of RIT each patient received a daily dietary fat intake ranging between 50 g. and 100 g.; in most the intake was 75 g. This diet continued through the period of the collection of faeces. Following the practice of Lubran and Pearson (1958), several out-patient studies were performed. These subjects received a simple diet sheet which was carefully explained. In addition, each patient received potassium iodide to block thyroidal uptake of ^{131}I .

Radiotriolein.—Of the 100 cases 82 received RIT labelled with ^{131}I as iodine monochloride by the method of Lubran and Pearson. The remaining 18 received RIT purchased from the Radiochemical Centre at Amersham. Doses were prepared by emulsification with Tween 80 and water and dispensed in a volume of 10 ml. in a glass container. Each dose was individually calibrated for radioactivity against an Na^{131}I standard. The administered dose of radioactivity varied between 10 and 15 μc of ^{131}I .

Dosing Procedure.—Half the patients received their dose after a 12-hour fast and the remainder two hours after a normal breakfast. The patient drank the active emulsion direct from the dose container, which was then washed four times with water; the patient also swallowed these washings. No appreciable amount of radioactivity remained after this procedure. Immediately after the dose 250 ml. of milk was taken.

Faecal Collection.—Faeces were collected for a period of four to six days, starting with the first motion after the administration of RIT. Stools were passed direct into a rigid polythene container lined with a plastic bag. Special stress was laid on the importance of complete stool collection and on the avoidance of urinary contamination of the faeces. Where extended metabolic studies were in progress the faeces were collected between carmine markers; in patients having a regular bowel habit this was not considered necessary.

Measurements.—(i) Faecal Chemical Fat:—A sample of the total faecal homogenate was used for the determination of faecal chemical fat by the method of van de Kamer *et al.* (1949). (ii) Faecal RIT:—The total faecal collection was measured for radioactivity in a multi-tube γ -ray assay apparatus (Veall and Vetter, 1958). The containers used for faecal collection fitted

into this apparatus. A solid standard was prepared in one of these containers, using a sample of the active fat emulsion or of Na^{131}I of suitable activity. "Instant whip" was found to be an ideal material for making the standard solid.

In all cases the faeces were homogenized to obtain uniform dispersal of excreted RIT. In some cases the faecal specimen was also counted prior to homogenization in order to assess the necessity for this procedure. Using a counter with 10-cm. Geiger-Mueller tubes, relatively poor agreement was obtained between the pre- and post-homogenization results. When a counter with 26-cm. tubes became available the correlation was greatly improved (Fig. 1) and faecal homogenization was unnecessary with this apparatus.

Results

Faecal Chemical Fat.—A daily faecal chemical fat excretion of 7 g. or more was taken as the criterion for steatorrhoea. On this basis, 67 cases were normal and the remaining 33 had steatorrhoea. The cases of steatorrhoea were analysed according to the condition causing the increase in fat excretion (Table I).

TABLE I.—*Steatorrhoea Cases*

Disease	No. of Cases
Previous gastric surgery	15
Pancreatic disease	6
Idiopathic steatorrhoea	7
Crohn's disease	3
Bile-duct obstruction	1
Carcinoma of colon	1
Total	33

Faecal RIT.—The investigation was designed to assess the reliability of the RIT test by comparing it with the results of the faecal chemical fat excretion. The results of this comparison are given graphically in Fig. 2. The faecal RIT excretion results have been divided into two groups according to the presence or absence of steatorrhoea as judged by the estimation of chemical fat (Table II).

FIG. 1.—Percentage of radiotriolein dose in faeces. Comparison of the two graphs shows that agreement between the pre- and post-homogenization results is better in the counter with 26-cm. Geiger-Mueller tubes than in the counter with 10-cm. G.-M. tubes.

FIG. 2.—Diagram showing comparison between faecal chemical fat and faecal radiotriolein excretion in 100 cases. The broken lines indicate the upper levels of normal faecal chemical fat excretion (7 g./day) and normal faecal radiotriolein excretion (5% of administered dose).

TABLE II.—Summary of Results of Concurrent Faecal Fat and Faecal RIT Excretion in 100 Cases

		Cases without Steatorrhoea (67 Cases)	Cases with Steatorrhoea		
			All 33 Cases	18 Cases Faecal RIT < 5%	15 Cases Faecal RIT > 5%
Faecal chemical fat (g./day)	Mean	3.9	15.6	14.5	16.9
	S.D.	± 1.4	± 9.0	± 10.0	± 7.7
Faecal RIT (% of dose)	Mean	2.3	10.4	2.7	19.0
	S.D.	± 1.3	± 12.4	± 1.2	± 14.1

(i) *Faecal RIT Excretion in Normal Subjects.*—The 67 cases without steatorrhoea excreted between 0.6% and 8.7% of the dose of RIT. The mean was 2.3% with a statistical range of 0 to 4.9% (mean $\pm$ 2 S.D.). On this basis, 5% has been taken as the upper normal limit of faecal RIT excretion. Two cases excreted over 5% (5.7% and 8.7%), results which may be regarded as “false positives.”

(ii) *Faecal RIT Excretion in Cases with Steatorrhoea.*—The 33 cases with steatorrhoea excreted between 1.0% and 47.7% of the dose of RIT. Taking 5% as the upper normal limit of faecal RIT excretion, these cases can be further subdivided into two groups (Table II). Fifteen cases excreted more than 5% and were thus differentiated from the normal material. Eighteen cases excreted less than 5% and were not so differentiated; the results in these cases may be regarded as “false negatives.”

Analysis of Results

The figure of 5% as the upper normal limit of faecal RIT excretion was chosen on statistical grounds. As other workers have used different values, the results were analysed to see if an alternative figure would improve the diagnostic reliability of the RIT test (Table III). Lubran and Pearson regard a range of 5–7% as equivocal, and they perform a chemical fat determination to establish the diagnosis in such cases; Vaughan Jones adopts a similar device but takes a wider

TABLE III.—Effect of Taking Different Values for Normal Faecal RIT Excretion on the Number and Incidence of False Results

		Faecal RIT Excretion taken as Normal (% of Dose)						Equivocal Ranges	
		3	4	5	6	7		5–7	3–7
67 cases without steatorrhoea	No. of false pos.	13	6	2	1	1	1	1	1
	% of false pos. . .	19%	9%	3%	2%	2%	2%	2%	2%
33 cases with steatorrhoea	No. of false neg.	10	14	18	20	20	18	10	
	% of false neg. . .	30%	42%	54%	60%	60%	54%	30%	
100 cases in whole series	Total No. of false results	23	20	20	21	21	19	11	
	% of false results . .	23%	20%	20%	21%	21%	19%	11%	

range of 3–7%. In the series reported here the total number of false results is not appreciably reduced except when a range of 3–7% is taken as equivocal. In these circumstances there are only 11% of false results in the whole series, but it is important to appreciate that this figure includes an incidence of 30% of false negative results in the group of cases with steatorrhoea.

The data on the steatorrhoea cases were examined to see if any obvious differences existed between the

patients who excreted less than 5% of the RIT dose and those who excreted more than 5%. The degree of steatorrhoea was similar in both groups (Fig. 3). The other factors considered were age, sex, bowel habit, mode of faecal collection, method of administration of RIT, type of RIT, and type of steatorrhoea (Table IV). Although there are small differences, these factors do not provide an adequate explanation for the observed discrepancies, partly because of the relatively small number of cases studied.

FIG. 3.—Diagram showing the faecal chemical fat excretion in the 33 cases of steatorrhoea, divided into those excreting less than 5% and those excreting more than 5% of the administered dose of radiotriolein.

TABLE IV.—Analysis of the Two Groups of Steatorrhoea Cases

Details of Factors Considered		33 Cases with Steatorrhoea	
		Faecal RIT below 5% of Dose	Faecal RIT over 5% of Dose
Age (years)	Range . . .	21–69	23–69
	Mean . . .	45.5	50.5
Sex (No. of cases)	Male . . .	16	9
	Female . . .	2	6
Bowel habit (No. of motions/day)	Range . . .	1–4	1–5
	Mean . . .	2.0	2.5
Mode of stool collection (No. of cases)	In-patients . . .	11	10
	Out-patients . . .	7	5
	Between markers . . .	3	2
	4–6 day collection . . .	15	13
Method of dosing (No. of cases)	Fasting . . .	9	9
	After breakfast . . .	9	6
Type of ¹³¹ I Triolein (No. of cases)	Lubran and Pearson . . .	12	13
	Amersham . . .	6	2
Type of steatorrhoea (No. of cases)	Digestive . . .	3	4
	Absorptive . . .	5	5
	Gastric surgery . . .	9	6
	Carcinoma of colon . . .	1	0

Comparison with Similar Studies

Five studies similar to the present one have been found in the literature, and the combined results are given in Table V. This summary shows that, in a total of 391 subjects studied by concurrent measurements of faecal RIT and faecal chemical fat the RIT test gave 26% of false negative results and 6% of false positives. More recently, Lubran (1960) has found "complete agreement" between faecal chemical fat and faecal RIT excretion in 76% of a large series of cases, which included both normal subjects and cases of steatorrhea.

TABLE V.—Summary of Results of Six Separate Studies in Which Faecal Chemical Fat and Faecal RIT Have Been Compared

Authors	No. of Cases		Incidence of False Results		Normal Values Adopted	
	Whole Series	With Steatorrhea	False Neg.	False Pos.	Faecal Fat g./Day	Faecal RIT % of Dose
Grossman and Jordan (1958)	47	14	0%	0%	14.1 g.†	<5.1%
Lubran and Pearson (1958)	26	9	11%	0%	6.0 g.	5-7%
Playoust, <i>et al.</i> (1959)	48	12	0%	11%	6.5 "	<3%
Pimparkar <i>et al.</i> (1960)	115	54	24%	16%	7.0 "	<7%
Jones (1960)*	55	18	28%	5%	7.0 "	3-7%
Present Series	100	33	54%	3%	7.0 "	<5%
Totals	391	140	26%	6%		

* Complete data not yet published. † Total faecal lipids.

The present study gave the lowest success rate for the diagnosis of steatorrhea by the RIT test, although the number of false positive results was lower than in other series. Despite the disparities between the different studies, the fact remains that several groups of workers have failed to obtain consistently reliable results with the RIT test.

Discussion

The main conclusion from this study is clearly that the test was unreliable in the diagnosis of steatorrhea. The first section of this discussion deals with the effect of errors in stool collection on the results obtained. This is followed by a consideration of the theoretical aspects of the RIT test.

Stool Collection

In the RIT test, mistakes in faecal collection can give rise to misleading results in two ways.

Firstly, an incomplete stool collection can cause a falsely low result. This applies both to the RIT test and to the fat balance, but in the former it is a particularly important source of error. This is because most of the RIT excreted in the faeces appears in one or two motions, whereas faecal chemical fat is more evenly distributed throughout the motions passed during the test. If the motion containing the majority of the unabsorbed RIT is lost the result of the RIT test will be affected to a greater degree than the result of the chemical fat balance. This may be the cause of a "false negative" result—that is, a low faecal RIT excretion in cases with a high faecal chemical fat excretion.

The second possible source of error arises because of the urinary excretion of 50% or more of the *absorbed* radioactivity in the first two days after the administration of RIT. Therefore urinary contamination of the faeces can cause "false positive" results—that is, the appearance of a high percentage of the RIT dose in the faeces of subjects without steatorrhea. Playoust *et al.* (1959) interpret false positive results as indicating that the RIT test is more sensitive than the fat balance in the diagnosis of steatorrhea, but the possibility of

urinary contamination as a cause of this anomaly must always be considered.

In this series, one of the false negative results could be safely ascribed to faulty stool collection, and this also seemed to be a likely explanation in a second case. If the other discrepant results were caused by errors in faecal collection, the practical value of the RIT test remains in doubt, since determined efforts were made to ensure a proper collection in every case—efforts which would not reasonably be expected in routine practice.

Theoretical Aspects of the RIT Test

Although the temptation to ascribe anomalous results to technical errors is considerable, the possibility that more fundamental errors may provide at least a partial explanation merits consideration. The validity of the RIT test rests on at least four fundamental assumptions.

(i) Validity of Faecal Measurement of RIT

The measurement of the faecal excretion of RIT is generally accepted as a valid procedure in the RIT test. While several workers have advocated plasma or urinary measurements as satisfactory alternatives, few claim that they rival the faecal determination in sensitivity. Fierst *et al.* (1958) are alone in denying the validity of faecal measurements on the grounds that excretion of iodine and iodine-containing compounds *into* the gut vitiates the results of faecal determinations.

Some evidence on this point is provided by studies in which faecal radioactivity has been measured after the parenteral administration of substances containing ¹³¹I. Berson and Yalow (1954) recorded negligible radioactivity after the intravenous injection of ¹³¹I as Na¹³¹I. Van Middlesworth (1960) has shown that intravenously administered ¹³¹I-labelled thyroxine is excreted in the faeces in appreciable amounts in the four days after injection. Using RIT, two groups of workers have performed similar experiments which may be expected to give the most direct evidence: in mice, Rutenburg, Seligman, and Fine (1949) found only 1% of the dose in the faeces after injection; in 5 human subjects without steatorrhea, Lamberg *et al.* (1960) were unable to detect any faecal radioactivity in the two days following the intravenous administration of a RIT emulsion.

However unlikely Fierst's belief may appear at first sight, the question must remain open until more experimental evidence is available. This may be provided by extending the work of Lamberg and his colleagues to a study of cases with steatorrhea.

(ii) Origin of Faecal Fat

Since RIT is used as a tracer for dietary fat, the test relies on the assumption that faecal chemical fat is derived solely from unabsorbed dietary fat. However, the origin of faecal fat is still a matter for debate (Frazer, 1959). It may be of dietary or non-dietary origin; alternatively, both sources may contribute appreciable amounts. Various sources of endogenous (that is, non-dietary) faecal fat have been suggested, including active secretion of fat into the lumen of the gut (Lewis and Partin, 1954), synthesis of fat by the bowel mucosa (Clark and Hübscher, 1960), excretion of fat in the bile (McClure *et al.*, 1934) and synthesis of fat by alimentary flora (Sammons *et al.*, 1956).

The evidence on this subject is not conclusive. Krakower (1934) and Annegers *et al.* (1948) found that alterations in the dietary fat intake in normal subjects

did not alter faecal fat output and concluded that an endogenous origin accounts for most of the faecal chemical fat in normal subjects. However, in observations on two normal subjects Wollaeger *et al.* (1953) found that faecal fat fell substantially on a lipid-free diet; their conclusion that faecal fat was mainly of dietary origin was in keeping with a previous study (Wollaeger, Comfort, and Osterberg, 1947) in which the output of faecal fat rose appreciably when the dietary intake was increased from 100 to 200 g. daily.

In patients with steatorrhoea, the general view is that faecal fat is largely of dietary origin. However, Comfort *et al.* (1953), Cooke *et al.* (1953), and Jiménez-Díaz *et al.* (1959) have reported studies in which the faecal fat output was in excess of the dietary intake. In these cases a substantial endogenous component must be accepted. In subjects studied by the RIT test a high faecal chemical fat excretion with a low faecal RIT excretion (that is, a "false negative" result) might be explained if the faecal chemical fat was chiefly of endogenous origin.

Seeking an explanation for the discrepancy between the faecal RIT excretion and chemical fat excretion in one of his cases, Jones (1960) cultured the intestinal contents in an unsuccessful attempt to repeat the work of Sammons *et al.* (1956). These workers claim to have isolated a faecal organism (from a patient with steatorrhoea) capable of synthesizing fat.

Jiménez-Díaz *et al.* (1959) used ^{131}I -labelled triolein as a tracer for dietary fat in an investigation into the origin of faecal fat. Their conclusion was that faecal fat was mainly derived from endogenous sources, both in normal subjects and in cases of steatorrhoea. Unfortunately the particular ^{131}I label used by these workers has not gained wide acceptance; furthermore, the validity of labelled triolein as a tracer material for dietary fat is a matter for further study. However, the possibility remains that, under suitable conditions, RIT may provide a useful means of assessing the dietary contribution of faecal fat, even though it may be rejected as a means of diagnosing steatorrhoea.

The answer to some of these questions might be supplied by the use of ^{14}C -labelled lipids. Unfortunately these materials are not acceptable for routine use because of the counting difficulties and because of the long half-life of the isotope.

(iii) Behaviour of RIT in the Alimentary Tract

To be acceptable as a tracer material, RIT must behave like dietary fat in the alimentary tract. Lack of evidence on this fundamental requirement is due, in large measure, to the inaccessibility of the small intestine. The assimilation of relevant data must await the development of suitable techniques. Meanwhile, RIT dosing procedures have an important practical bearing on this problem and merit further consideration.

Grossman and Jordan (1958) studied the effect of giving different fat loads with the RIT dose and concluded that the faecal RIT excretion did not vary. Similar findings have been reported by Cheers *et al.* (1958). However, the latter group confined their observations to normal subjects, and Grossman and Jordan included only one case of steatorrhoea.

Playoust *et al.* (1959) have stressed the importance of determining the best dosing procedure. They reported a few cases of steatorrhoea in which the absorption of RIT was reduced by increasing the fat

load given with the dose of RIT. Similar observations have been made in this department, and a series of cases is being studied with a modified dosing procedure to see if the incidence of false results can be reduced.

Of great theoretical interest is the suggestion of J. C. Charlton (personal communication, 1960) that the behaviour of RIT in the gut may be altered by the degree of saturation of the triolein molecule with the ^{131}I label. The physico-chemical properties of triolein are changed by radio-iodination, and this may be expected to have some bearing on its biological behaviour. However, it is known from experience that the same batch of RIT may successfully diagnose steatorrhoea in one case and yet fail in another. Therefore it seems unlikely that Charlton's theory will provide a complete explanation of the false results.

(iv) Stability of the RIT Bond

The assumption is generally made that the radio-iodinated triolein bond is stable in the alimentary tract. If this assumption proves to be incorrect and a substantial amount of the ^{131}I label is split off within the lumen of the gut, the RIT test is vitiated, since the metabolic pathway of iodine differs from that of fat.

Turner (1958) has conducted an extensive series of experiments which rely on the observation that the circulating radioactivity of absorbed RIT exists partly as lipid-bound ^{131}I and partly as unbound ^{131}I , liberated from the RIT bond. This observation has been confirmed by many workers. Van Handel and Zilvermit (1958) gave ^{131}I -labelled fat and unlabelled fat simultaneously to dogs and rats, and showed that the plasma and lymph concentrations of the labelled fat were lower than those of the unlabelled fat, and that some of the circulating ^{131}I was not lipid-bound. In the same study they found that ^{14}C -labelled fats behaved in the same way as the unlabelled fats. The anomalous behaviour of RIT was ascribed to liberation of the ^{131}I label either in the lumen of the gut or in the mucosal cells.

The exact site of liberation of the ^{131}I label remains uncertain. Most authors favour the suggestion that this occurs in the mucosal cells of the alimentary tract, and this is supported by the *in vitro* tests of Balint *et al.* (1960), in which appreciable liberation of free ^{131}I occurred when RIT was incubated in extracts of intestinal mucosa. Similar experiments by the same workers, and by Beres *et al.* (1957), failed to detect free ^{131}I when RIT was incubated in a variety of intestinal secretions; however, their periods of incubation were relatively short. The use of an anion exchange resin to determine free ^{131}I in radio-iodinated lipids offered a simple means of studying the behaviour of the RIT bond over a longer period of time. Using this method, the most striking finding was a steady rise in the amount of free ^{131}I when RIT was incubated in human duodenal juice over a period of four days (Cox and Hinchliffe, 1961). This appeared to be due to the enzymes, because free ^{131}I was not detected when the incubation medium was *boiled* duodenal juice. Since the lipolytic activity of duodenal juice falls off very rapidly *in vitro* (Lagerlöf, 1942), its bond-splitting potency may be less in laboratory experiments than in the alimentary tract. The possibility that the RIT bond is appreciably unstable under the conditions of the RIT test remains to be explored by *in vivo* experiments.

Summary

The value of radiotriolein in the diagnosis of steatorrhea was assessed in 100 subjects by comparing the faecal radiotriolein excretion with concurrent faecal chemical fat determinations.

Sixty-seven cases did not have steatorrhea as judged by a faecal chemical fat excretion below 7 g. daily. In these the upper limit of faecal radiotriolein excretion was 5% of the administered dose.

Thirty-three cases had steatorrhea as judged by the faecal chemical fat excretion. Of these, 15 excreted more than 5% of the dose of radiotriolein. The remaining 18 excreted less than 5% and were not differentiated from the normal material.

Analysis of these results failed to explain the discrepancies. Comparison with similar studies has shown that some other workers have also found the radiotriolein test to be unreliable in the diagnosis of steatorrhea.

If technical errors are the explanation of the false results, the practical value of the radiotriolein test is lessened.

Several possible defects and a few alternative applications of the radiotriolein test are discussed.

This study was assisted by the Tuberculosis Research Fund of the University of Sheffield. I am indebted to Professor A. W. Kay for invaluable advice and encouragement throughout; to the following consultants for allowing me to study their patients: Dr. H. P. Brody, Dr. C. E. Davies, Mr. F. J. P. O'Gorman, Dr. E. G. G. Rhind, Dr. E. W. Skipper, and Professor G. M. Wilson; to Dr. A. Jordan for faecal chemical fat determinations performed in his department; to Mrs. O. Fisher for guidance in radioisotope techniques; to Messrs. A. Bird and Sons Ltd. for supplies of "instant whip"; and to Miss R. Chalmers and Miss Z. Hinchliffe for technical assistance.

REFERENCES

- Annegers, J. H., Boutwell, J. H., and Ivy, A. C. (1948). *Gastroenterology*, **10**, 486.
 Balint, J., Pendower, J., and Ramsey, N. W. (1960). *Clin. Sci.*, **19**, 321.
 Beres, P., Wenger, J., and Kirsner, J. B. (1957). *Gastroenterology*, **32**, 1.
 Berkowitz, D., Sklaroff, D., Woldow, A., Jacobs, A. G., and Likoff, W. (1959). *Ann. intern. Med.*, **50**, 247.
 Berson, S. A., and Yalow, R. S. (1954). *J. clin. Invest.*, **33**, 1533.
 Chears, W. C., McGraw, B. H., Tyor, M. P., and Ruffin, J. M. (1958). *Sth. med. J. (Bgham, Ala.)*, **51**, 433.
 Clark, B., and Hübscher, G. (1960). *Nature (Lond.)*, **185**, 35.
 Comfort, M. W., Wollaege, E. E., and Taylor, A. B. (1953). *Gastroenterology*, **23**, 155.
 Cooke, W. T., Thomas, G., Mangall, D., and Cross, H. (1953). *Clin. Sci.*, **12**, 223.
 Cox, A. G., and Hinchliffe, Z. (1961). *Gut*, **2**, 131.
 Fast, B. B., Wolfe, S. J., Stormont, J. M., and Davidson, C. S. (1959). *Gastroenterology*, **37**, 321.
 Fierst, S. M., Feldman, S. M., Solomon, N., and Langsam, A. (1958). *Ibid.*, **35**, 381.
 Frazer, A. C. (1959). *Proceedings of World Congress of Gastroenterology*, 1958, **1**, 619.
 Grossman, M. I., and Jordan, P. H. (1958). *Gastroenterology*, **34**, 892.
 Hall, G. V., George, E. P., and Hickie, J. B. (1959). *Aust. Ann. Med.*, **8**, 307.
 Jiménez-Díaz, C., Linazasoro, J. M., Marina, C., and Romeo, J. M. (1959). *Bull. Inst. med. Res. (Mad.)*, **12**, 41.
 Jones, R. V. (1960). *Brit. med. J.*, **2**, 1236.
 Krakower, A. (1934). *Amer. J. Physiol.*, **107**, 49.
 Lagerlöf, H. O. (1942). *Acta. med. scand.*, Suppl. 128, pp. 55-61.
 Lamberg, B.-A., Siurala, M., Turula, K., Hakkila, R., and Harjanne, A. (1960). *Scand. J. clin. Lab. Invest.*, **12**, 107.
 Lewis, G. T., and Partin, H. C. (1954). *J. Lab. clin. Med.*, **44**, 91.
 Lubran, M. (1960). *Lancet*, **2**, 907.
 — and Pearson, J. D. (1958). *J. clin. Path.*, **11**, 165.
 McClure, C. W., Huntsinger, M. E., and Fernald, A. T. (1934). *Amer. J. Physiol.*, **107**, 1.
 Mäkelä, T. E., Hakkila, R. L., and Hakkila, J. (1960). *Acta med. scand.*, **167**, 121.

- Pimparkar, B. D., Tulskey, E. G., Kalser, M. H., and Bockus, H. L. (1960). *Brit. med. J.*, **2**, 894.
 Playoust, M. R., Wyatt, J. V., and Blackburn, C. R. B. (1959). *Aust. Ann. Med.*, **8**, 245.
 Reemtsma, K., Malm, J. R., and Barker, H. G. (1957). *Surgery*, **42**, 22.
 Ruffin, J. M., Shingleton, W. W., Baylin, G. J., Hymans, J. C., Isley, J. K., Sanders, A. P., and Sohmer, M. F. (1956). *New Engl. J. Med.*, **255**, 594.
 Rutenburg, A. M., Seligman, A. M., and Fine, J. (1949). *J. clin. Invest.*, **28**, 1110.
 Sammons, H. G., Vaughan, D. J., and Frazer, A. C. (1956). *Nature (Lond.)*, **177**, 237.
 Sandberg, H., Min, B. S., Feinberg, L., and Bellet, S. (1960). *Arch. intern. Med.*, **105**, 866.
 Stanley, M. M., and Thannhauser, S. J. (1949). *J. Lab. clin. Med.*, **34**, 1634.
 Turner, D. A. (1958). *Amer. J. dig. Dis.*, **3**, 594.
 van de Kamer, J. H., Huinink, H. ten B., and Weyers, H. A. (1949). *J. Biol. Chem.*, **177**, 347.
 van Handel, E., and Zilvermit, D. B. (1958). *J. Lab. clin. Med.*, **52**, 831.
 van Middlesworth, L. (1960). *Recent Progr. Hormone Res.*, **16**, 405.
 Veall, N., and Vetter, H. (1958). *Radioisotope Techniques in Clinical Research and Diagnosis*. Butterworth, London.
 Walker, W. F., Stewart, W. K., Morgan, H. G., and McKie, J. (1960). *Brit. med. J.*, **1**, 1403.
 Wollaege, E. E., Comfort, M. W., and Osterberg, A. E. (1947). *Gastroenterology*, **9**, 272.
 — Lundberg, W. O., Chipault, J. R., and Mason, H. L. (1953). *Ibid.*, **24**, 422.

Medical Memoranda

Perforated Peptic Ulcer in Late Pregnancy

Peptic ulcer rarely occurs in pregnancy. This had probably been known to the astute physician since time immemorial, but Avery Jones's (1947) figures came to most as a surprise. He was unable to find a single case of peptic ulcer occurring among 10,000 pregnancies and 2,000 abortions reviewed. If peptic ulcer is rare, complications of peptic ulcer are, not unnaturally, exceedingly rare, and when Sandweiss *et al.* (1943) reviewed the world literature they were able to find only 13 recorded cases of complications of peptic ulcer occurring during pregnancy—nine perforations and four haemorrhages.

In this country two cases of perforated peptic ulcer in late pregnancy have been recorded during the past 13 years. James's (1948) case occurred at the 36th week, and ended satisfactorily for mother and child. The perforation was repaired, and the mother was delivered of a live child four days later. Both did well. Ten years later a case was described by Horwich (1958), occurring in the 32nd week. Conservative treatment was adopted, but this was not successful, a stillborn child being born the following day. Laparotomy was eventually necessary 60 hours after the onset of the perforation. The perforation was sutured, and after a very stormy convalescence the patient recovered.

The present case, in which twins were born the day after a partial gastrectomy, would appear to be unique.

CASE HISTORY

A married woman, aged 38, and 31 weeks pregnant, was admitted to the Maternity Department of Upton Hospital on January 7, 1961, as a case of suspected hyperemesis gravidarum. She had been vomiting persistently for three weeks, prior to which the pregnancy had been normal. A year previously she had had some abdominal pain, for which she had taken medicine; but she was not a known case of peptic ulcer, though there was a family history of it. In the early hours of the morning following her admission she began to complain of severe abdominal pain, and Dr. Ralph Evans, the house-surgeon, wisely suspected the possibility of a perforated peptic ulcer. When I saw