adds considerably to the nutritional deficiency caused by loss of calories and defective absorption of mineral elements and vitamins, which are known to be associated with steatorrhoea of long standing.

We wish to express our gratitude to Sir Charles Harington, F.R.S., and to Dr. A. S. McFarlane for permission to use the mass spectrometer at the National Institute for Medical Research, Mill Hill, and to Mr. G. Dickenson for valuable co-operation in carrying out the very large number of determinations of $^{15}N$. We thank Dr. Margot Shiner, of the Gastroenterological Unit, the Central Middlesex Hospital, for performing jejunal biopsies on the patients and for the estimation of duodenal enzymes; Dr. E. Miller of the Distillers Co. Ltd., Great Burgh, Epsom, Surrey, for gifts of yeast cultures; and Miss Sheila Wilkie, late dietitian of St. Mary's Hospital, for supervising the diets of one patient. Our thanks are also due to Professor W. S. Peart, Dr. W. D. W. Brooks, and Dr. T. A. Kemp, of St. Mary's Hospital, and Dr. F. Avery Jones, of the Gastroenterological Unit, the Central Middlesex Hospital, for permission to study patients under their care. We are also indebted to the Board of Governors of St. Mary's Hospital for a grant from endowment funds for the purchase of $^{15}N$. Finally, one of us (C. W. C.) wishes to thank the British Medical Association for the award of a scientific scholarship during 1957–8 when a part of this work was carried out.

REFERENCES

Albright, F., Forbes, A. P., Bartter, F. C., Reifenstein, E. C., Bryant, D., Cox, L. D., and Dempsey, E. F. (1950). In *Plasma Proteins, Robert Gould Research Foundation Symposia on Nutrition*, vol. 2, p. 155, edited by J. B. Youmans. Thomas, Springfield, Ill.
Borgström, B., Dahlqvist, A., Lundh, G., and Sjövall, J. (1957). *J. clin. Invest.*, **36**, 1521.
Citrin, Y., Sterling, K., and Halsted, J. A. (1957). *New Engl. J. Med.*, **257**, 906.
Cooke, W. T., Thomas, G., Mangall, D., and Cross, H. (1953). *Clin. Sci.*, **12**, 223.
Cope, C. L., and Goadby, H. K. (1935). *Lancet*, **1**, 1038.
Crane, C. W., and Neuberger, A. (1960a). *Biochem. J.*, **74**, 313.
—— —— (1960b). *Brit. med. J.*, **2**, 815.
Geiger, E., Human, L. E., and Middleton, M. J. (1958). *Proc. Soc. exp. Biol. (N.Y.)*, **97**, 232.
Gordon, R. S (1959). *Lancet*, **1**, 325.
Holman, H., Nickel, W. F., and Sleisenger, M. H. (1959). *Amer. J. Med.*, **27**, 963.
Leblond, C. P., and Stevens, C. E. (1948). *Anat. Rec.*, **100**, 357.
Lusk, G. (1928). *The Elements of the Science of Nutrition*, 4th ed. Saunders, Philadelphia and London.
McCrudden, F. H., and Fales, H. L. (1912). *J. exp. Med.*, **15**, 113, 450.
—— —— (1913). Ibid., **17**, 20.
McMinn, R. M. H. (1954). *J. Anat. (Lond.)*, **88**, 527.
Mendel, L. B., and Fine, M. S. (1912). *J. biol. Chem.*, **11**, 5.
Mosenthal, H. O. (1911). *J. exp. Med.*, **13**, 319.
Nasset, E. S. (1957). *J. Amer. med. Ass.*, **164**, 172.
Schwartz, M., and Jarnum, S. (1959). *Lancet*, **1**, 327.
—— and Thomsen, B. (1957). *Brit. med. J.*, **1**, 14.
Sharp, G. S., Lassen, S., Shankman, S., Gebhart, A. F., and Hazlet, J. W. (1956). *J. Nutr.*, **58**, 443.
Voit, C. (1894). *Z. Biol.*, **30**, 548.
Voit, F. (1892). Ibid., **29**, 325.
Walser, M., and Bodenlos, L. J. (1959). *J. clin. Invest.*, **38**, 1617.
Wollaeger, E. E., Comfort, M. W., and Osterberg, A. E. (1947). *Gastroenterology*, **9**, 272.

Dr. F. TROSS, leader of the World Health Organization's yaws control team in the South Pacific, has made a three-month visit to the Cook Islands, where he conducted a survey and trained staff in the eradication of yaws. Dr. Tross has been working since 1954 in co-operation with local governments in South Pacific territories in a campaign against this disease. It involved the mass treatment of the entire indigenous population of these territories with penicillin, followed by several extensive surveys. As a result the incidence of yaws in Fiji, Western Samoa, British Solomon Islands, Gilbert and Ellice Islands, and the New Hebrides has dropped from an average of 15% to a few residual cases. (N.Z. Release No. A26/60.)

# CORRELATION OF RADIOACTIVE AND CHEMICAL FAECAL FAT IN DIFFERENT MALABSORPTION SYNDROMES*

BY

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Many methods of studying fat-absorption from the gastro-intestinal tract have been used. The most accurate method of quantitatively determining faulty assimilation of fat and protein is the balance technique accurately calculating the components in ingested food and chemically determining the residue of the stools (Cooke *et al.*, 1946, 1953; Wollaeger *et al.*, 1947; Annegers *et al.*, 1948; Comfort *et al.*, 1953; Weijers and van de Kamer, 1953; Frazer, 1955; French, 1955; Crowe and Blackburn, 1956; Comfort, 1957; Kalser, 1957). This method has certain disadvantages as a routine clinical diagnostic aid in that it is time-consuming, laborious, and expensive, requiring a metabolic ward and three to five days for the collection of stools. Such facilities are seldom available in the average hospital.

Since the advent of radioisotopes, particularly the $^{131}I$ labelled fats, the absorption tests in humans are becoming much more common. These tests are relatively simple to perform and may be carried out in any radioisotope laboratory. They do not require the special facilities needed for faecal chemical balance study.

In view of the simplicity of $^{131}I$ labelled fat studies as against the time-consuming, expensive, and laborious technique of faecal chemical-balance studies, it is important that controlled studies to correlate these two types of tests be done in the same subjects. No such studies to our knowledge were published until those of Grossman and Jordan (1958).

It is the purpose of this project to compare in a large series the accuracy of radioactive $^{131}I$ labelled triolein studies with faecal chemical intake-excretion studies as a diagnostic aid in the various malabsorption syndromes.

## Methods

Twenty-four normal volunteers consisting of members of the house staff and laboratory personnel were studied as normal controls.

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One hundred patients from the gastro-intestinal service of the Graduate Hospital of the University of Pennsylvania who were suspected of having malabsorption were studied. The clinical diagnoses in these 100 patients were as follows: idiopathic steatorrhoea, 10; non-specific regional enteritis, 12; diseases of pancreas, 18; diseases of hepatobiliary system, 15; functional enterocolonopathy, 13; gastric resections, 11; non-specific idiopathic ulcerative colitis, 5; and miscellaneous, 16.

All of the patients had a complete clinical evaluation, including history and physical examination. Appropriate radiological examinations had been performed. Each person also had routine haematological and biochemical examinations (haemograms, fasting blood-sugar, blood urea nitrogen, total proteins with albumin/globulin ratio, serum calcium, prothrombin time, cholesterol, etc.).

Each individual was given 10 min. (0.6 ml.) of Lugol's solution three times a day for two days prior to the test meal to block the thyroid uptake of radioactive $^{131}I$. Each was placed on a standard diet containing 100 g. of fat, 120 g. of protein, and 270 g. of carbohydrate per day for about 48 hours prior to the test meal and during the intake-excretion studies. All of the non-consumed diet was returned to the diet kitchen for calculation. In each test it was established that the subject ate at least 50 g. of fat per day. Carmine was used as a marker for the balance study.

The $^{131}I$ triolein meal was prepared in emulsion and capsule forms according to the methods of Shingleton *et al.* (1957) and Isley *et al.* (1958) respectively. This radioactive triolein meal was administered to the fasting patient about one to two hours after the first dose of carmine was given. Blood was withdrawn every two hours till a peak was reached and the blood radioactivity was determined according to the method of Shingleton *et al.*, except that the blood volume was presumed to be 3,000 ml. per square metre of body-surface area. Stools were collected in a wide-mouthed jar and faecal radioactivity and faecal chemical fat were determined on the same specimen. In each instance stools were collected till the last specimen did not show significant radioactivity. The usual collection period was four days, with a range of three to six days. Blood peak radioactivity was expressed in terms of percentage of the administered dose in the calculated whole blood volume at the time of drawing of the specimen. The faecal radioactivity was expressed as the percentage excretion of the administered dose. The faecal chemical fat was determined by the method of Van de Kamer *et al.* (1949) and expressed as the number of grammes of total fat† excreted per day.

## Results

Fig. 1 shows the mean blood peak radioactivity at different times in 20 normal volunteers who had both emulsion and capsule types of the triolein meal. The absorptive pattern after the emulsion meal was much more uniform, with a narrower range of values than that with the capsule type of meal. Although the mean peak occurred at four hours with each type of meal, there were four volunteers in whom the peak did not occur until 10 hours after the capsule meal. Fig. 2 shows the mean values after the emulsion and the capsule meals and after both meals together in 45 tests on 24 normal volunteers. Since the peak level is the most important value in the blood absorptive pattern, only these values are considered in the subsequent discussion. The mean blood peak radioactivity value in 45 tests on 24 normal volunteers after the emulsion and capsule meals was 19 $\pm$ 5% of administered dose with a range of 10 to 32% of the administered dose and a calculated lower limit of normal (mean $\pm$ 2 S.D.) of 9% of the administered dose in the whole blood volume.

The mean faecal radioactivity value in 31 experiments on 20 normal volunteers was 3 $\pm$ 1.94% of the administered dose with a range of 1 to 9% of the administered dose and a calculated upper limit of normal (mean $\pm$ 2 S.D.) of 6.9% of the administered dose.

The mean faecal chemical fat value in the same 31 specimens on 20 normal volunteers was 4 $\pm$ 1.6 g. per

†Fat is used in its broadest sense, and means the total neutral fat, excluding sterols and phospholipid.

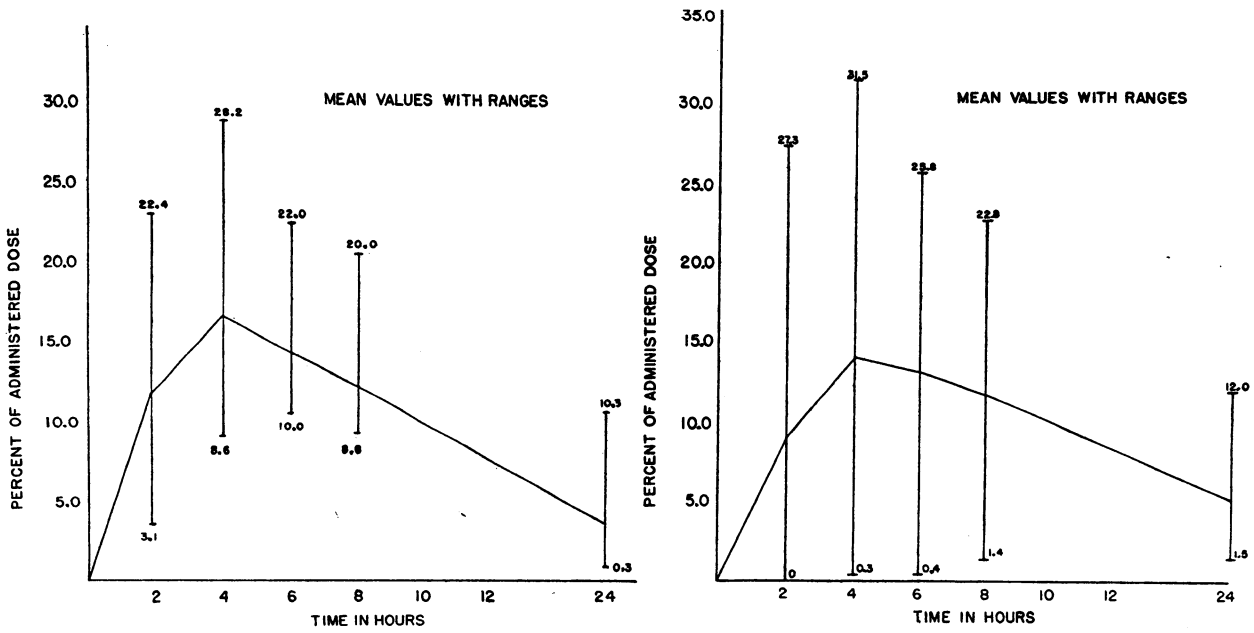


FIG. 1.—Mean blood peak radioactivity in 20 volunteers with emulsion of $^{131}I$ triolein (left) and with capsule of $^{131}I$ triolein (right).

day with a range of 2 to 9 g. per day and a calculated upper limit of normal (mean ± 2 S.D.) of 7.2 g. per day.

In the subsequent discussion 7% of the administered dose as faecal radioactivity and 7 g. per day of faecal chemical fat have been taken as the upper limit of normal for the stool studies, while 9% of the administered dose in the whole blood volume at any time has been taken as the lower limit of normal blood peak radioactivity.

During this study 115 tests were performed on 102 patients and these are analysed in the following discussion. Some of these patients had these studies on two occasions at an interval of one month to one year. Their clinical condition was changed because of the specific or non-specific medical therapy, and hence each test is regarded as a separate patient.

In Figs. 3, 4, and 5 the blood absorptive pattern of normals is compared with that of patients with different types of malabsorption syndromes. From these figures it will be seen that the absorptive pattern was nearly

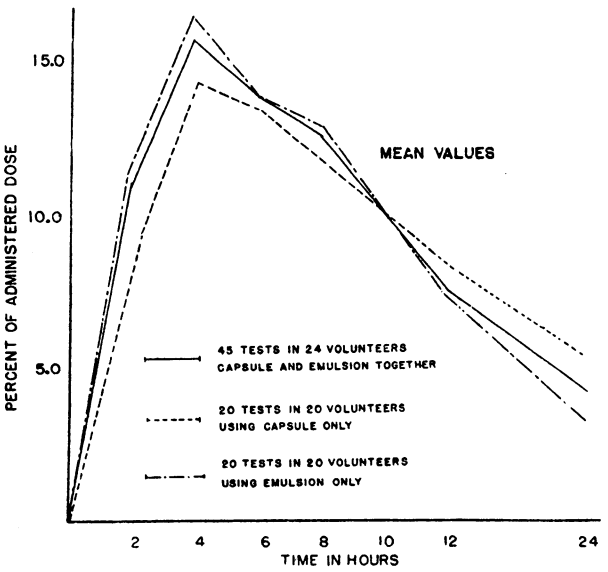


FIG. 2.—Blood radioactivity after the emulsion and the capsule meals.

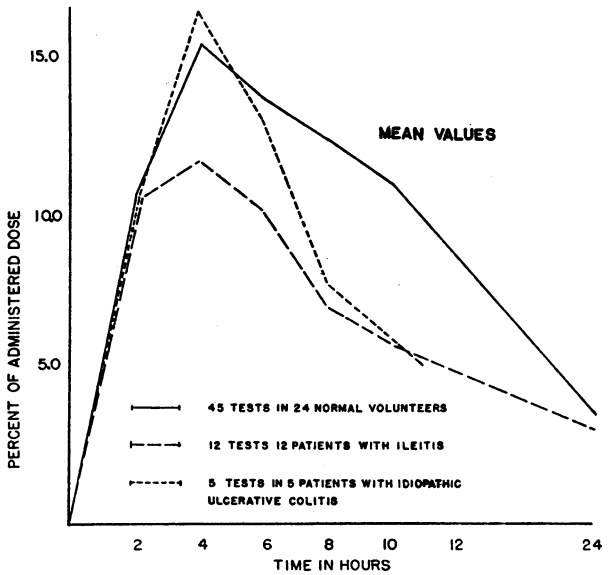


FIG. 3.—Blood radioactivity after oral $^{131}$I triolein in patients with ileitis and with idiopathic ulcerative colitis, compared with normal volunteers.

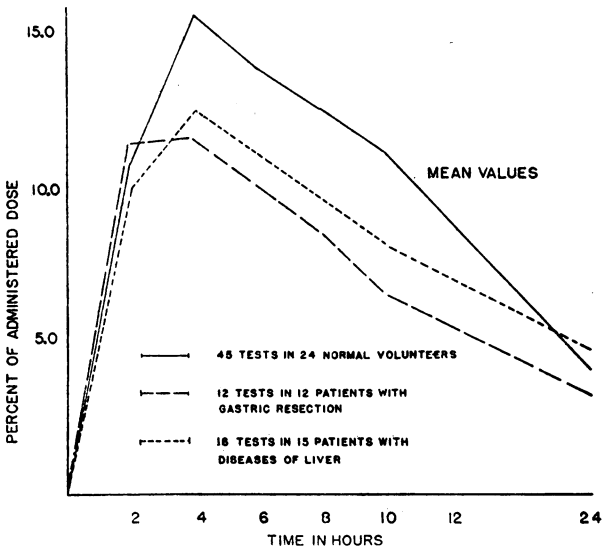


FIG. 4.—Blood radioactivity after oral $^{131}$I triolein in patients with gastric resection and with liver diseases, compared with normal volunteers.

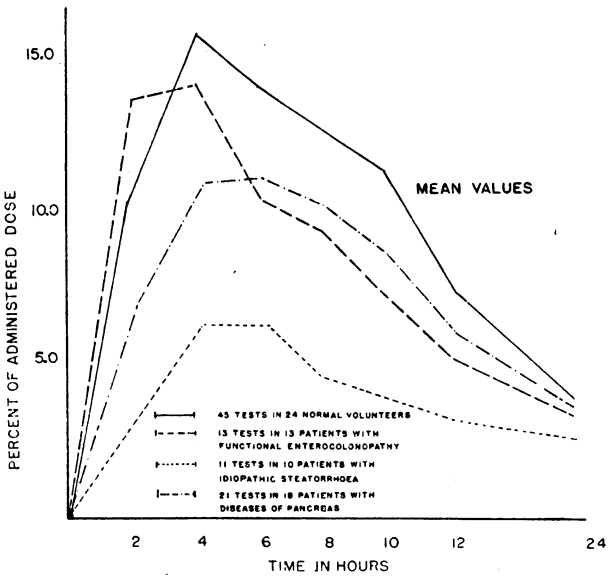


FIG. 5.—Blood radioactivity after oral $^{131}$I triolein in patients with functional enterocolonopathy, with idiopathic steatorrhoea, and with diseases of pancreas, compared with normal volunteers.

normal in patients with non-specific ulcerative colitis and in patients with functional enterocolonopathy, while it was moderately impaired in patients with pancreatic disease, diseases of the hepatobiliary system, non-specific regional ileitis, and gastric resection. It was markedly impaired only in idiopathic steatorrhoea.

TABLE I.—*Blood Peak Radioactivity Values in Different Groups of Patients*

| Name of Group and Total No. in Each | Mean Blood Peak Radioactivity, with S.D. | Range in the Blood Peak Radioactivity | Difference from the Normals, p Value |
|---|---|---|---|
| Normal volunteers, 24 .. | 19·0±5·0 | 10·0–32·0 | — |
| Idiopathic steatorrhoea, 15 | 7·5±5·1 | 1·0–17·0 | <0·001 |
| Non-specific regional enteritis, 12 .. .. | 12·8±6·7 | 1·0–25·0 | <0·01 |
| Diseases of pancreas, 25 .. | 11·6±6·6 | 1·0–24·0 | <0·001 |
| Diseases of hepatobiliary system, 18 .. .. | 13·3±8·3 | 1·0–21·0 | <0·01 |
| Functional enterocolonopathy, 13 .. .. | 17·1±6·5 | 7·0–31·0 | <0·2 |
| Gastric surgery, 11 .. | 13·0±5·5 | 3·0–20·0 | <0·01 |
| Non-specific ulcerative colitis, 5 .. .. | 16·2±7·2 | 12·0–21·0 | <0·5 |

Table I shows the mean blood peak radioactivity values in the various groups with standard deviations and ranges. Attention is called to the last column in that table, which shows the differences from the normal. The p value was considered significant if it was less than 0.05. It was significant in all groups except functional enterocolonopathy and non-specific ulcerative colitis.

TABLE II.—*Faecal Radioactivity Values in Different Groups of Patients*

| Name of Group and Total No. in Each | Mean Faecal Radioactivity with S.D. | Range in the Faecal Radioactivity | Differences from the Normals, p Value |
|---|---|---|---|
| Normal volunteers, 24 | 3·0 ± 1·94 | 1·0– 9·0 | — |
| Idiopathic steatorrhoea, 15 | 29·1 ±22·7 | 1·0–63·0 | <0·001 |
| Non-specific regional enteritis, 12 | 22·8 ±22·2 | 1·0–68·0 | <0·001 |
| Diseases of pancreas, 25 | 18·8 ±26·7 | 1·0–95·0 | <0·02 |
| Diseases of hepatobiliary system, 18 | 15·6 ±23·3 | 1·0–87·0 | <0·05 |
| Functional enterocolonopathy, 13 | 1·92± 1·5 | 1·0– 5·0 | <0·05 |
| Gastric surgery, 11 | 12·8 ±19·3 | 1·0–67·0 | <0·05 |
| Non-specific ulcerative colitis, 5 | 9·6 ± 7·3 | 1·0–17·0 | <0·01 |

Table II shows the mean faecal radioactivity values in different groups, with their corresponding standard deviations and ranges. The mean faecal radioactivity was significantly different from the normals in all groups except functional enterocolonopathy.

TABLE III.—*Faecal Chemical Fat Values in Different Groups of Patients*

| Name of Group and Total No. in Each | Mean Faecal Chemical Fat with S.D. | Range in Faecal Chemical Fat Values | Difference from the Normals, p Value |
|---|---|---|---|
| Normal volunteers, 24 | 4·0± 1·6 | 2·0– 9·0 | — |
| Idiopathic steatorrhoea, 15 | 22·3±13·7 | 7·0–59·0 | <0·001 |
| Non-specific regional enteritis, 12 | 23·2±23·0 | 1·0–66·0 | <0·001 |
| Diseases of pancreas, 25 | 11·2±13·2 | 2·0–51·0 | <0·02 |
| Diseases of hepatobiliary system, 18 | 16·3±11·7 | 3·0±44·0 | <0·001 |
| Functional enterocolonopathy, 13 | 2·8± 1·6 | 1·0– 6·0 | <0·05 |
| Gastric surgery, 11 | 9·5± 9·2 | 1·0–29·0 | <0·02 |
| Non-specific ulcerative colitis, 5 | 3·8± 1·9 | 2·0– 7·0 | <1·0 |

Table III demonstrates the mean faecal chemical fat values in different groups with their corresponding standard deviations and ranges. The mean faecal chemical fat was significantly abnormal in all groups except those with non-specific ulcerative colitis and functional enterocolonopathy. The faecal chemical fat was significantly lower than normal in patients with functional enterocolonopathy.

Table IV shows the results of the three studies in all of the groups with the patients classified into normals and abnormals according to the criteria described previously.

In each division except for the ulcerative colitis and miscellaneous groups more patients were abnormal percentage wise by the faecal chemical fat determination, intermediate by the faecal radioactivity determination, and least by the blood peak radioactivity determination. For the detection of steatorrhoea the faecal chemical fat determination was the most sensitive, followed by the faecal radioactivity determination and then the blood peak radioactivity determination. Of the three tests there was much better correlation between the faecal chemical fat test and the faecal radioactivity test than between any other two tests.

When only normals are considered (Table IV) the opposite is seen—that is, there were more people who had normal faecal and blood radioactivity as compared with a faecal chemical fat.

These results suggest that $^{131}I$ triolein studies are not as sensitive a diagnostic aid in detection of steatorrhoea as is the faecal chemical fat determination.

When the values for faecal chemical fat, faecal radioactivity, and blood peak radioactivity were all normal, or were all abnormal, we defined this as complete agreement of the three tests. On the other hand, if the faecal chemical fat was normal and both blood peak and faecal radioactivity were abnormal, or vice versa (abnormal faecal chemical fat with normal blood peak and faecal radioactivity), we defined this as complete disagreement of the three tests.

With the use of these criteria in analysing the 115 patients (Table V) there was complete agreement in 74 patients or in 64% and there was complete disagreement in 13%. Table VI shows the incidences of complete agreement and complete disagreement in all the groups. It should be noted that the incidence of complete agreement varied from 40 to 93%, with a mean of 62%, while

TABLE V.—*Correlation of Faecal Chemical Intake-Excretion Studies and $^{131}I$ Triolein Test in 115 Patients as a Whole Group*

| | | Faecal Chemical Fat | | | |
|---|---|---|---|---|---|
| | | Normal 7 g./Day | | Abnormal 7 g./Day | |
| | Total No. 115 | No. | % | No. | % |
| | | 61 | 53 | 54 | 47 |
| Faecal radioactivity % adm. dose | Normal, 7% | 51 | 84 | 13 | 24 |
| | Abnormal, 7% | 10 | 16 | 41 | 76 |
| Blood peak radioactivity | Normal, 9% | 54 | 89 | 24 | 46 |
| | Abnormal, 9% | 7 | 11 | 30 | 54 |
| Combined faecal and blood peak radioactivity | Both normal | 47 | 77 | 11 | 21 |
| | One or both disagree | 14 | 23 | 27 | 50 |
| | Both abnormal | 4 | 7 | 27 | 50 |

TABLE IV.—*Normal and Abnormal Results by Three Tests in Different Groups of Patients*

| Name of Group and Total Cases in Each | Faecal Chemical Fat | | | | Faecal Radioactivity | | | | Blood Peak Radioactivity | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Normal ≤7 g./Day | | Abnormal >7 g./Day | | Normal ≤7% | | Abnormal >7% | | Normal ≥9% | | Abnormal <9% | |
| | Tests | | Tests | | Tests | | Tests | | Tests | | Tests | |
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| 115 tests as a whole irrespective of clinical diagnosis | 61 | 53 | 54 | 47 | 64 | 56 | 51 | 44 | 78 | 68 | 37 | 32 |
| Idiopathic steatorrhoea, 15 | 1 | 7 | 14 | 93 | 4 | 27 | 11 | 73 | 5 | 33 | 10 | 66 |
| Non-specific regional enteritis, 12 | 4 | 33 | 8 | 66 | 5 | 42 | 7 | 58 | 9 | 66 | 3 | 33 |
| Diseases of pancreas, 25 | 15 | 60 | 10 | 40 | 15 | 60 | 10 | 40 | 16 | 64 | 9 | 36 |
| ,, ,, liver, 18 | 5 | 28 | 13 | 72 | 11 | 61 | 7 | 39 | 12 | 66 | 6 | 33 |
| Functional enterocolonopathy, 13 | 13 | 100 | 0 | 0 | 13 | 100 | 0 | 0 | 12 | 92 | 1 | 8 |
| Gastric surgery, 11 | 6 | 55 | 5 | 45 | 6 | 55 | 5 | 45 | 8 | 73 | 3 | 27 |
| Non-specific idiopathic ulcerative colitis, 5 | 5 | 100 | 0 | 0 | 2 | 40 | 3 | 60 | 5 | 100 | 0 | 0 |
| Miscellaneous, 16 | 12 | 75 | 4 | 25 | 8 | 50 | 8 | 50 | 11 | 69 | 5 | 31 |

TABLE VI.—*Complete Agreement and Complete Disagreement Between Faecal Chemical Fat Determination and Faecal and Blood Peak Radioactivity Determination*

| Name of Group | Percentage of Complete Three Tests | |
|---|---|---|
| | Agreement | Disagreement |
| Idiopathic steatorrhoea | 66 | 14 |
| Non-specific regional enteritis | 58 | 8 |
| Diseases of pancreas | 72 | 4 |
| ,, ,, hepatobiliary system | 50 | 33 |
| Functional enterocolonopathy | 93 | 0 |
| Gastric surgery | 58 | 0 |
| Ulcerative colitis | 40 | 0 |
| Miscellaneous | 56 | 25 |
| Mean | 62 | 10·4 |
| 115 patients as a whole group | 64 | 13 |

the incidence of complete disagreement ranged from 0 to 33%, with a mean of 10%. Thus there was complete agreement in about two-thirds and complete disagreement in another one-eighth, so that about one-third of the patients were either false positive or false negative.

When, in a given patient, the faecal chemical fat was abnormal and the faecal radioactivity and/or blood peak radioactivity was in the range of normal, this patient was said to be false negative. On the other hand, if the chemical fat was normal and the faecal and/or blood peak radioactivity was abnormal then this patient was a false positive for steatorrhoea.

TABLE VII.—*Percentage False Negative by $^{131}I$ Triolein Test as Compared with Faecal Intake-Excretion Studies*

| Name of Group | Percentage of False Negative | | |
|---|---|---|---|
| | By Blood Peak Radioactivity | By Both | By Faecal Radioactivity |
| Idiopathic steatorrhoea | 29 | 14 | 21 |
| Non-specific regional enteritis | 63 | 12 | 12 |
| Diseases of pancreas | 40 | 10 | 10 |
| ,, ,, hepatobiliary system | 54 | 46 | 54 |
| Gastric surgery | 60 | 0 | 0 |
| Ulcerative colitis | 0 | 0 | 0 |
| Miscellaneous | 50 | 25 | 25 |
| Mean | 43 | 14 | 17 |
| 115 patients as a whole group | 46 | 21 | 24 |

Table VII shows the incidence of false negatives in different groups of patients by the blood peak radioactivity test alone, by the faecal radioactivity test alone, and by both tests together. The incidence of false negatives by blood peak radioactivity tests ranged from 0 to 63%, with a mean of 43% in the different groups and 46% in the 115 patients as a whole group. The incidence of false negatives by faecal radioactivity tests ranged from 0 to 54%, with a mean of 17% in different groups and 24% in the whole group of 115 patients. The differences between blood peak radioactivity test and faecal radioactivity test are quite significant. Also, when both blood peak radioactivity and faecal radioactivity are considered, the incidence of false negatives ranged from 0 to 46%, with a mean of 14% in different groups and 21% in the 115 patients as a whole group.

These results suggest that the triolein test is likely to be abnormal in patients with steatorrhoea in about 50% by blood peak, in 75% by faecal radioactivity tests, and in about 80 to 85% by both faecal and blood peak radioactivity tests.

Table VIII shows the incidence of false positives in the different groups. The incidence of false positives by the blood peak radioactivity test ranged from 0 to 25% with a mean of 8.5% in different groups and 11% in the whole group of 115 patients. The incidence of false positive by the faecal radioactivity test ranged from 0 to 60%, with a mean of 16% in different groups and 16% in the entire series of 115 patients. When the false-positive patients in the ulcerative colitis group, where exudation of protein and inorganic $^{131}I$ into the colon which may account for the increased radioactivity are omitted, the mean incidence of false positives by faecal radioactivity is the same as that by blood peak

TABLE VIII.—*Percentage False Positive by $^{131}I$ Triolein Test as Compared with Faecal Intake-Excretion Studies*

| Name of Group | Percentage of False Positive | | |
|---|---|---|---|
| | By Blood Peak Radioactivity | By Both | By Faecal Radioactivity |
| Idiopathic steatorrhoea | 0 | 0 | 0 |
| Non-specific regional enteritis | 0 | 0 | 0 |
| Diseases of pancreas | 20 | 0 | 6 |
| ,, ,, hepatobiliary system | 0 | 0 | 20 |
| Functional enterocolonopathy | 7 | 0 | 0 |
| Gastric surgery | 16 | 0 | 0 |
| Ulcerative colitis | 0 | 0 | 60 |
| Miscellaneous | 25 | 25 | 42 |
| Mean | 8·5 | 3·0 | 16·0 |
| 115 patients as a whole group | 11 | 7 | 16 |

radioactivity—namely, 9%. On the other hand, when both faecal and blood peak radioactivity are taken into consideration, the incidence of false-positive tests ranges from 0 to 25%, with a mean of 3% in different groups and 7% in the entire group.

These results suggest that the triolein test is likely to be normal in about 80 to 95% of patients who do not have steatorrhoea, if both blood peak and faecal radioactivity are determined, while if blood peak radioactivity alone is determined it is likely to be normal in about 85 to 90%. If only faecal radioactivity is determined, the study is likely to be normal in about 80 to 85%. When Tables VII and VIII are compared it is seen that the incidence of false-positive results is much less than the incidence of false-negative results by either blood peak radioactivity or a faecal radioactivity, or by both tests. This finding again suggests that the radioactive triolein studies are not as sensitive an index of steatorrhoea as is the faecal chemical fat determination.

## Discussion

The use of radio-iodinated $^{131}I$ fat in the investigation of indigestion and absorption involves some important sources of error. In determining the efficiency of the labelled-fat meal it must be remembered that one is using a fat which is not usually present in such amounts in the diet. The iodine is partly split off from the organic compound both in the intestinal contents by the action of bacterial enzymes and in the cells after absorption. $^{131}I$ exists in the blood in two forms after the ingestion of the labelled triolein. The bulk of the radioactivity is present as inorganic $^{131}I$; the remainder is bound to lipid. This lipid-bound $^{131}I$ represents the ingested fat which is in transport in the blood as lipoprotein and chylomicrons. The lipid fraction usually contains 20 to 35% of the whole blood radioactivity, though the range extends from 0 to 50% (Beres *et al.*, 1957; Turner, 1958). The absorbed $^{131}I$ is excreted mainly by the kidneys as inorganic $^{131}I$.

Beres *et al.* found that normally the mean 24-hour urinary excretion was 55 ± 11%, with a range of 24 to 68%. Since this $^{131}I$ is in the form of inorganic iodide, the value represents the result of several meta-

bolic processes: fat absorption, fat transport, fat utilization, completeness of thyroid blockade, and renal function. Hence it is not possible to get quantitative information from blood-activity studies on the extent and rate of absorption, since both are influenced by the rate of elimination by the kidney, which may vary for inorganic iodide and different organic iodine compounds. However, if the radioactivity in the blood is followed, valuable information may be obtained as regards the time relationship in absorption. The inorganic $^{131}I$ level is dependent upon the rate of utilization of the fat (at which time the iodine–fatty-acid bond is apparently broken).

Turner (1958) demonstrated that in dogs after feeding a labelled-fat meal the changes in the plasma $^{131}I$ lipid curves paralleled the changes in the turbidity, but as the quantity of olive oil fed with the $^{131}I$ triolein was increased there were changes in the plasma turbidity and the $^{131}I$ lipid activity decreased, while the plasma turbidity increased as the amount of fat was increased. This, however, was not observed in humans (Grossman and Jordan, 1958). Turner also noted differences between young and old dogs in their response to fat administered by the oral and intravenous routes. The plasma $^{131}I$ lipid activity and turbidity after the ingestion of fat were greatly increased in the old dogs as compared with the young dogs. The elevated levels were shown to be the result of an unexplained decrease in the rate of removal of fat from the blood in the dogs. Van Handel and Zilversmit (1958) studied the validity of $^{131}I$ labelling of fat by: (*a*) comparing $^{131}I$ lipid radioactivity with chemically determined fat in the lymph and lipaemic blood, and (*b*) mixing $^{131}I$-labelled fat or fatty acid with radioactive-carbon ($^{14}C$)-labelled fat or fatty acid and determining the ratio of lipid $^{131}I$ to $^{14}C$ in lymph fat and in the neutral fat and phospholipid fraction of tissues. Their results confirmed Turner's observations that the $^{131}I$-labelled triolein administered intravenously as an emulsion disappears from the blood at the same rate as neutral fat, although differences were seen in the lymph.

After the oral administration of $^{131}I$ triolein the concentration of $^{131}I$ triglyceride in the dog plasma during the period of alimentary hyperlipaemia is lower than that of the chemically determined fat. This difference between the specific activity of fed fat and plasma fat already exists in the lymph as shown by the low specific activity of dog and rat lymph compared with that of the administered fat. Comparison of $^{131}I$ and $^{14}C$ triolein showed that dilution by an endogenous triglyceride pool cannot account for the absorbed decrease in specific activity. Those authors state that $^{131}I$ triolein does not appear to give a quantitative measure of the amount of fat absorbed no matter whether part of the $^{131}I$ is broken off the fat or whether $^{131}I$ triolein is absorbed at a rate different from triolein. This finding does not, however, affect the use of $^{131}I$ triolein as an empiric clinical test for the malabsorption syndrome.

Grossman and Jordan (1958) report normal blood radioactivity in 10 patients or 71% of 14 patients with pancreatic steatorrhoea. All 14 patients had abnormal faecal radioactivity. Beres *et al.* (1957) also found this discrepancy between blood radioactivity and faecal radioactivity in cases of pancreatic disease, liver disease, gastric surgery, and regional enteritis. McKenna *et al.* (1957) concluded that although the blood curve is a good indicator of the absorption rate, the stool recovery of $^{131}I$ is a better indicator of the total absorption of the labelled fat. Beres *et al.* (1957), McKenna *et al.* (1957), and Berkowitz and Sklaroff (1957) found variable absorption patterns in patients with gastric resections. In this group 40 to 60% of the patients had abnormally low values.

The question of origin of faecal fat is not definitely settled. There are two sources of faecal fat: endogenous (Hill and Bloor, 1922; Sperry and Bloor, 1924; Sperry, 1926, 1932; Sperry and Angevine, 1932; Bloor, 1943; Norcia and Lundberg, 1954) and exogenous (Wollaeger *et al.*, 1947; Annegers *et al.*, 1948; Crowe and Blackburn, 1956; Crowe *et al.*, 1956; Asenjo *et al.*, 1957).

So far as the faecal analysis of radioactivity is concerned, the enterohepatic circulation of iodine as well as the secretion of $^{131}I$ lipid into the gut should be taken into consideration. Beres *et al.* (1957) report that only 0.5% of the administered dose was recovered in the four-day collection of bile in the patient with a biliary fistula. This is quite insignificant and would not affect the final analysis of faecal radioactivity. Whether there is any secretion of $^{131}I$ lipid into the gastro-intestinal tract remains to be studied.

Further, the sources of error by contamination of faeces by urine can be very great in the $^{131}I$ triolein tests, as a large quantity of $^{131}I$ is excreted by the kidney in the first 24 hours. If there is only minimal contamination of faeces by urine, faecal radioactivity will be greatly increased. In our studies we tried to exclude all those patients in whom the faeces might have been contaminated with urine. Moreover, in general there were more false-positive or false-negative results with the blood peak radioactivity determination than by the faecal radioactivity study. Also, with a few exceptions, faecal nitrogen was increased only when faecal chemical fat was also increased. These two facts may indicate that there was no urinary contamination of faeces in our series.

## Summary and Conclusions

The accuracy of the radioactive $^{131}I$-labelled triolein test and the faecal chemical balance studies as a diagnostic aid in the various malabsorption syndromes is compared in a series of 24 normal volunteers and 102 patients suspected of having malabsorption.

Blood peak radioactivity, faecal radioactivity, and faecal chemical fat were determined in 160 tests, 146 tests, and 146 tests respectively, performed on 126 persons. These consisted of the following groups: normal volunteers, 24; idiopathic steatorrhoea, 10; non-specific regional enteritis, 12; diseases of pancreas, 20; diseases of hepatobiliary system, 15; functional enterocolonopathy, 13; gastric surgery, 11; non-specific idiopathic ulcerative colitis, 5; and a miscellaneous group of 16 patients.

The mean blood peak radioactivity in 45 tests on 24 normal volunteers was 19 $\pm$ 5% of the administered dose, with a calculated lower limit of normal (mean $\pm$ 2 S.D.), being 9% of the administered dose. The mean faecal radioactivity in 31 tests on 20 normal volunteers was 3 $\pm$ 1.94% of the administered dose, with a range of 1 to 9% of the administered dose and with a calculated lower limit of normal (mean $\pm$ 2 S.D.) being 6.9% of the administered dose. The mean faecal chemical fat in the same 31 tests was 4 $\pm$ 1.6 g. per day, with a range of 2 to 9 g. per day and a calculated upper limit of normal (mean $\pm$ 2 S.D.) being 7.2 g. per day.

In general, in each group of those who had abnormal faecal chemical fat the faecal radioactivity determination was abnormal in about 75%, while the blood peak radioactivity was abnormal in only about 50%. On the other hand, in nearly each group, of those who had normal faecal chemical fat, nearly 80% had a normal faecal radioactivity, while the blood peak radioactivity was normal in nearly 85%.

Of the two $^{131}I$ triolein determinations the faecal radioactivity determination was found to be a much better index of the presence of steatorrhoea than the blood peak radioactivity test. When both studies were carried out the index of accuracy was increased.

If a patient has normal blood peak and faecal radioactivity values after the $^{131}I$ triolein meals, the chances of his being normal are about 85 to 95%, while the chance of his having steatorrhoea (false negative) are about 15 to 25%. On the other hand, if both values are abnormal the chances of his being normal are about 10% (false positive), while the chances of his having steatorrhoea are about 75%.

Administration of the $^{131}I$-labelled triolein does not afford an adequate quantitation of steatorrhoea, as does the faecal chemical balance study.

Although the $^{131}I$ triolein studies are good, simple exploratory tests in the detection of steatorrhoea, particularly if both faecal and blood peak radioactivity are determined, show by our results that $^{131}I$ triolein is not as sensitive an index of accuracy in the detection of steatorrhoea as is the faecal chemical fat determination. However, if facilities for metabolic balance studies are not available, then because of its simplicity the triolein test (using both blood peak and faecal radioactivity determination) may be used as a diagnostic aid in the detection of steatorrhoea, provided its limitations are fully appreciated.

It is also recommended that, in a given patient, if both blood peak and faecal radioactivity are abnormal, that patient should have faecal chemical balance studies to establish the diagnosis definitely and for the quantitative estimation of steatorrhoea.

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REFERENCES

Annegers, J. H., Boutwell, J. H., and Ivy, A. C. (1948). *Gastroenterology*, **10**, 486.
Asenjo, C. F., Rodriguez Molina, R., and Cancio, M. (1957). *Fed. Proc.*, **16**, 380.
Beres, P., Wenger, J., and Kirsner, J. B. (1957). *Gastroenterology*, **32**, 1.
Berkowitz, D., and Sklaroff, D. (1957). *A.M.A. Arch. intern. Med.*, **100**, 951.
Bloor, W. R (1943). *Biochemistry of the Fatty Acids*. Reinhold Publishing Corp., New York.
Comfort, M. W. (1957). *Gastroenterology*, **33**, 34.
—— Wollaeger, E. E., Taylor, A. B., and Power, M. H. (1953). Ibid., **23**, 155.
Cooke, W. T., Elkes, J. J., Frazer, A. C., Parkes, J., Peeney, A. L. P. Sammons, H. G., and Thomas, G. (1946). *Quart. J. Med.*, **15**, 141.
—— Thomas, G., Mangall, D., and Cross, H. (1953). *Clin. Sci.*, **12**, 223.
Crowe, P. J., and Blackburn, C. R. B. (1956). *Aust. Ann. Med.*, **5**, 32.
—— —— Mashford, M. L., and Reed, C. S. H. (1956). Ibid., **5**, 36.
Frazer, A. C. (1955). *Brit. med. J.*, **2**, 805.
French, J. M. (1955). *Postgrad. med. J.*, **31**, 299.
Grossman, M. I., and Jordan, P. H. (1958). *Gastroenterology*, **34**, 892.
Hill, E., and Bloor, W. R. (1922). *J. biol. Chem.*, **53**, 171.
Isley, J. K., Sanders, A. P., Baylin, G. J., Ruffin, J. M., Shingleton, W. W., Anlyan, W. G., and Sharpe, K. W. (1958). *Gastroenterology*, **35**, 482.
Kalser, M. H. (1957). *Med. clin. N. Amer.*, **41**, 1553.
McKenna, R. D., Bourne, R. H., and Matzko, A. (1957). *Gastroenterology*, **32**, 17.
Norcia, L. N., and Lundberg, W. O. (1954). *J. Nutr.*, **54**, 491.
Shingleton, W. W., Isley, J. K., Floyd, R. D., Sanders, A. P., Baylin, G. J., Postlethwait, R. W., and Ruffin, J. M. (1957). *Surgery*, **42**, 12.
Sperry, W. M. (1926). *J. biol. Chem.*, **68**, 357.
—— (1932). Ibid., **96**, 759.
—— and Angevine, R. W. (1932). Ibid., **96**, 769.
—— and Bloor, W. R. (1924). Ibid., **60**, 261.
Turner, D. A. (1958). *Amer. J. dig. Dis.*, **3**, 594, 682.
van de Kamer, J. H., Huinink, H. ten Bokkel, and Weyers, H. A. (1949). *J. biol. Chem.*, **177**, 347.
Van Handel, E., and Zilversmit, D. B. (1958). *J. Lab. clin. Med.*, **52**, 831.
Weijers, H. A., and van de Kamer, J. H. (1953). *Acta Paediat. (Uppsala)*, **42**, 24, 97.
Wollaeger, E. E., Comfort, M. W., and Osterberg, A. E. (1947). *Gastroenterology*, **9**, 272.

# STAPHYLOCOCCAL SEPSIS IN OUT-PATIENTS

## RELATION OF PENICILLIN RESISTANCE TO PREVIOUS CONTACT WITH HOSPITALS

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It is in hospital that the majority of antibiotic-resistant bacteria are thought to originate. For *Staphylococcus aureus* there is abundant evidence that patients, and babies born in hospital, may become nasal carriers of penicillin-resistant staphylococci and may take resistant staphylococci home. Additional and rather different support for the view that hospitals are the main source of penicillin-resistant staphylococci has been put forward recently by Galbraith (1960). Working with septic patients in general practice, he was able to relate the presence of penicillin-resistant staphylococci in lesions to previous hospital contacts. Similarly, McDonald *et al.* (1960) in a study of recruits joining the Royal Air Force concluded that the high proportion of penicillin-resistant staphylococci carried by men with a history of recent admission to hospital or contact with a baby born in hospital could be attributed to acquisition of staphylococci from hospital.

From this hospital over the last ten years we have reported the increasing proportion of out-patients infected with penicillin-resistant strains of *Staph. aureus*. In this paper we describe our most recent findings and also the results of a survey undertaken to determine if patients with resistant staphylococci had previously been in direct or indirect contact with hospitals.

### Materials and Methods

The patients in the survey comprised 208 unselected out-patients attending the casualty department with acute infections of the skin and subcutaneous tissues between October, 1959, and March, 1960. In addition, there were 214 patients with other non-septic conditions, such as lacerations and contusions, attending the same casualty