Diss 52. B25H5

THE METABOLISM OF UNDER-NOURISHED INFANTS.

BY

EVELYN MARION HICKMANS.

(From the Biochemical Department of The Children's Hospital, Birmingham.)

A thesis presented for the degree of Ph.D. in the Faculty of Science, Birmingham University.

May 1925.

UNIVERSITY OF
BIRMINGHAM

University of Birmingham Research Archive

e-theses repository

This unpublished thesis/dissertation is copyright of the author and/or third parties. The intellectual property rights of the author or third parties in respect of this work are as defined by The Copyright Designs and Patents Act 1988 or as modified by any successor legislation.

Any use made of information contained in this thesis/dissertation must be in accordance with that legislation and must be properly acknowledged. Further distribution or reproduction in any format is prohibited without the permission of the copyright holder.

THE METABOLISM OF UNDER-NOURISHED INFANTS.

The condition known as infantile atrophy, athrepsia or marasmus is found most frequently among babies fed entirely on artificial foods. In an analysis of 100 cases recently admitted to hospital, only 2 had been entirely breast-fed, 19 had been fed completely on artificial foods and the remainder were partially breast-fed. [Parsons (1)]. Utheim (2) states that of 102 cases studied by her, all but one had been fed artificially. It seems probable therefore, that food may be at any rate an important factor, and that the condition may be to some extent caused by the inability of the infant to digest and absorb cow's milk or its modifications as easily as human milk.

Various studies have been made during recent years on the metabolism of atrophic infants. In most records, only a few cases have been observed, and frequently over a very short period. The literature dealing with the absorption of fat is often conflicting and seems inconclusive. Few observations have been made, beyond a series of 17 cases by Utheim (ibid), on the calcium metabolism of definitely atrophic children, and the information on the metabolism of the other constituents of food is vague. Moreover, none of the available records are classified according to the kind of milk, whether ordinary whole milk modified, whole milk dried or condensed, or modified and dried. This has proved to be a very important point in the discussion.

This investigation on the metabolism of atrophic infants was undertaken at the request of Dr. Leonard G. Parsons, Physician to the Children's Hospital, Birmingham, on cases under his care. The infants selected for observation were, with 2 exceptions, under 6 months of age. Two were just 6 months and most of the others were about 3 months old. They were all less than 80% of the expected weight for their age, since Talbot (3) has shown that there is no change in the metabolism of these infants till there is a loss of 20% of the body-weight; and none of them showed other evidence of disease.

Preliminary observations showed that there is considerable variation in the composition and amount of excreta from day to day; it was therefore deemed advisable to make the period of observation five days if possible. Since also it was found, as Lesage has said, "Chaque organisme a sa personalité, son coefficient de fixation", it was considered impossible to draw any definite conclusions from a few cases only. Eighty-two cases of simple atrophy and 9 cases of pyloric stenosis have been observed for fat metabolism and the metabolism of many of these for other factors also at the same time, so that the relationship between them could be established. The actual intake was rigidly ascertained by analysis and not by calculation from percentage composition of foodstuffs already published. The following routine was observed.

COLLECTION OF SPECIMENS.

The time required for food to pass through the alimentary canal of atrophic infants varies from 8 hours to 3 days [Parsons (I)]. In order to obtain stools therefore from a known intake of any of the constitutuents of food, the infant was given the specified diet for at least 3 whole days before the stools were collected as well as during the period of collection. Since the composition of milk varies from day to day and the composition of the feeds depends on the proper mixing of the milk and accuracy in dilution, half an ounce extra was prepared for each meal and these samples were put together with a trace of formalin and analysed for the respective constitutuents every 24 hours for 5 days, The actual food intake was also observed and any food vomited was noted and subtracted from the intake. There was little vomiting in the cases reported in this communication. At the end of 3 days, the infant was placed on the metabolism bed* and stools and urine were collected separately

---

* A canvas covered frame or hammock so arranged that the excreta could be collected quantitatively.

for 5 consecutive days. (Any variation in the period of collection of specimens is noted in the tables.) The specimens were removed at short intervals from the metabolism bed and kept cold till the 24-hours collection was complete, when they were taken to the laboratory and the analysis was begun as soon as possible. The urine was collected under toluene.

The mean of five 24-hours specimens is taken as the daily average for both intake and output of any of the constituents.

Since it had been shown previously by Holt, Courtney and Fales (4) that in diarrhœa the digestion of fat may be seriously affected, probably by the rapid passage of the food through the intestinal tract, no case showing diarrhœa is included in this series though many of the stools were loose. Most of them were formed or semi-formed. A few were constipated.

The results are classified according to the kind of diet.

1. FAT METABOLISM.

Literature.

The following figures for fat absorption by athreptic infants are quoted by Ütheim (ibid).

Rubner & Heubner (1899); 84.5% on a milk diet } 1 case, age 3½ months.
56.9% " " carbohydrate. diet. }

Bendix (1909); 59%. Age not given: 1 case.

Meyer (1910); 74.2%, 24.9%, 51%, 68.3% and 78% for 5 periods. Age 3 months: 1 case.

Fife & Veeder (1911) found in 2 cases that the absorption was less than in healthy children.

Freund (1909) found absorptions of 90%, 97%, and 81.8% in 3 cases. Age not given.

In 1912, Czerny (5) expressed the opinion that the main cause of infantile atrophy is difficulty in dealing with

fat, and he insisted on the occurence of Milchnährschaden and especially of Fettnährschaden. Czerny's theory was based on work previously done by Keller in 1897, and Steinitz in 1903 (both quoted Utheim) who stated that there was increased output of ammonia in the urine of athreptic children and that it was increased by a high fat diet. Czerny believed that in order to neutralise the excess of free fatty acid in the intestinal tract from the unabsorbed food fat, alkalies were taken from the tissues and excreted. In constipation with soap stools calcium, and in diarrhoea potassium and sodium are thus excreted; and in order to make up for the loss of alkali, ammonia was formed in the body and excreted in the urine. The basis of this theory has been criticised from time to time; and in 1922 Utheim (ibid) stated that while she was of the opinion that athreptic children do have a low assimilative power for fat, and that the ammonia excretion is higher than in normal children, found that there was only a relatively small increase in the excretion of ammonia following a great increase in the fat of the diet in 2 cases, and no variation in a third case. The output of ammonia in the urine of 34 of the cases of marasmus in this investigation has been observed and the results show that on a diet of humanised dried milk with a high fat content, the output of ammonia is considerably lower than with a diet of ordinary milk and water with a medium or low fat content, or a dried milk preparation with a low fat content. (See Tables 12 & 13) This was also found to be the case quite definitely for an infant on the same kind of food, but of a different strength in two 5-day periods of observation, - viz:-

% Fat in diet.	mg. NH_3 in 100 c.c. in urine	Total output NH_3 mg. in 24 hours.
2.4	10.9	36.5
4.9	8.2	23.0

It may be, however, that the difference in the output of ammonia on diets of humanised milk and skim milk is not

altogether connected with the fat intake, but depends somewhat on the nitrogen intake. This is discussed later in this communication (Page 22).

Failure to confirm the theory that the output of ammonia in the urine of athreptic children is increased by a high fat diet is supported by an examination of Fig. V. which shows that the output of free fatty acid in the stools from humanised milk diet with a high fat content is much greater than in the cases on diets of low fat content. If Czerny's theory were correct, there should of course be a greater output of ammonia on a humanised milk diet than on a skim milk diet.

It seems clear then that Czerny's theory as to the cause of athrepsia is based on an incorrect assumption. The output of ammonia may be a little higher than normal. (It has only been possible to investigate 2 cases of normal infants for comparison here). The percentage of ammonia found in the urine of athreptic infants on milk and water diets in this series of observations is certainly a little higher than that of the cases of pyloric stenosis on milk and water diets where the fat metabolism is normal. [Parsons & Barling (6)]. But according to these observations, it is not increased by increasing the fat in the diet.

Whether the absorptive power of athreptic infants for fat is, as stated by Czerny and Utheim, really lower than that of normal infants will now be discussed.

Figures given by various authors for the percentage absorption of fat have been quoted. They are not in agreement with each other, but the observations were made on one or two cases only from which no definite conclusions can, in my opinion, be drawn as there is a very great variation in individuals and even in the same individual from day to day. Hutchison in 1919 (7) however, examined 22 normal and 22 atrophic children, but he did not state the ages, nor give information as to how the fat intake was estimated or

whether the figures given were for one 24-hour period or the average of a number of 24-hour periods. He found the average absorption of fat to be 73.5% in the atrophic group and 98.4% in the normal children; but the argument is not convincing nor confirmed by figures quoted by Fleming & Hutchison (8) in a later report of a set of observations on 4 healthy and 8 marasmic children, each experiment lasting for at least 3 days, no gastro-intestinal disturbance being present. Hutchison attributes this low value of 73.5% absorption to the low fat intake, which averaged 17.8g. in 24 hours as against 35g. in the normal infants. In the present series a high percentage absorption has been found when the fat intake was low. The arguments set forth in Fleming & Hutchison's papers are based on the assumption that the fat excreted is constant at about 1/3 of the weight of the dried faeces. The observations recorded in this paper do not confirm this as the average daily faecal output of fat has been found to vary from 5 to 63% of the dry faecal weight in 82 cases of marasmus on varying diets, the average being 36.8%. Hutchison also states that the daily faecal output by atrophic infants is about 10g. and continues the argument after reducing the faecal weight to this level in all cases. As a matter of fact, the faecal weights vary very much in actual life. In this investigation, it was found that the average of the 82 cases observed was only 6.0g. This covers 396 days' observations.

Holt, Courtney and Fales (ibid) examined the fat metabolism of a larger number of cases both of breast-fed and artificially fed infants. They state that "most cases examined were normal, though some had digestive disturbances of varying severity", and their figures are classified according to the nature of the stools. They found that in the case of breast-fed infants the percentage fat in the dried faeces varied from 4.4 to 57.7%, the average of 44 estimations being 34.5%. The daily excretion of fat in sick children may be,

Table 1. Fat absorption - (various workers)

	Wt. of dried faeces daily.	% Total fat in D.F.	Daily Intake of fat.	Daily output of fat.	Retention of fat.	% absorption.
	G.		G.	G.		
Hutchison - for healthy infants quoted by Fleming & Hutchison	10.0	36.8	14.0	3.68	10.3	73.7
Hutchison - for healthy infants - Quoted by Hutchison & Fleming.	9.9	33.3	35.2	3.3	31.9	90.6
Hutchison & Fleming - for atrophic infants.	10.2	35.2	20.4	3.6	16.8	84.3
Hutchison - for atrophic - Quoted by Hutchison & Fleming.	11.9	35.1	17.8	4.2	13.6	76.1
Utheim - for atrophic infants - All cases up to 9 months.	-	-	19.5	4.6	14.9	77.0
Utheim - for atrophic infants - Omitting 2 day cases, but including diarrhoea.	-	-	13.5	4.1	9.4	78.0
Utheim - for atrophic infants. Omitting 2 day cases & excluding diarrhoea.	-	-	19.6	4.1	15.5	80.0
Holt, Courtney & Fales. All cases including infants over 6 months.	Range 11.2 to 82.6	34.1	24.2	2.7	21.4	88.6
Holt, Courtney & Fales. Cases up to 6 months, excluding diarrhoea.	-	37.1	-	-	-	78.4

(Contd.

Table 1 Fat absorption -(various workers.)

(Contd.)

	Wt. of dried faeces daily.	% Total fat in D.F.	Daily intake of fat.	Daily Output of fat.	Retention of fat.	% Absorption.
Holt, Courtney & Fales. Cases up to 6 months, including cases not quite normal but excluding diarrhoea.	-	-	-	-	-	81.1
Holt, Courtney & Fales. Stools definitely normal.	-	-	-	-	-	87.7
Holt, Courtney & Fales. Breast fed infants.	-	34.5	-	-	-	95.1 (for children gaining weight.
Hickmans. (average of 82 cases of marasmus on different diets.	6.0	36.8	19.4	2.4	17.0	87.7

according to these workers, up to 12 grams and the average absorption 52.5 to 79.0%. The average absorption of fat in children gaining weight was 95.1% the range being 90.3 to 99.2%. In Holt's series of cases fed on modified cow's milk, 128 specimens from 77 infants of 2 - 18 months of age were analysed for fat, the figures reported being averages for 2 or 3 days, frequently longer. Their results, together with those of Fleming & Hutchison and of Utheim are given in Table 1 for comparison with the present series.

Utheim's series of 20 estimations for the fat absorption of 13 athreptic infants includes some cases suffering from diarrhoea and also 5 cases observed for a period of 1 or 2 days only. These 5 have been excluded for comparison with this series. She reached the conclusion that fat absorption is low in athreptic infants - resulting in a high caloric loss through the intestine.

Fat absorption on different diets.

The present series of figures has been obtained by an examination of 469 specimens from 82 sets of observations on cases of simple atrophy or marasmus and 69 specimens from 9 sets of observations on cases of pyloric stenosis. Cases of pyloric stenosis after the Rammstedt operation have been examined and reported for comparison with the cases of marasmus because here the wasting is unquestionably due to starvation. [Parsons (1)]. In the earlier part of the investigation every stool was examined separately; but in the majority of cases the-24 hours complete collection was analysed.

A few of the cases reported are of the same child at different times and on different diets. Sixty-three of these cases have already been quoted and commented on by Parsons (10.

It is to be regretted that up to the present time only 2 cases of infants of normal weight within the age limit of this series have been available for metabolism investigation. They are given here for comparison (Table 8.)

Method of Analysis.

The moist stool was mixed very thoroughly to make it as homogeneous as possible. The whole of a proportionate part was dried for 24 hours (or longer if big) over an electric heater, thus ensuring a moderate temperature of 60 - 80°, and then weighed.

Since the most complete study of the fat metabolism of infants has been made by Holt, Courtney and Fales (4), it was decided to use a comparable method and to record the observations in this series in the same way. The total weight of the dried faeces for the 24 hours having been estimated, about 0.5g. of the dry pulverised material was weighed into each of two fat extraction tubes. To one was added 10 c.c. of 30% H Cl. and to the other 10 c.c. of distilled water. Both were heated in a boiling water-bath for half an hour, cooled and extracted with 40 c.c. of ether by shaking. After settling, 20 c.c. of the clear ether solution was transferred with a pipette to a weighed flask of about 50 c.c. capacity and evaporated. Repeated experiments under the same conditions but without the material to be extracted showed that on the average 3.4c.c. of the ether dissolved in the water or dilute acid, so that the weight of the residue from 20c.c. of the extract must be multiplied by 183 to give the total weight of the fat extracted from the known weight of the dried faeces. This eliminated the filtering process which is essential when all the ether extract is evaporated as in the modified Rose-Gottieb method used by Holt and his co-workers.

This method was tested out by estimating the fat in specimens of milk powder by this process and by a Soxhlet extraction process. The following figures were obtained:-

	Soxhlet.	Hickmans.
1.	22.87%	23.19% 22.52
2.	28.63	28.64 28.47
3.	30.38	30.84 29.52

The residue from the ether extract of the dried faeces after treating with hydrochloric acid is reported as "total fat". The ether extract after heating with water only is reported as "unsaponified fat". "Total fat" - "unsaponified fat" gives "saponified fat", all being in terms of free fatty acid. The free fatty acid was determined by re-dissolving the "unsaponified fat" in 10c.c. of ether and 5.c.c. of alcohol and titrating with $\frac{N}{100}$ NaOH using phenolphthalein as indicater, and calculating to stearic acid. Holt, Courtney and Fales have shown that in drying the stools of children fed on cow's milk, the amount of total fat and the distribution of fat is unchanged except in cases of diarrhoeal acid stools. Such have been excluded from this series. The results are given in Tables 2 - 9.

Table 2. Fat metabolism on Humanised Milk.

Case No.	Age in weeks	No. of days observation.	No. of estimations.	Gain or loss in wt.	Approximate amt. of food in 24 hours.	% Fat in Food.	wt. of dried faeces per 24 hrs.	% Total Fat in D.F.	Distribution % Total Fat. Sap.	Free fatty acid.	Neutral.	Fat intake per 24 hours.	Fat Output.	wt. of Fat absorbed.			Wt. of Fat Absorbed.
				oz.	oz.		G.					G.	G.	G.			G.
1	14	5	5	+1½	30	4.9	17.1	43.3	48.1	41.8	10.1	41.5	7.4	34.1	82.2	10.8	1.9	8.9
2	17	4	4	+3	25	4.2	13.5	57.3	66.6	21.7	11.7	29.6	7.8	21.8	73.7	8.6	2.3	6.3
3	18	4	4	+3	24	4.2	11.4	53.9	48.9	28.0	23.1	29.1	6.1	22.9	78.9	8.2	1.7	6.5
4	14	5	5	+¾	26	4.2	4.2	44.0	83.5	15.4	1.1	30.9	1.8	29.1	94.1	7.7	0.4	7.3
49	15	17	17	0	36	3.8	7.9	49.2	87.4	9.3	3.3	38.7	3.9	34.8	89.9	7.9	0.8	7.1
50	11	5	16	+1	28	3.7	9.4	50.3	71.4	18.0	10.6	29.7	4.8	25.0	84.0	8.3	1.4	7.4
51	13	5	17	+3	26	3.6	12.8	57.9	71.7	19.6	8.7	25.9	7.4	18.4	71.2	6.8	1.9	4.9
52	19	5	10	-4½	-	3.6	-	45.1	64.3	19.9	15.8	-	-	-	-	-	-	-
6	22	5	5	+1	26	3.5	3.8	40.6	79.0	16.3	4.8	26.2	1.6	24.7	94.1	7.0	0.4	6.6
5	8	5	5	+2	16	3.2	4.9	25.4	62.7	37.3	0	14.4	1.2	13.2	91.4	5.3	0.4	4.9
53	17	5	5	-	28	2.9	7.2	29.0	76.9	21.2	1.9	23.3	2.1	21.2	91.0	-	-	-
			Average		-	-	9.2	45.1	69.1	22.6	8.3	28.9	4.4	24.5	85.1	7.9	1.3	6.6

Table 3. Fat Metabolism on "Food A".

81	23	5	5	-1½	31	4.4	4.6	37.2	57.4	16.5	26.1	38.7	1.7	37.0	95.6	9.6	0.4	9.2
82	28	5	5	+2¾	34	3.8	4.3	33.8	32.6	41.9	25.6	36.4	1.4	35.0	96.0	7.1	0.3	6.8
			Average		-	-	4.45	35.5	45.0	29.2	25.8	37.5	1.5	36.0	95.8	8.3	0.3	8.0

Table 4. Fat Metabolism on Dried Milk.

Case No.	Age in weeks.	No. of days observation.	No. of estimations.	Gain or loss in wt.	Approximate amt. of food in 24 hours.	% Fat in Food.	Wt. of dried faeces per 24 hours.	% Total Fat in D.F.	Distribution % Total Fat. Sap.	Free fatty acid.	Neutral.	Per 24 hours. Fat intake.	Fat Output.	Wt. of Fat absorbed	% absorption.	Per kilo. body wt. Fat intake.	Fat Output.	Wt. of fat absorbed.
	Group A Full Cream.			oz.	oz.		g.					g.	g.	g.		g.	g.	g.
7	32	5	5	+6	43	3.1	21.5	55.1	46.4	39.4	14.5	38.3	11.9	26.4	69.0	7.3	2.3	5.0
80	19	5	5	+2	32	2.6	5.2	29.2	80.9	12.0	7.1	23.5	1.5	22.0	93.5	3.7	0.2	3.5
8	25	5	5	+3	33	2.1	5.9	42.4	81.3	7.8	11.0	19.4	2.5	16.9	87.1	3.8	0.5	3.3
	Average						10.9	42.2	69.5	19.7	10.9	27.1	5.3	21.8	83.2	4.9	1.0	3.9
	Group B Half Cream.																	
54	19	5	4	+3	33	1.5	6.0	20.9	91.1	4.8	4.1	13.9	1.3	12.6	91.0	2.9	0.3	2.6
55	11	5	4	+1	24	1.5	4.5	21.1	52.5	16.0	31.5	10.0	1.0	9.0	90.4	2.8	0.3	2.5
9	18	5	5	+1	30	1.4	4.0	24.9	88.9	11.3	0.8	11.5	1.0	10.5	91.3	2.7	0.2	2.5
10	14	5	5	+2	20	1.3	2.0	26.5	91.9	6.9	1.0	7.5	0.5	7.0	93.1	4.0	0.3	3.7
11	16	5	5	+2	31	1.2	1.9	27.9	66.0	-	-	10.6	0.5	10.1	88.7	4.1	0.2	3.9
	Average						3.7	24.3	78.1	9.7	9.4	10.7	0.9	9.8	90.9	3.3	0.3	3.0

Table 5. Fat Metabolism on Condensed Milk.

56	11	5	5	-	21	3.2	5.7	44.0	-	-	-	19.0	2.5	16.5	86.9	5.9	0.8	5.1
57	23	5	5	-8	28	2.5	3.6	34.5	71.9	21.2	6.8	20.0	1.2	18.6	93.8	4.9	0.3	4.6
12	7	5	5	-3¾	18	2.0	4.8	63.5	56.9	36.8	6.3	10.2	3.1	7.1	69.8	3.3	1.0	2.3
58	22	4	6	+5	-	-	-	40.7	89.4	5.4	5.2	-	-	-	-	-	-	-
	Average						4.7	45.7	72.7	21.1	6.1	16.4	2.3	14.1	83.5	4.7	0.7	4.0

Table 6 Fat Metabolism on Cow's Milk diluted & Sweetened.

Case No.	Age in weeks.	No. of days observation.	No. of estimations.	Gain or loss in wt.	Approximate amt. of food in 24 hours.	% Fat in Food.	Wt. of dried faeces per 24 hours.	% Total Fat in D.F.	Distribution % Total Fat. Sap.	Free fatty acid.	Neutral.	Per 24 hours. Fat intake.	Fat output.	Wt. of Fat absorbed.	% absorption.	Per kilo. body wt. Fat intake.	Fat output.	Wt. of fat absorbed.
				oz.	oz.		g.					g.	g.	g.		g.	g.	g.
Group A. Sweetened with Lactose.																		
59	18	5	13	+½	24	2.4	-	51.1	62.5	23.0	17.0	-	-	-	-	-	-	-
60	25	3	6	+1½	33	2.2	-	30.4	78.9	12.0	18.7	-	-	-	-	-	-	-
61	27	4	8	+3	33	2.1	-	45.5	67.4	13.4	22.0	-	-	-	-	-	-	-
62	16	4	7	+3	39	2.1	-	38.2	76.0	18.0	6.0	-	-	-	-	-	-	-
63	18	3	5	+2½	24	2.0	-	41.0	81.0	8.0	8.3	-	-	-	-	-	-	-
	Average							41.2	73.0	14.9	14.4	-	-	-	-	-	-	-
Group B. Sweetened with Sucrose.																		
13	25	5	5	+8½	33	3.3	7.3	34.6	79.6	13.9	6.4	30.9	2.5	28.4	91.8	6.9	0.6	6.3
14	20	5	6	+4½	33	3.2	7.5	34.0	92.2	4.8	3.0	29.0	2.6	26.4	91.2	6.2	0.6	5.6
15	21	5	5	+7½	30	3.0	6.3	47.6	64.6	32.5	2.9	25.0	3.0	22.0	87.2	5.7	0.7	5.0
16	24	5	5	+1	36	2.6	7.7	37.1	70.8	26.3	2.9	26.1	2.8	23.3	89.2	4.9	0.5	4.4
17	16	5	5	+3½	30	2.4	7.5	41.0	77.0	21.9	1.1	19.9	3.1	16.8	84.6	4.4	0.7	3.7
18	18	5	5	0	24	2.4	3.2	33.7	91.8	7.4	0.8	16.3	1.1	15.2	93.4	3.9	0.3	3.6
64	24	4	5	-4	36	2.3	-	40.1	69.6	18.5	11.9	23.2	-	-	-	-	-	-
65	11	5	9	+3	34	1.9	2.7	33.0	75.6	18.8	5.6	18.0	0.9	17.1	95.1	4.1	0.2	3.9
19	10	5	5	+2½	31	1.7	8.9	42.8	56.2	34.1	9.7	14.7	3.8	10.9	73.9	4.5	1.6	2.9
20	9	4	4	-4	24	1.6	1.4	25.8	68.4	23.8	8.2	10.5	0.4	10.1	96.6	2.8	0.1	2.7
66	12	5	5	-13	29	1.6	-	43.4	38.1	46.8	15.1	12.7						
	Average						5.8	37.6	71.3	22.6	6.1	20.6	2.2	18.9	89.2	4.8	0.6	4.2

Table No. 6 (Contd:-

Group C. Sweetened with Mead's Dextri-Maltose.

Case No.	Age in weeks.	No. of days observation.	No. of estimations.	Gain or loss in wt.	Approximate amt. of food in 24 hours.	% Fat in Food.	WT. of dried faeces per 24 hours.	% Total Fat in D.F.	Sap.	Free fatty acid.	Neutral.	Fat intake.	Fat output.	Wt. of Fat absorbed.	% absorption.	Fat intake.	Fat output	Wt. of fat absorbed.
67	19	5	5	+3 oz.	46 oz.	4.0	5.3	46.9	78.8	18.6	6.5	30.7	2.5	28.2	92.1	6.9	0.5	6.4
68	23	5	5	+1½	27	3.4	6.2	37.8	66.4	14.3	7.3	26.4	2.2	24.2	92.0	6.6	0.5	6.1
22	14	5	5	+3	36	3.1	7.3	37.0	74.2	31.9	1.0	33.2	3.1	30.1	90.6	7.3	0.6	6.7
69	19	5	5	+1½	30	3.0	7.8	34.5	73.6	22.7	4.4	27.1	2.7	24.4	90.0	6.0	0.6	5.4
70	19	5	5	+2½	27	3.1	6.2	37.8	84.9	14.4	1.7	16.1	1.7	14.4	89.4	4.7	0.5	4.2
71	17	5	5	+3½	39	3.0	6.3	45.8	61.7	10.4	1.4	11.8	1.2	10.6	89.8	4.6	0.4	4.2
23	19	5	5	+1½	19	3.1	3.2	42.2	76.2	36.9	5.0	41.9	4.1	37.8	90.2	4.9	0.4	4.5
24	12	5	5	+1½	23	2.8	3.6	45.8	82.5	21.0	7.5	28.5	2.9	25.6	89.8	6.9	0.7	6.2
72	19	5	5	+2½	23	2.8	3.9	42.2	76.2	10.0	7.5	17.5	1.7	15.8	90.2	6.9	0.6	6.3
25 (1)	24	5	5	+3	46	4.0	5.3	46.9	78.8	18.6	6.5	30.7	2.5	28.2	92.1	6.9	0.5	6.4
27	14	5	5	+1½	21	2.7	3.2	42.2	74.2	31.9	1.0	33.2	3.1	30.1	90.6	7.3	0.6	6.7
73	11	5	5	+2	20	2.6	3.3	37.8	66.4	22.7	4.4	27.1	2.7	24.4	90.0	6.0	0.6	5.4
30	11	5	5	+1½	24	2.6	3.2	37.8	73.6	14.4	1.7	16.1	1.7	14.4	89.4	4.7	0.5	4.2
31	22	5	5	0	18	2.2	2.4	37.8	84.9	14.4	1.7	16.1	1.7	14.4	89.4	4.6	0.4	4.2
32	22	5	5	+1½	32	2.2	3.3	37.8	76.2	36.9	5.0	41.9	4.1	37.8	90.2	4.9	0.4	4.5
74	22	5	5	+2½	30	2.2	3.3	37.8	82.5	21.0	7.5	28.5	2.9	25.6	89.8	6.9	0.7	6.2
75	23	5	5	+3½	43	2.2	3.3	37.8	76.2	10.0	7.5	17.5	1.7	15.8	90.2	6.9	0.6	6.3
33	6	5	5	+1½	20	2.0	3.3	37.8	82.5	21.0	7.5	28.5	2.9	25.6	89.8	6.9	0.7	6.2
34	11	5	5	+1½	22	2.0	3.3	37.8	76.2	10.0	7.5	17.5	1.7	15.8	90.2	6.9	0.6	6.3
36	15	5	5	0	23	2.0	3.2	37.8	82.5	21.0	7.5	28.5	2.9	25.6	89.8	6.9	0.7	6.2
37	14	5	5	+1½	22	2.0	3.3	37.8	76.2	10.0	7.5	17.5	1.7	15.8	90.2	6.9	0.6	6.3
39	9	5	5	+1½	40	1.8	3.3	37.8	82.5	21.0	7.5	28.5	2.9	25.6	89.8	6.9	0.7	6.2
38	11	5	5	+1½	19	1.7	3.3	37.8	76.2	10.0	7.5	17.5	1.7	15.8	90.2	6.9	0.6	6.3
40	8	5	5	+1½	23	1.7	3.3	37.8	82.5	21.0	7.5	28.5	2.9	25.6	89.8	6.9	0.7	6.2
41	4	5	5	+1½	19	1.7	3.3	37.8	76.2	10.0	7.5	17.5	1.7	15.8	90.2	6.9	0.6	6.3

(Contd.

Table No.6 (Contd.)

Case No.	Age in weeks.	No. of days observation.	No. of estimations.	gain or loss in wt.	Approximate amt. of food in 24 hours.	% Fat in Food.	Wt. of dried faeces per 24 hours.	% Total Fat in D.F.	Distribution % Total Fat.			Per 24. hours			% absorption.	Per kilo body wt.		
									Sap.	Free fatty acid.	Neutral.	Fate intake.	Fat Output.	Wt. of Fat absorbed.		Fat intake.	Fat output.	Wt. of fat absorbed.
76	9	5	4	+2	31	1.7	6.5	40.1	73.3	25.2	1.4	14.6	2.6	12.0	82.1	5.0	0.9	4.1
77	7	5	5	+2	28	1.7	2.7	37.1	61.6	32.6	5.8	13.5	1.0	12.5	92.6	4.3	0.3	4.0
42	13	5	5	+7½	40	1.6	7.7	40.2	62.9	26.0	11.1	18.0	3.1	14.9	82.9	4.9	0.8	4.1
43	14	5	5	-½	17	1.4	4.4	33.0	48.3	46.0	5.7	6.6	1.4	5.2	78.0	2.9	0.6	2.3
		Average.			—	—	5.4	38.3	70.5	23.2	6.9	18.7	2.1	18.1	87.5	5.0	0.6	4.4
Group D. Acid added to bring p_H to 5.2 to 6.0																		
29	13	5	5	+6	25	2.3	7.3	36.5	84.3	-	-	16.4	2.6	13.8	83.9	5.9	0.9	5.0
26	18	5	5	-2½	21	2.7	2.6	31.5	66.6	-	-	16.0	0.8	15.2	94.8	5.5	0.3	5.2
28	22	5	5	+1½	32	2.4	8.5	54.7	52.9	43.5	3.6	22.1	4.7	17.4	78.9	6.7	1.4	5.3
21	16	5	5	+2½	27	2.6	3.7	39.2	88.0	6.3	5.6	18.5	1.5	17.0	92.1	5.4	0.4	5.0
		Average.			—	—	5.5	40.5	72.9	24.9	4.6	18.2	2.4	15.9	87.4	5.9	0.75	5.1
Group E. (on skim milk sweetened)																		
44(2)	9	5	5	+1½	21	1.6	4.1	19.9	86.6	6.3	7.1	9.3	0.8	8.5	91.1	3.1	0.3	2.8
45(2)	25	5	4	+3	44	1.1	1.8	18.2	85.0	10.6	4.5	13.9	0.3	13.6	97.7	2.7	0.1	2.6
46(2)	19	5	5	+2	35	6.9	6.4	14.4	71.7	9.6	18.8	8.6	0.9	7.7	89.4	1.8	0.2	1.6
47(2)	11	5	5	-4	27	0.8	7.8	13.0	76.4	14.6	8.9	6.3	1.0	5.3	83.9	1.8	0.3	1.5
48(2)	15	5	5	+5½	30	0.6	4.4	11.5	87.7	9.1	3.3	5.1	0.5	4.6	90.1	1.1	0.1	1.0
78(3)	19	3	3	0	23	0.6	3.7	10.5	-	-	-	3.9	0.4	3.5	90.1	0.51	0.07	0.44
79(4)		5	5	+1½	22	0.2	4.1	4.9	-	-	-	1.5	0.2	1.3	86.4	1.2	0.1	1.1
		Average.			—	—	4.6	13.2	81.5	10.0	8.5	6.9	0.6	6.4	89.8	1.7	0.2	1.5

(1) Mead's "Casec" added
(2) Ordinary milk skimmed and sweetened.
(3) "Casec" + "Secwa" in water, sweetened.
(4) Skimmed dried milk sweetened.

Table 7. Fat Metabolism in Pyloric Stenosis.

Case No.	Age in weeks.	No. of days observation.	No. of estimations.	Gain or loss in wt.	Approximate amt. of food in 24 hours.	% Fat in Food.	Wt. of dried faeces per 24 hours	% Total Fat in D.F.	Distribution % Total Fat. Sap.	Free fatty acid.	Neutral.	Per 24 hours Fat Intake.	Fat Output.	% of Wt./Fat absorbed.	% Absorption.	Per kilo body wt. Fat intake.	Fat output.	Wt. of fats absorbed.
				oz.	oz.		g.					g.	g.	g.		g.	g.	g.
83(5)	-	4	5	-	48	1.6	-	28.5	95.2	3.7	1.0	23.0	-	-	-	-	-	-
84	4½	5	5	+1	9	1.6	2.1	25.7	62.6	19.6	17.8	4.4	0.5	3.9	87.5	1.6	0.2	1.4
85	8	5	5	-1	15	1.6	2.6	34.4	49.7	34.6	15.7	6.7	0.9	5.8	86.7	2.4	0.3	2.1
86	8	5	5	+6	23	1.7	3.5	37.4	85.2	7.1	7.8	11.4	1.3	10.1	88.5	4.2	0.5	3.7
87	12	4	14	+2	13	1.8	3.5	38.6	68.7	22.3	10.9	6.5	1.3	5.2	79.4	1.9	0.4	1.5
88	13	5	10	+4	20	2.2	5.1	39.3	76.3	20.5	3.3	12.5	2.0	10.5	84.0	3.5	0.6	2.9
89	13½	5	11	+3	23	1.8	5.1	32.3	80.2	14.7	5.1	11.6	1.6	10.0	85.9	3.1	0.4	2.7
90	14	6	10	+2	27	1.8	4.6	35.3	90.3	11.4	1.0	13.3	1.6	11.7	87.8	3.5	0.4	3.1
91	15	4	4	0	28	1.5	4.0	23.2	92.1	7.1	0.8	11.7	0.9	10.8	92.0	3.0	0.2	2.8
		Average.					3.8	32.7	77.8	15.7	5.8	11.2	1.3	8.5	86.5	2.9	0.4	2.5

(5) Treated medically.

Table 8. Infants of normal weight on Milk & water diet.

92	13	5	5	0	33	2.8	4.6	29.4	76.3	10.2	13.5	26.4	1.3	25.1	94.8	4.7	0.2	4.5
93	6	8	8	0	31	2.0	11.7	32.6	58.5	35.4	6.1	17.7	3.8	13.9	78.5	4.7	1.0	3.7

Table 9.

Summary of Fat Metabolism (average.)

	Wt D.F. per 24 hrs.	% Total Fat. m'D.F	Distribution. % Total Fat: Sap.	Free Fatty Acid.	Neutral.	per 24 hours. In-take.	Out-put.	Ab-sorbed.	per Kilo Body wt. % Ab-sorp-tion.	In-take.	Out-put.	Absorb-ed.
	g.					g.	g.	g.		g.	g.	g.
Dried Humanised Milk.	9.2	45.1	69.1	22.6	8.3	28.9	4.4	24.5	85.1	7.9	1.3	6.6
Food A	4.4	35.5	45.0	29.2	25.8	37.5	1.5	36.0	95.8	8.3	0.35	8.0
Dried Milk Full Cream	10.9	42.2	69.5	19.7	10.9	27.1	5.3	21.8	83.2	4.9	1.0	3.9
" " half "	3.7	24.3	78.1	9.7	9.4	10.7	0.9	9.8	90.9	3.3	0.3	3.0
Condensed Milk	4.7	45.7	72.7	21.1	6.1	16.4	2.3	14.1	83.5	4.7	0.7	4.0
Milk, Water & Caetose	-	41.2	73.0	14.9	14.4	-	-	-	-	-	-	-
" " " Sucrose	5.8	37.6	71.3	22.6	6.1	20.6	2.2	18.9	89.2	4.8	0.6	4.2
" " " D.M.	5.4	38.3	70.5	23.2	6.9	18.7	2.1	18.1	87.5	5.0	0.6	4.4
" " (sweetened) + acid.	5.5	40.5	72.9	24.9	4.6	18.2	2.4	15.9	87.4	5.9	0.8	5.1
Skimmed Milk.	4.6	13.2	81.5	10.0	8.5	6.9	0.6	6.4	89.8	17	0.2	1.5
Grand Average. (82 cases)	6.0	36.8	71.3	20.9	8.3	19.4	2.4	17.0	87.7	5.1	0.6	4.5
Pyloric Stenosis av. of 9 cases.	3.8	32.7	77.8	15.7	5.8	11.2	1.3	8.5	86.5	2.9	0.4	2.5

Discussion of Results.

It may be stated at once that the results of this investigation show that in general, there is no defect in the power of the atrophic infant to absorb fat, The type of case described by Czerny as Milchnährschaden or Fettnährechaden, and by Finkelstein as Bilanzstörung, in which there is diminished tolerance for fat, does not appear to be common. In the 82 cases of marasmus reported and many others not completely investigated and therefore not reported here, only one case, in the opinion of Dr. Parsons, approached this condition - viz. No.37. Here, while fat splitting was normal, the fat absorbed was only 55.8%, the intake being about the same as that of the others in the group. The fact that this case was only found when more than half of this extensive series was done points to the importance of not drawing any very definite conclusions unless a large number of cases are observed. But while generally speaking the absorption of fat is normal, it differs very much on different diets; a fact which is very important in its relation to infant feeding generally.

Relationship between Intake and Output of Fat. It must be understood that in this communication, by "fat absorbed" is meant the difference in weight between the fat intake and fat excreted in the stools. Whether excreted fat has the same chemical composition as the diet fat has been discussed by Hill & Bloor (9) working with adults, and by Holmes & Kerr (10) working with dogs and cats. The latter state that whatever kind of fat the diet contains, the ether extract of the faeces appears to be uniform and that the saponification and iodine values of the faecal fat are quite different from those of the diet fat. Hill & Bloor state that there is always fat in the faeces even when there is none in the food; that the addition of moderate amounts of fat does not increase the faecal fat to any considerable extent, and that the composition and properties of the excreted fatty material is largely independent of the fat of the food. They believe that

the comparative constancy of the amount and composition of faecal fat under a variety of conditions indicates that it is not to be regarded as unabsorbed food fat, but rather as an excretion.

In a later paper by Sperry & Bloor (11) this idea is reaffirmed - that the faecal fat does not arise directly from the unabsorbed fatty material of the food, and that the output of fat during fasting (which is considerable in amount) is similar in properties and in the relations of its components to that excreted when food is given. They also state that the composition of the faecal fat is different from that of the food fat.

While not prepared to express an opinion at present as to whether the faecal fat differs in composition from the food fat in the case of atrophic infants, the writer is not in agreement with Hill & Bloor when they state that the addition of a moderate amount of fat to the food does not increase the faecal fat to any considerable extent. A consideration of Fig. 1. which shows the average daily intake and output of fat in 91 cases of atrophic infants, indicates that where the fat intake is decidedly low (less than 12g. daily) the average daily fat output is fairly constant, but small in amount ; viz., about 1 gram or less. Possibly this amount represents the daily output of truly excreted fat. But for an intake about 12g., it may be 3 or 4 times this amount when the diet is cow's milk and water and up to 10 or 11 times this amount when the diet is a humanised dried milk or a dried milk mixture with a high fat content. The case showing fat excretion of 6.6g on a diet of ordinary milk and water mixture can be excluded from this argument, being the one referred to above as showing "fat intolerance".

Fig. 1. also shows that the amount of fat excreted on a diet of humanised milk appears to be greater on the whole than from a diet of cow's milk and water giving the same fat intake (Compare A---------B with C-------D.) Two cases included in this series of infants fed on a patent infant food A, which is

made from egg yolk, butter, malto-dextrins and decitrated fresh fruit juice and no milk, show a high fat intake and small output. If this observation is confirmed after investigating a number of cases on the same diet, it points to means of introducing a large quantity of fat into the diet without excessive excretion.

Relationship between Fat Intake, Fat Absorbed, Percentage of Fat in the Dried Feaces and the Weight of Dried Faeces. Fleming & Hutchison (ibid) state that the dried faeces always contain about 33% of fat. Holt 's figure for all cases artificially fed was 34.1% with a range from 11.2 to 82.6%; for breast-fed children 34.5%, but for children under 6 months artificially fed it was 37.1%. The average for the 82 cases of marasmus reported here is 36.8%, but it varies very much, Fig II shows that where the fat intake is less than 12g. daily (below x on the graph), the faceal fat is, with one exception 33% or less, the average of 13 cases being 21.9%, corresponding to an average daily output of less than 0.9g. The average percentage fat in the dried faeces of 50 cases on a normal diet of milk and water with a medium fat content (No. 37) being excluded) is 37.4 higher than Hutchison's figure for atrophic infants, but the same as calculated for Holt's cases up to six months and excluding diarrhoea. The average of 11 cases on humanised dried milk is 45.1%. The two cases on food A showed faecal fat 33.8 and 37.2%. The nine cases of pyloric stenosis show an average percentage faecal fat of 32.7. Again, by comparing A----------B with C----------D in Fig 11, it is clear that for the same fat intake from humanised milk and milk and water, the percentage fat in the dried faeces is much higher on the humanised milk diet than on the milk and water diet or on the food A.

The average weight of the daily faecal output (dried) from atrophic infants is stated by Hutchison to be about 10g. The average found in this investigation of 396 days' specimens from 32 atrophic infants (excluding pyloric stenosis) is 6.0g., but it varies on different diets. The average of 13

observations on humanised dried milk and full-cream dried milk is 9.5g. while the 2 cases on food A with a high fat intake shows an average of 4.4g. dried faeces. On the ordinary milk and water diet, the weight of the dried faeces tends to decrease slightly with a decided decrease in the daily fat intake down to 12g. but below that it tends to rise. This is obviously due to the general increase in the output of total mineral matter as shown in Fig. 111. Again the faecal matter from humanised milk tends to be greater than from ordinary milk and water diet giving the same intake of fat. The average weight of the dried faeces from the humanised milk diet is 9.2g. for 6 cases as compared with 6.9g for 7 cases on ordinary milk and water diet. (Compare E------F with G------H in Fig.II.)

Since the percentage of fat in the dried faeces from humanised milk diet is higher than from milk and water diet, and since the weight of faecal matter is also greater, it follows that less fat is absorbed from the same fat intake with humanised milk than with ordinary milk and water diet. (Compare K------M with N------P Fig.II.) The conclusion to be drawn is that although the amount of fat absorbed from humanised milk may actually be very high when the fat intake is high, it is absorbed with the expenditure of more anergy than is the fat fram ordinary milk and water.

It seems evident from Fig. II that if the fat supply is less than 12 g. daily, it is insufficient, A similar conclusion is reached from a consideration of the calcium metabolism, which depends to some extent on the fat supply. The fat intake must be not less than 12 - 14 grams daily to ensure an adequate absorption of calcium [Hickmans (12)].

The high percentage absorption with a low fat diet seems to indicate that more fat could be absorbed if supplied.

<u>The Amount of Fat Absorbed.</u> The average percentage absorption in 82 cases of marasmus was found to be 87.7%. Since this average figure includes a very wide range (55.8 to 97.7) it

is better to consider the actual amount of fat absorbed. It is clear that with a high fat intake, there can be a high actual absorption. These cases show a maximum figure of 31.6g. per day on cow's milk and water, 34.8g. on humanised milk and the two cases on food A 35.0g and 37.0g. respectively.

The greatest gains in weight on milk and water and the corresponding amounts actually absorbed and the amount absorbed per kilogram of body-weight are given here for comparison with some other figures.

Diet.	Age. (weeks)	Absorption per day.	Absorption per kilo of body wt.	Intake per kilo g.	Gain or loss in wt.
Cow's milk & Water.	25	28.4g.	6.3g.	6.9g.	+8½oz.
"	21	22.0	5.0	5.7	+7½
" + (Casec)	24	31.6	6.2	6.9	+7½
"	13	14.9	4.1	4.9	+7½
" + (HCl.)	13	13.8	5.0	5.9	+ 6
Humanised Milk	15	34.8	7.1	7.9	+ 0
"	14	34.1	8.9	10.8	+1½
Food A	23	37.0	9.2	9.6	+1¼
"	28	35.0	6.8	7.1	+2¾

Lindberg's normal infant quoted by Hamilton (13) absorbed 27.3g. or 6.3g. per kilo daily. This is practically the same firgure as found in the case here with the best gain in weight. Holt & Fales (14), state that healthy nursing children require 20g. of fat daily, increasing to 40g. at 6 - 7 months, or 4g. per kilo; but that infants on cow's milk should have smaller amounts than this. Galbraith (15) says that the amount is 18g. in the first month, rising to 28g. in the seventh month. It is clear from this investigation that many atrophic infants of 6 months of age or under can actually absorb as much fat as is suggested for healthy nursing children by Holt &

Fales and more than suggested by Galbraith, i.e, - up to 31.6g. on cow's milk and water, and up to 34.8g. and 37.0g. on humanised milk and food A respectively: and while the average absorption in 82 cases is 4.0g. per kilo, individuals can absorb per kilo more than this - viz. up to 6g. per kilo on cow's milk and up tp about 9g. per kilo on humanised milk or on food A. This higher absorption is only to be expected when under-nourished children are pulling their weight up to normal in the absence of gastro-intestinal disturbances. But in the opinion of Dr. Parsons the absorption of such large amounts of fat from such an uneconical food as humanised milk appears to be, because the excretion is somewhat excessive, may place such a strain on the child's resources that it may eventually lead to fat intolerance if continued for any length of time.

Digestion of Fat. The proportion of neutral fat in the total fat excreted has not exceede 14.4% in any group except that on food A, though individuals show a higher figure. An analysis of the results shows:-

Neutral fat less than 5% of total fecal fat in less than 37% of the cases.

" " between 5% & 10% " " " 34% of the cases
" " over 10% " " " less than 30% of the cases.

Two out of 4 cases showing over 20% neutral fat occur on food A. Here however, the actual amount of neutral fat excreted is fairly low because the total fat excreted was small. (See Figs.IV & V). It is difficult to account for the high percentage of neutral fat in cases 61 and 55.

Holt's observation showed that fat splitting was good in all cases he examined except in diarrhoea. There is here no indication that lipase is deficient in marasmus in the absence of diarrhoea; and since the average neutral fat for the group of pyloris stenosis cases is 5.8% total fat, there is no deficiency there either.

Holt states that the free fatty acid is 17% in normal cases, increasing to 30% in diarrhoea. Although the average of 82 cases

here examined is 20.9%, there are 17 cases where 30% is exceeded without showing diarrhoea. Three were, however, very ill at the time of observation and died a few days later. One is the case showing fat intolerance, previously commented on, and one was a case of pyloric stenosis who also died a few days later. Five of the remainder were on foods other than ordinary milk and water mixtures.

Fig.1V. showing the intake of fat daily and the distribution of the saponified fat, free fatty acid and neutral fat in the faecal fat, does not show any particular relationship between these beyond the fact that the proportion of total fat excreted in the form of saponified fat remains about the same (within fairly large limits) whether the intake is large or small, except in the faeces from food A where it is decidedly low. The percentage of neutral fat tends however, to increase when the fat intake becomes very small, both in marasmus and pyloric stenosis. The percentage of neutral fat is also higher for the same intake of fat from humanised milk than from cow's milk and water. (Compare A----------B with C----------D Fig.1V.) This is possibly explained by the lower amount of calcium in the humanised milk than in the cow's milk and water [Hickmans (12)].

Fig. V shows that there is much less variation in the actual output of saponified fat, free fatty acid and neutral fat when the intake is below 12g. This would tend to confirm the idea that all fat excreted when the intake is less than 12 grams is truly excreted fat.

Summary of Fat Metabolism.

1. Fat digestion and absorption, in the absence of diarrhoea, is in general normal in atrophic infants fed artificially. It differs very much however, on different diets. The occurence of ~~fat~~ "fat intolerance" is very rare.
2. The output of fat is affected to some extent by the intake of fat. It appears to be fairly constant in amount when the intake is below 12g.: but is considerably increased in

amount on dried milk preparations giving a high fat intake. Broadly speaking however, a high fat intake results in a high fat absorption, particularly in the cases fed on food A, the fat of which is egg and butter fat combined.

3. The average faecal fat for 82 cases of marasmus in infants up to 6 months of age fed on different diets was found to be 36.8% of dried faeces. It was 37.4% for the cases on ordinary milk and water diet of medium fat content, but considerably higher in those cases fed on dried milk preparations with a high fat content. The faeces from humanised milk contained a higher percentage of fat than the faeces from ordinary milk and water giving the same fat intake.
4. The average weight of dried faeces in 82 cases of marasmus was found to be 6.0g. but was considerably higher in the cases fed on dried milk with high fat content and lowest in the cases fed on skim milk and food A.
5. The output of faecal matter tends to increase when the fat intake is below 12-14g. corresponding to an increase in the output of total mineral matter.
6. Fat up to 37.0g. per 24 hours can be absorbed by atrophic infants under 6 months of age on certain diets.
7. Individual cases have shown an absorption of 6g. per kilogram of body weight on ordinary milk and water diet, and 9g. per kilo on humanised milk or food A.
8. Although the absorption on humanised milk is good, it involves excessive fat excretion which may lead to fat intolerance if continued for any length of time.
9. Fat digestion is good in the absence of diarrhoea in all groups. The percentage of neutral fat excreted was found to be highest in the cases fed on food A. A few exceptional cases on milk and water diet showed stools with a high percentage of free fatty acid; also some of the cases on prepared foods.
10. Probably there should be at least 12g. of fat in the diet per

24 hours.

11. This investigation fails to confirm the theory of Czerny that the output of ammonia in the urine of athreptic infants is increased by a high fat diet, or that the main cause of infantile atrophy is difficulty in dealing with fat.

Table 10. Calcium Metabolism.

Per 24 hrs.

Case No.	Food	% Fat in Food.	% CaO. in Food.	Wt. of D.F.	% Total Ash in D.F.	% CaO. in D.F.	Fat Intake	CaO Intake.	CaO Output.	Ca. Absorbed.	% Absorption.
53	Humanised Dried Milk.	2.9	.110	7.2	22.3	9.9	23.3	0.87	0.72	0.15	17.8
80	Dried milk; full cream.	2.6	.144	5.2	30.2	14.5	23.5	1.32	0.75	0.57	43.1
54	Dried Milk; half cream.	1.5	.147	6.0	31.8	17.5	13.9	1.38	1.01	0.37	26.4
55	" "	2.4	.125	4.5	24.1	13.6	10.0	0.85	0.64	0.21	25.3
56	Condensed	3.2	.126	5.6	16.9	6.9	6.7	19.0	0.75	0.37	49.9
57	"	2.5	.169	3.6	25.5	10.7	20.0	1.35	0.37	0.98	72.2
68	Milk + water + Dextri-maltose.	3.4	.128	5.9	26.1	12.4	37.5	1.42	0.73	0.68	48.3
70	"	3.0	.128	3.2	20.0	9.5	22.5	0.96	0.33	0.63	66.1
72	"	2.3	.130	3.6	24.0	13.6	18.5	0.85	0.51	0.34	39.7
76	"	1.7	.113	6.5	23.6	10.4	14.6	1.00	0.68	0.32	31.7
78	Skimmed & Dried.	0.60	.112	3.7	18.8	8.9	3.9	0.78	0.30	0.48	61.5
79	"	0.24	.223	4.1	40.4	20.1	1.5	1.37	0.84	0.53	38.5
										Average	43.3
81	Food A.	4.4	.118	4.6	8.3	5.3	38.7	1.04	0.24	0.80	76.8
82	"	3.8	.093	4.3	11.6	5.4	36.4	0.90	0.23	0.67	74.3

II CALCIUM METABOLISM.

The calcium metabolism of 62 of the 82 cases of marasmus just described has been studied and the relationship between the fat and calcium metabolism established. The results obtained in 48 of these cases have been published in the Biochemical Journal (1924, 18, 5), a copy of which is appended. The results obtained for the remaining 14 cases are given in Table 10, and are in general agreement with the 48 cases, the average absorption for the 12 cases on humanised milk, dried milk, condensed milk and dried skim milk preparations being 43.4% as against 43.0% for the 48 cases.

The 2 cases on food A are of especial interest however. They both show a normal intake, but an abnormally low output of calcium, resulting in a high percentage absorption. If this is confirmed by the investigation of further cases, this food will be highly valuable from the calcium standpoint as well as from the fat standpoint.

III PROTEIN METABOLISM.

The literature on the protein metabolism of atrophic infants is not extensive. In a study made by Heubner and Rubner (quoted by Utheim - ibid) in 1899 on an atrophic baby, 3½ months old, the nitrogen loss through the intestine is given as 18.27% as compared with 6.38% for a normal weight baby of 7 months; that is - the absorption is only 81.73% compared with 93.6% normally. In 1910 Meyer (quoted by Utheim) found a negative balance in 2 cases out of 3 which he considers due to salt loss. Utheim, in the paper previously quoted, has reported total nitrogen determinations on 18 atrophic children. Some of these estimations were for 1 or 2 days only and 5 were over 6 months of age. Eliminating these for comparison with this series, the averages of 22 observations on 14 infants are:- absorption 75.4% and retention 36.0%, the average intake being

1.70g. (range 0.6 to 3.6g.). She found that the nitrogen balance might be negative even with increasing weight. The estimations were done on moist fresh stools preserved under toluol and kept on ice and analysed immediately after collection was complete.

Utheim concludes that nitrogen absorption is fairly normal, but that the retention is poor "due to a deficient utilization throughout the organism or to actual destruction of the body tissues".

Fleming & Hutchison (8) maintain also that nitrogen absorption in marasmus is not impaired, and state that in atrophy, nitrogen can be satisfactorily retained in the body.

The average percentage absorption found by them for 37 daily observations over 10 periods is 85.0%, and the retention68.4%, the average intake being 3.96g. of nitrogen per day. They state that there was no example of a negative balance in any of these observations "probably due to the large intake of nitrogen in nearly all the cases".

The present series of observations on nitrogen absorption consists of 143 days' observations on 29 atrophic infants and 2 infants of normal weight, the results being shown in Table 11. The analyses were made by the Kjeldahi - Gunning method on a proportionate part of the 24-hrs. specimens of moist faeces, collected as previously described. The output of nitrogen by the urine was determined in 18 cases only owing to loss of urine during the collection period.

Table 11. Protein Metabolism.

Case No.	Kind of Food.	% N in Food.	N. intake per 24 hrs.	Fecal Output of N.	Wt. of N. absorbed.	Urine output of N.	Total Output of N.	Wt. of N. retained.	% Absorption.	% Retention.
			g.	g.	g.	g.	g.	g.		
53	Humanised.	.25	1.99	0.41	1.58	-	-	-	79.2	-
5	"	.17	0.78	0.33	0.45	-	-	-	57.7	-
82	Food A.	.27	2.57	0.23	2.34	-	-	-	90.9	-
81	"	.26	2.34	0.36	1.98	0.83	1.18	1.15	84.7	47.4
80	Dried Milk Full Cream	.48	4.39	0.300	4.09	1.90	2.20	2.18	93.2	-
54	" " half "	.46	4.42	0.32	4.10	2.10	2.42	2.00	92.8	45.3
55	" " " "	.37	2.52	0.27	2.25	1.26	1.52	1.00	89.4	39.5
57	Condensed.	.30	2.39	0.26	2.13	0.69	0.95	1.44	89.2	60.1
56	"	.41	2.44	0.30	2.13	-	-	-	87.5	-
68	Milk + water + D.M.	.43	4.76	0.31	4.45	1.63	1.94	2.82	93.5	59.3
42	" " "	.31	3.50	0.41	3.09	0.77	1.18	2.31	88.3	66.1
69	" " "	.31	3.15	0.27	2.88	1.63	1.90	1.25	91.3	39.6
70	" " "	.37	2.82	0.18	2.64	1.26	1.44	1.38	93.7	49.0
29	" " "	.38	2.70	0.31	2.39	0.57	0.88	1.82	88.6	67.5
40	" " "	.23	2.61	0.39	2.22	-	-	-	84.9	-
67	" " "	.33	2.52	0.21	2.31	1.37	1.57	0.95	91.8	37.6
76	" " "	.28	2.44	0.31	2.13	0.78	1.09	1.35	87.2	55.2
72	" " "	.37	2.42	0.21	2.22	1.54	1.75	0.67	91.5	27.9
34	" " "	.25	2.25	0.34	1.91	0.52	0.86	1.39	84.8	61.8
37	" " "	.25	2.08	0.33	1.75	-	-	-	84.1	-
19	" " "	.23	1.98	0.45	1.53	-	-	-	77.3	-
38	" " "	.28	1.82	0.15	1.67	0.51	0.67	1.16	91.6	63.4
77	" " "	.23	1.80	0.15	1.65	0.51	0.66	1.13	91.5	63.2
74	Milk + Water + D.M.	.30	1.69	0.14	1.56	-	-	-	91.8	-
35	" " "	.27	1.66	0.24	1.42	-	-	-	85.8	-
73	" " "	.28	1.61	0.28	1.32	0.74	1.02	0.59	82.4	36.6
43	" " "	.24	1.16	0.30	0.86	-	-	-	74.1	-
78	Casec & Secwa.	.32	2.07	0.24	1.83	0.95	1.19	0.88	88.4	42.3
79	Skim Dried Milk.	.56	3.43	0.33	3.10	2.05	2.38	1.05	90.3	30.6
	Average		2.50	0.29	2.20	1.14	-	-	86.8	49.6
	Normal Wt. infants.									
92	Milk + Water	.240	2.25	0.20	2.04	1.04	1.25	1.00	90.9	44.5
93	" "	.241	2.11	0.51	1.59	0.67	1.19	0.92	75.5	43.8

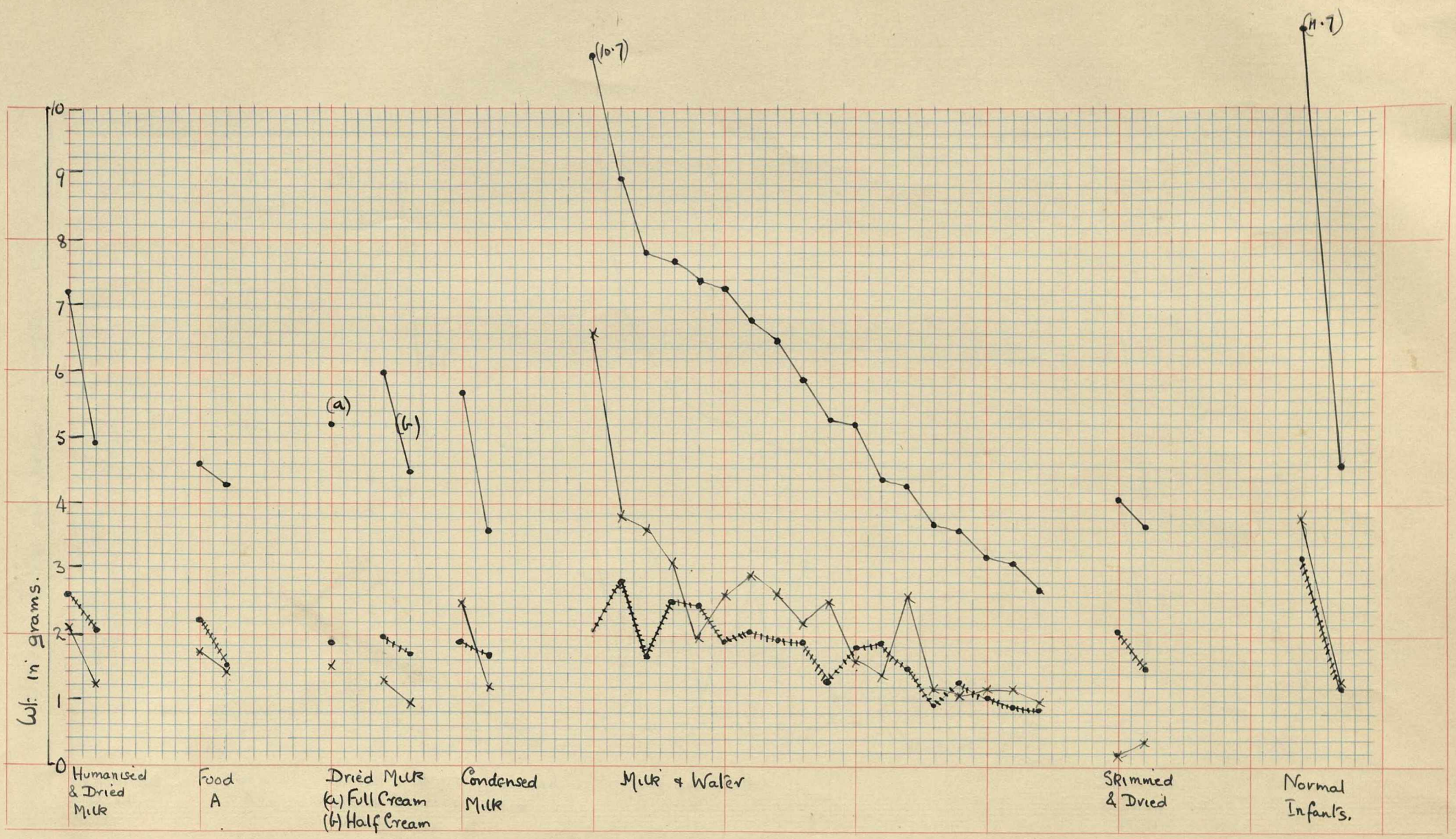


Fig VI. To show the relationship between Wt. of DRIED FAECES, OUTPUT of FAT and OUTPUT of PROTEIN (N x 6·25)

●——● Wt. of DRIED FAECES; ×——× Wt. of FAT; ●·····● Wt. of PROTEIN.

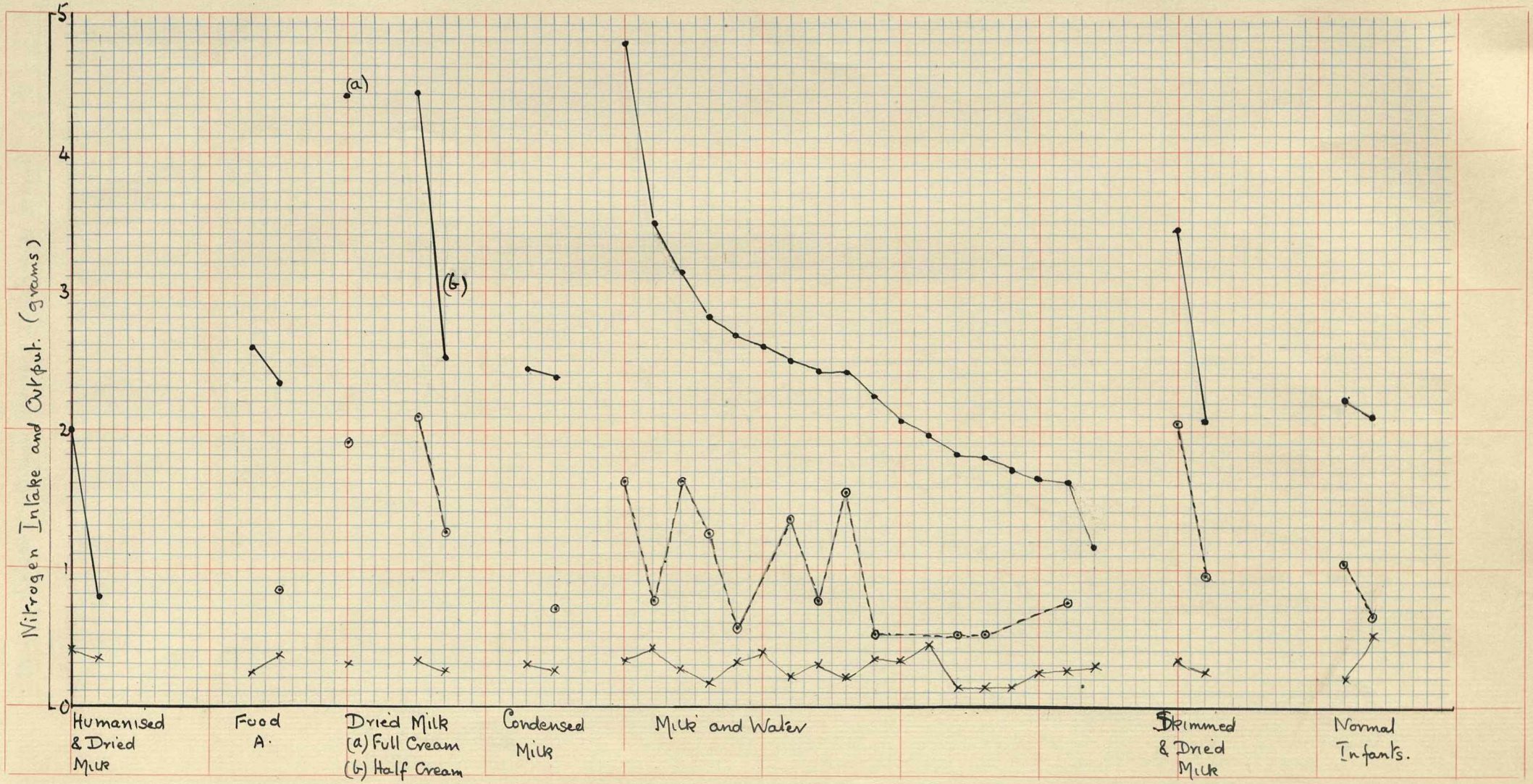


Fig. VII. To show relationship between Intake of Nitrogen, Faecal & Urine Output of Nitrogen.

——— Intake; x------x Faecal Output; o------o Urine Output.

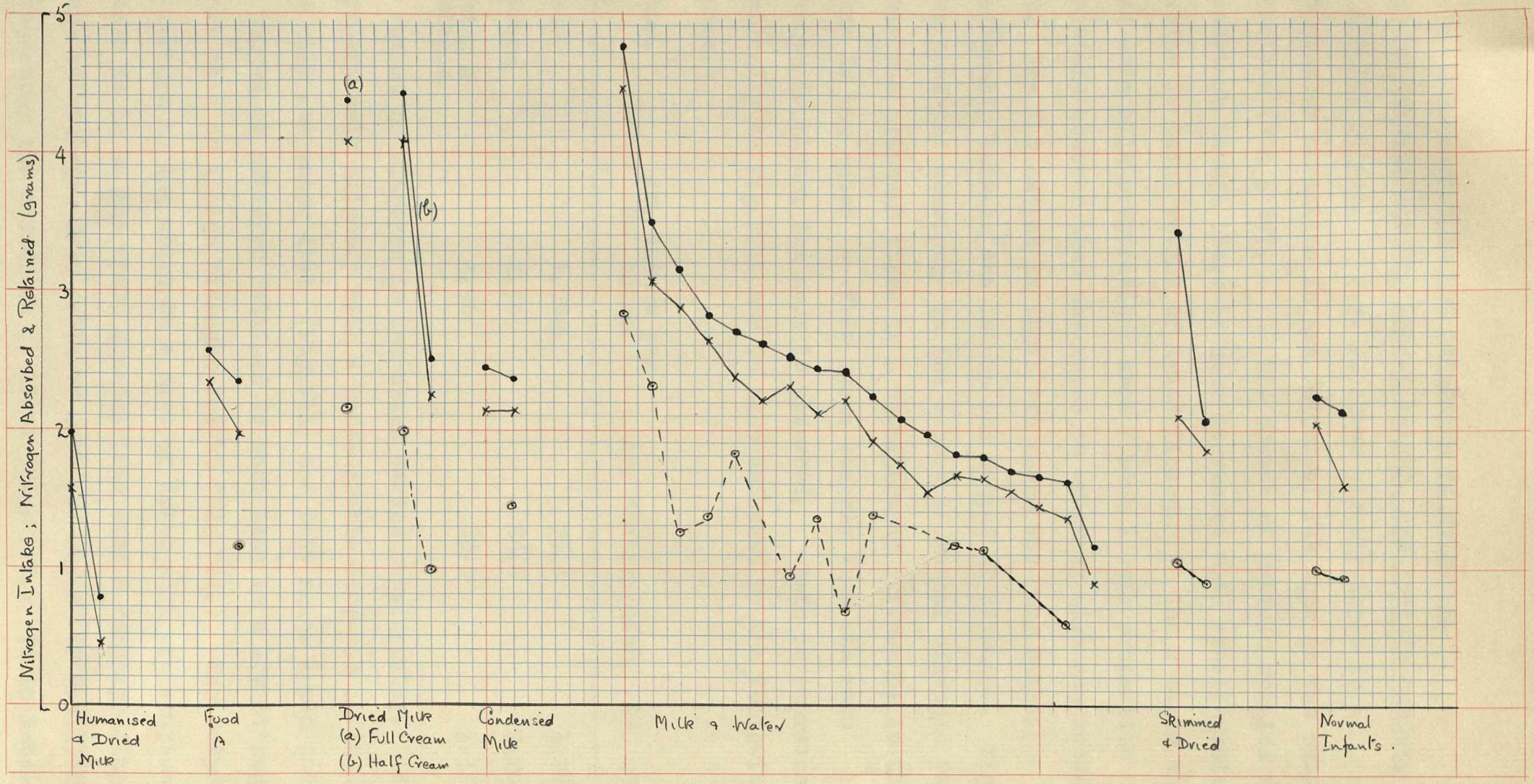


Fig. VIII To show the relationship between Nitrogen INTAKE ; Nitrogen ABSORBED or RETAINED

●——● Nitrogen Intake ; ×——× Nitrogen Absorbed ; ○——○ Nitrogen Retained.

The absorption and Retention of Nitrogen.

Relation between the Dry Faecal Weight, the Protein Output, and the Fat Output. Fig. V1 shows clearly there is a much greater variation in the output of fat than in the output of protein (N x 6·25). The output of protein remains fairly constant though there is some decreases with considerable decrease in total weight of dried faeces. - The 2 cases on dried skim milk preparations show a much larger proportion of protein however than the cases on ordinary milk and water diet. The fat output in these two cases was very small.

Relationship between the Intake and Output of Nitrogen. Fig.V11 shows that the constancy in the output of faecal nitrogen is maintained although there is a considerable difference in the intake in the cases - This means roughly that the more nitrogen is given, the more is absorbed. This is represented graphically in Fig.V111 and is also endorsed by the following figures:-

Author.	Av. intake per 24 hours.	Av. % absorption.	Av. wt.absorbe
Utheim	1.70g.	75.4	1.28g.
Hickmans	2.50	86.8	2.20
Fleming & Hutchison.	3.96	85.0	3.37

The output of nitrogen in the urine varies considerably. It decreases only slightly with a considerable decrease in intake on a milk and water diet (Fig.V11) and this means again that the weight of nitrogen retained is much less on a low nitrogen intake than on a high nitrogen intake (Fig.V11.) The output of nitrogen by the urine on a diet of dried milk preparations appears to be on the whole greater than with a corresponding intake of nitrogen from ordinary milk and water (Fig.v11) and consequently the retention is lower (Fig.V111.) It is impossible to say however, whether the dried milk protein is more difficult to utilise than protein from ordinary milk until further work has been done. The protein retention in the one

Table 12. Ammonia Excretion in Urine of Atrophic Infants.

Case No.	% Fat in food.	Fat intake per 24 hrs.		mg. NH_3 in 100cc urine.	mg NH_3 output in 24 hrs.
Humanised Milk.		g			
50	3.7	29.7		12.9	16.2
51	3.6	25.9		11.9	15.9
49	3.8	38.7		13.6	11.1
2	4.2	29.6		13.0	6.45
3	4.2	29.1		11.6	6.15
4	4.9	41.5		8.2	23.0
1	2.4	-		10.9	36.9
53	2.9	23.3		12.7	13.5
			Average.	11.8	16.2
Dried Milk. (Full Cream)					
8	2.1	19.4		26.1	84.2
80	2.6	23.5		13.1	48.7
			Average.	19.6	66.4
Milk and Water.					
33	2.0	27.5		7.8	-
17	2.4	19.9		50.6	238.2
15	3.0	25.0		19.0	-
13	3.3	30.9		83.5	340.6
14	3.2	29.0		68.6	206.8
21	2.6	18.5		21.0	77.1
41	1.7	9.2		13.1	-
16	2.6	26.1		26.3	119.1
22	3.1	26.3		55.1	214.1
27	2.6	15.7		29.9	64.5
31	2.3	11.9		25.9	77.5
29 (Acitric Acid)	2.3	16.4		11.2	-
34	2.0	17.3		9.2	-
38	1.8	11.4		6.9	15.5
42	1.6	18.0		7.3	21.6
76	1.7	14.6		5.0	15.8
68	3.4	37.5		13.0	56.4
72	2.8	18.5		26.3	99.6
70	3.0	22.5		19.3	60.7
			Average.	26.3	114.8
Skim Milk.					
46	0.9	8.6		40.6	128.6
47	0.8	6.3		39.6	136.4
44	1.6	9.9		44.8	121.2
78	0.24	1.5		50.5	164.5
			Average.	45.6	139.0
Normal Wt. Infants.					
93	2.0			3.5	9.7
92	2.8			16.4	51.1
(1) Skimmed & Dried milk preparations.			Average.	9.9	30.4

Table 12. Cont.

Case No.	% Fat in food	Fat intake per 24 hrs.	mg. NH_3 in 100cc urine.	mg. NH_3 output per 24 hrs.
Pyloric Stenosis.				
83	1.6	23.0	10.7	-
87	1.8	6.5	26.8	-
88	2.2	12.5	4.7	-
89	1.8	11.6	21.5	-
90	1.8	13.3	22.8	-
91	1.5	11.7	8.5	-
84	1.6	4.4	69.9	-
85	1.8	6.7	31.3	-
86	2.7	11.4	9.6	-
		Average.	23.9	-

Table 13. Ammonia Output in Urine.
(Summary)

Author.	Diet.	% Fat in Food.	Mg NH_3 in 100cc. Urine.	No. of Periods of observation.	Av. total output of NH_3 (Mg.) per 24 hrs.	No. of periods of observation.
Utheim	-	-	34.8	9 cases 56 1-day observation.	91.6	9
Hickmans	Humanised milk.	2.4 to 4.8	11.8	8	16.2	8
"	Milk & Water	1.6 to 3.4	26.3	19	114.8	14
"	Dried Milk.	2.0 to 2.6	19.6	2	66.4	2
"	Skim Milk.	0.2 to 1.6	45.6	5	139.0	5
For Hickmans 2 normal infants	Milk & Water.	2.3 to 2.8	9.9	2	30.4	2
Hickmans (For Pyloric Stenosis).	"	1.5 to 2.2	23.9	9	-	-

case on food A that has been examined so far appears to be comparable with that from ordinary milk and water diet. This protein is derived from egg yolk and not from milk. The low intake of nitrogen in the cases on humanised milk (where the fat content is fairly high) is noticeable. (Compare the low calcium intake on the same food.)

No case of a negative nitrogen balance has yet been found.

Output of Ammonia.

Observations have been made during this investigation on the ammonia output of 34 cases of marasmus, and are reported in Table 12. The estimations were made by the method of Folin and are therefore comparable with those of Utheim done by the same method. From her figures for volume and percent of "Ammonia" nitrogen in the urine of 9 of her cases (eliminating the one case over six months of age), the total ammonia eliminated in 24 hrs. has been calculated and is given for comparison in Table 13, together with the percentage ammonia in the urine during 9 periods of observation in pyloric stenosis (covering 42 observations), in which the fat absorption is not defective [Parsons & Barling, (6)].

These observations were made with the intention of establishing the relationship between the ammonia output and the fat ~~output~~ intake in marasmus, Czerny's theory of fat intolerance having been based on the assumption that ammonia output was abnormally high in atrophy and increased with an increased fat intake. Unfortunately in this investigation it has not been possible to examine the output of ammonia for many normal infants, but the output in the cases of pyloric stenosis (where although the fat absorption is normal, very small feeds were being given) is somewhat lower than that observed in marasmus on the same kind of diet (milk and water). The output of ammonia varies very much, however, on the different diets, being low in the cases on dried humanised milk with a high fat content, and high on skim milk diets, while the group on ordinary milk and water diet gives an inter-

mediate value, the range however, in this group, being large. The fact that there is a low output of ammonia on the humanised milk may be connected with the fact that the intake of nitrogen is low; and the high output of ammonia on skim milk due to the higher intake of nitrogen. (See Fig.Vll) It is regretable that up to the present the nitrogen and ammonia estimations were not always done on excreta from the same infant, but this point will be investigated as opportunity arises. Until further work has been done, no definite conclusions can be arrived at.

Summary of Protein Metabolism.

(1) The daily faecal output of nitrogen in the various cases is fairly constant, even with considerable variation in the intake.
(2) The weight of nitrogen absorbed increases with an increase in intake of nitrogen.
(3) The output of nitrogen in the urine shows considerable variation in the different cases and appears to be somewhat greater on diets of dried milk preparations than from diets of ordinary milk and water giving the same nitrogen intake.
(4) There has not been a case of negative nitrogen balance in this investigation.
(5) The ammonia output in the urine of atrophic infants was found to be low on humanised milk diet and high on skim milk diet This may be connected with nitrogen intake rather than with the fat intake, but this point remains to be investigated.
(6) The absorption of protein by atrophic infants on artificial diets is normal in the absence of diarrhoea, but the retention varies considerably, and may be low.

REFERENCES.

(1) Parsons. Lancet, 1924. 1. 687.
(2) Utheim. J. Metab. Research. 1922. 1. 808.
(3) Talbot. Amer. J. Dis. Child., 1921. 22. 358.
(4) Holt, Courtney & Fales. Amer. J. Dis. Child., 1919. 17. 241 & 423.
(5) Czerny. Amer. J. Dis. Child., 1912. 3. 170.
(6) Parsons & Barling. Lancet, 1923. 1. 59.
(7) Hutchison. Quart. J. Med., 1919. 13. 20.
(8) Fleming & Hutchison. Quart. J. Med., 1924. 17. 68.
(9) Hill & Bloor. J. Biol. Chem., 1922. 53. 171.
(10) Holmes & Kerr. J. Biol. Chem., 1923. 58. 377.
(11) Sperry & Bloor. J. Biol. Chem., 1924. 60. 261.
(12) Hickmans. Biochem. J., 1924. 18. 5.
(13) Hamilton. Acta. Paediatrica., 1922. 2. 1.
(14) Holt & Fales. Amer. J. Dis. Child., 1922. 23. 471.
(15) Galbraith. Quart. J. Med., 1923. 16. 321.

I have much pleasure in expressing my thanks to Dr. L. G. Parsons for suggesting this study; for making conditions possible for carrying it out and for his encouraging interest throughout. I wish also to express my thanks to the nursing staff of the hospital for their assistance in the collection of specimens. Finally I am indebted to the Medical Research Council for a grant made in connection with this research.

Evelyn M. Hickmans.

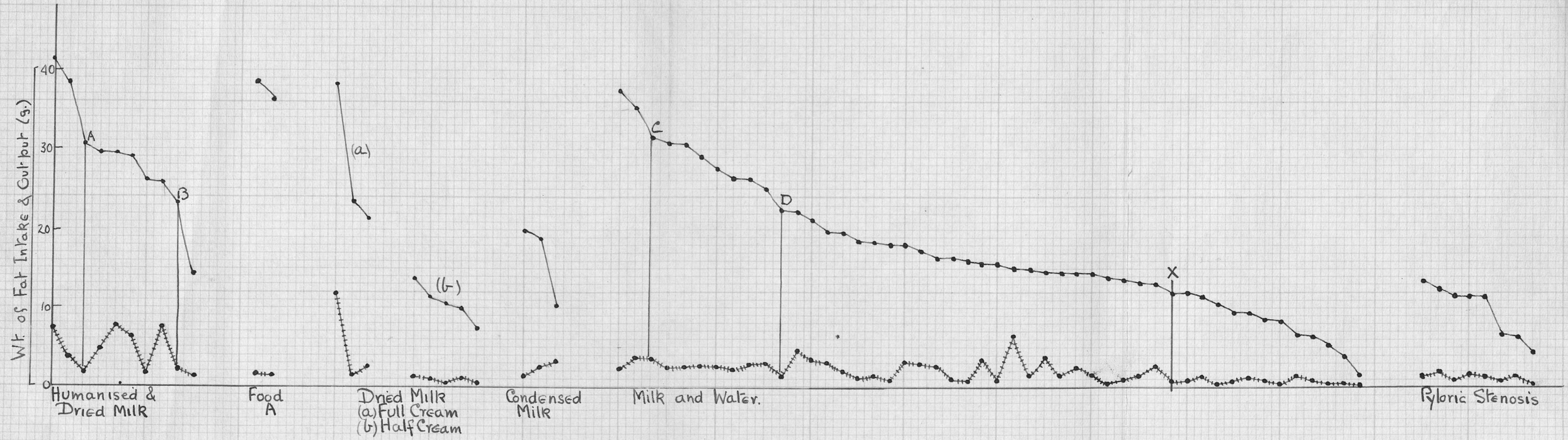


Fig 1. To show relationship between FAT INTAKE and OUTPUT. per 24 hours.

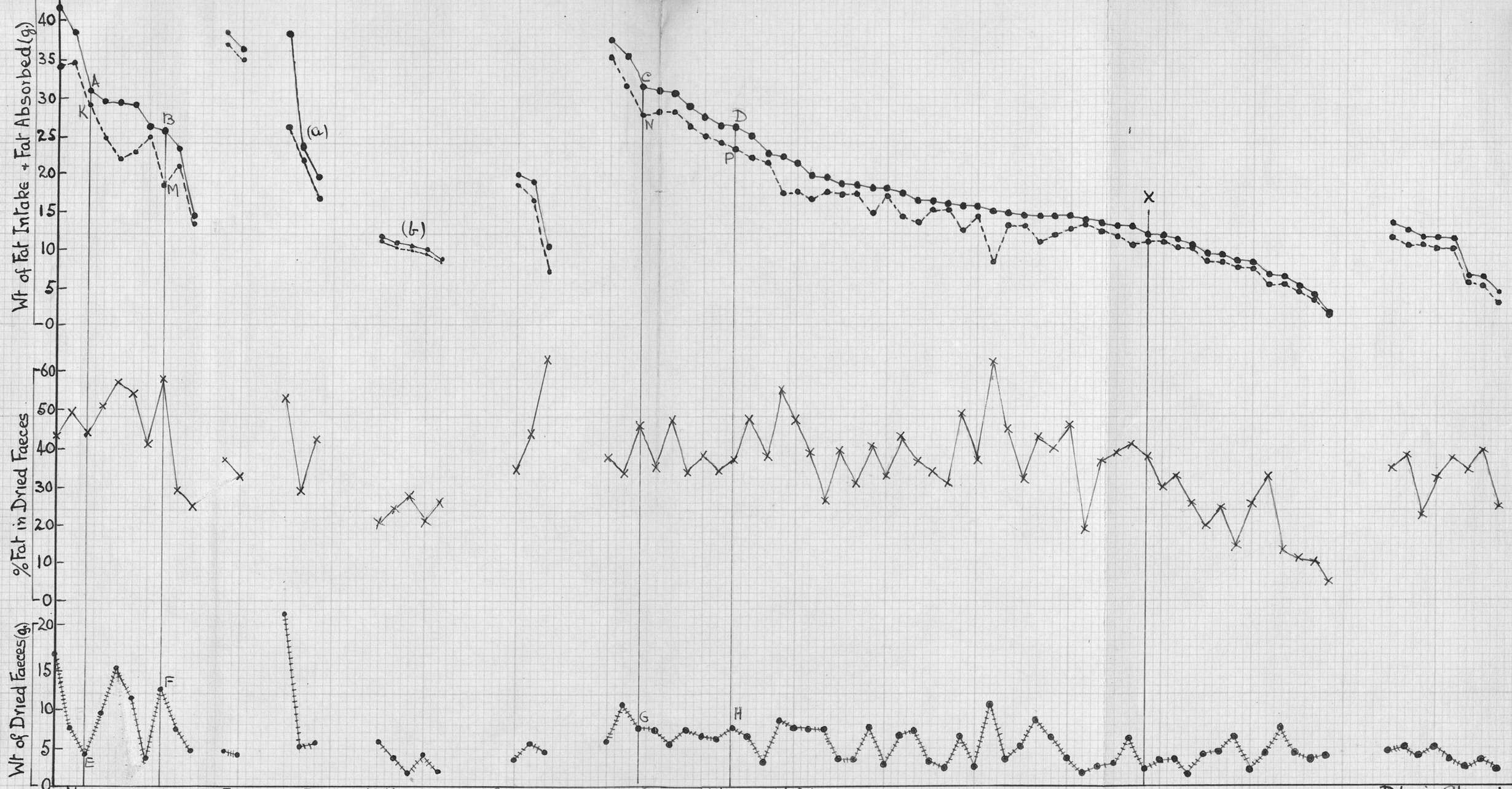


Fig. II. To shew relationship between FAT INTAKE, FAT ABSORBED, WEIGHT of DRIED FAECES and Percentage FAT in DRIED FAECES.

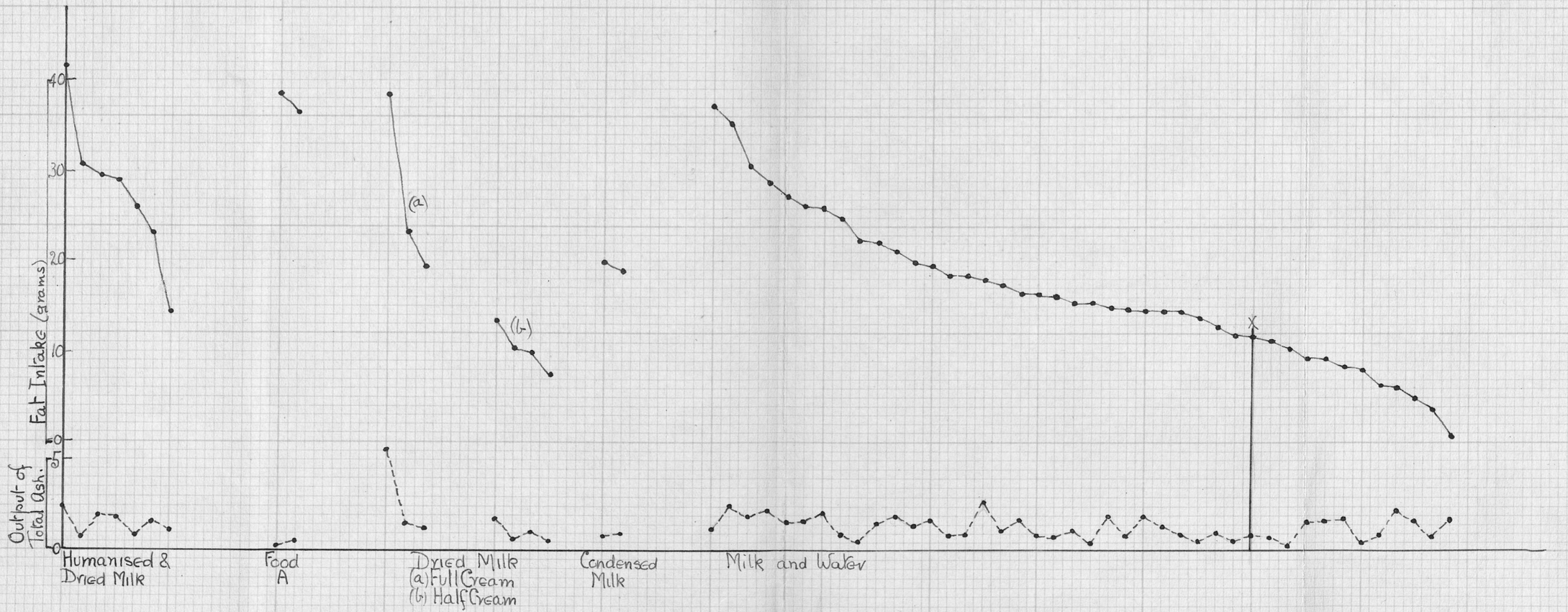


Fig III. To show the relationship between FAT INTAKE and TOTAL ASH OUTPUT (grams per 24 hrs).

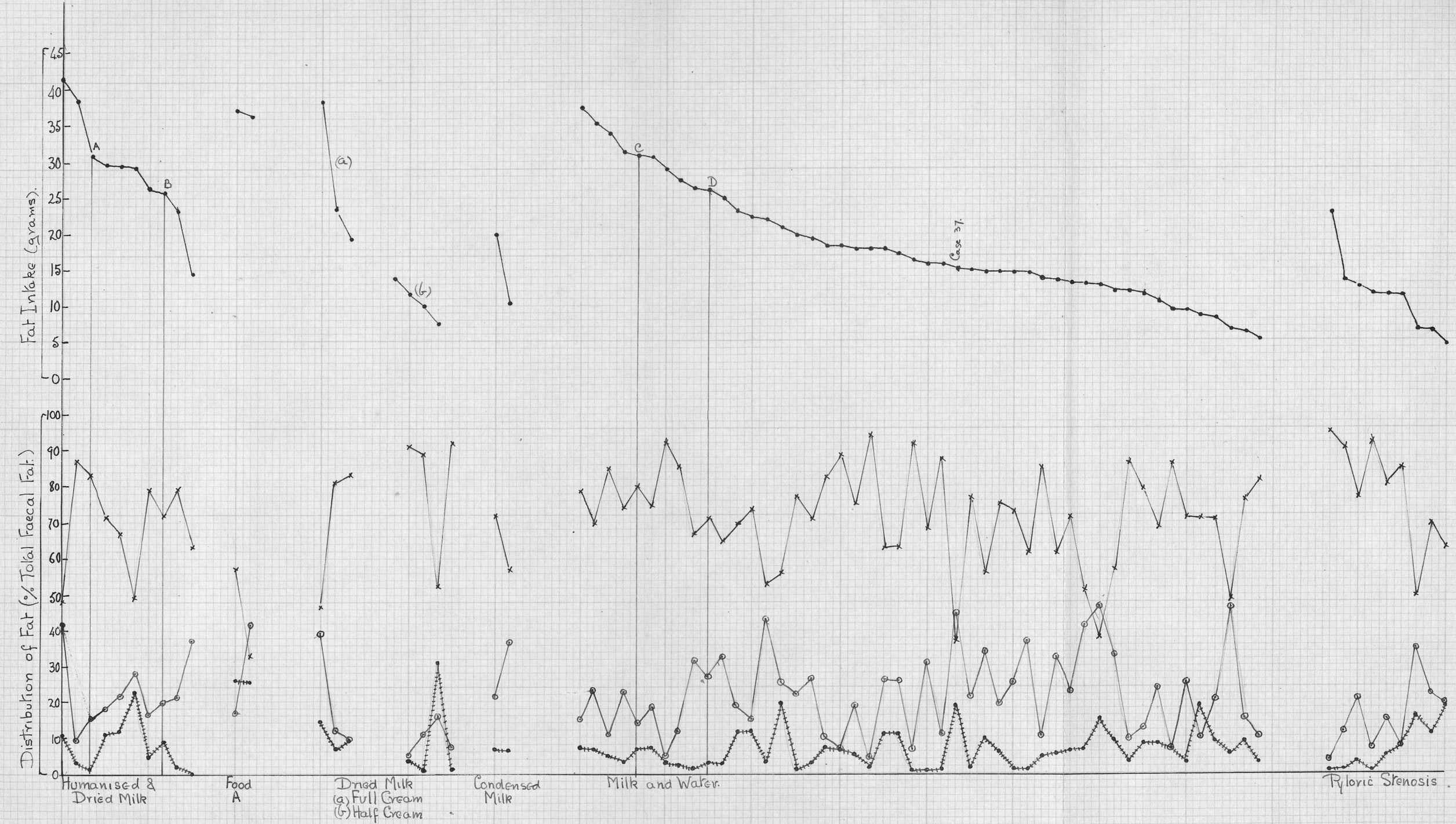


Fig. IV. To show the Distribution of Fat (% Total Faecal Fat) in Faeces. ×—× Saponified Fat; ○—○ Free Fatty Acid; •·····• Neutral Fat; •—• Fat Intake.

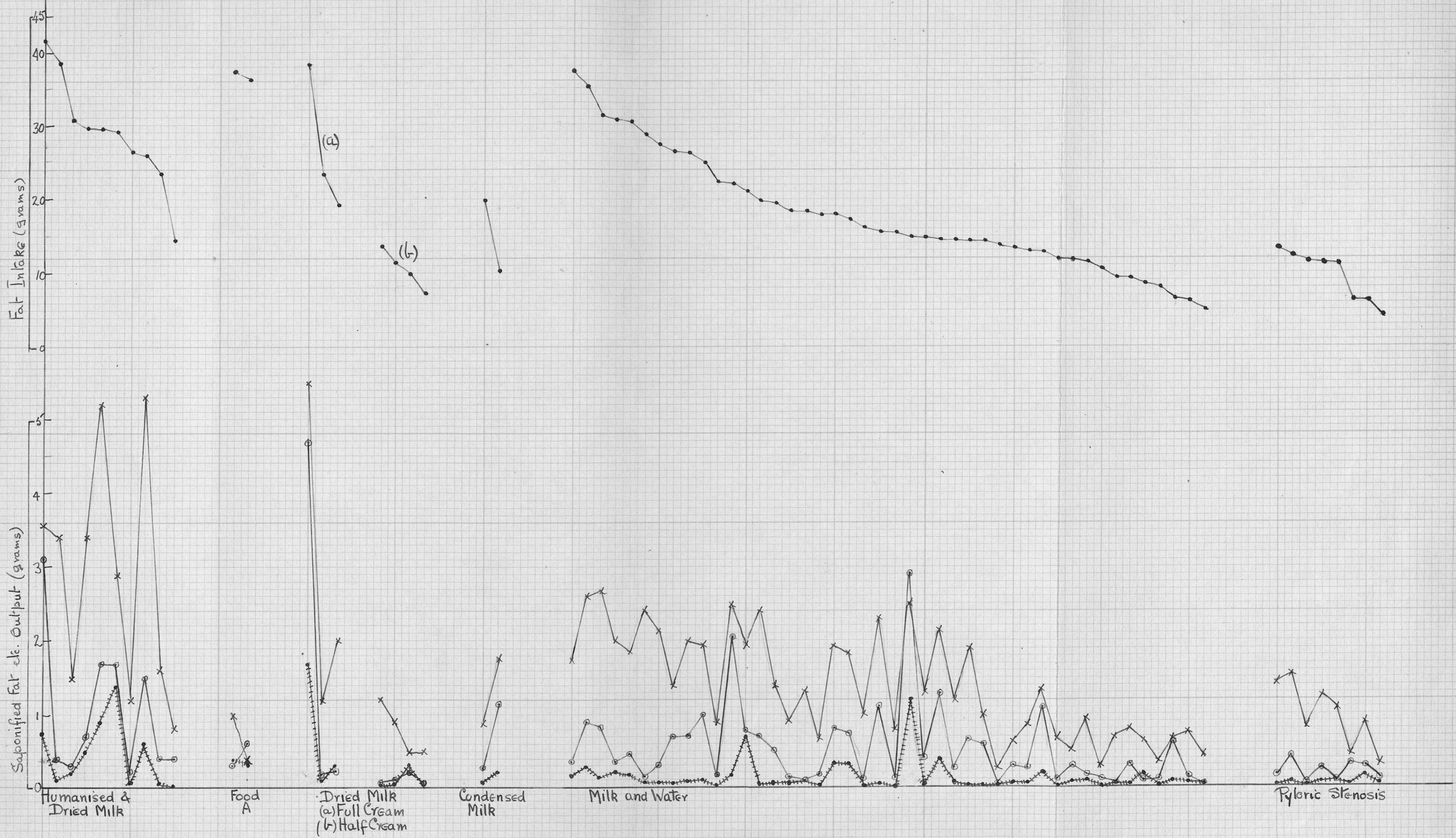


Fig V. Output of SAPONIFIED FAT, FREE FATTY ACID & NEUTRAL FAT per 24 hours. ×——× Saponified Fat; o——o Free Fatty Acid; o·····o Neutral Fat; •——• Fat Intake.