THE BILE-SALTS (GLYCO- AND TAURO-CHOLATE OF SODA) IN THEIR RELATION TO THE SECRETION OF UREA, &c. By G. H. EDINGTON, M.B. Glasgow. (PLATE VI.)[1]

THE following observations are the result of a research undertaken at the suggestion of Dr W. J. Fleming, Surgeon to the Glasgow Royal Infirmary, from a patient in whose wards the material was obtained.

The investigation was carried out in the Physiological Laboratory of the University of Glasgow, by the kind permission of Professor M'Kendrick, and was determined on in view of the small number of observations made during life on the composition of human bile.

It was hoped to have made analyses over an extended period; but from various causes—partly the delay in taking up the inquiry, and also the patient's anxiety to have the fistula closed—these did not exceed thirty in number. Even with this limited evidence, there seems to be shown, what was made the chief point in the inquiry, viz.:—a relation between the excretion of the Salts of the Bile-acids (Glycocholate and Taurocholate of Soda) and that of Urea.

I wish here to express my sincere thanks to Dr Fleming for the opportunities placed at my disposal in his wards, and for the assistance he so freely rendered me in every way; and I have also to thank Professor M'Kendrick for his kind permission to work in the Physiological Laboratory, and for the many practical hints he gave me while conducting the experiments.

This paper is arranged under the following headings:—

I. Narrative of Case. II. Limitation of the Inquiry. III. Methods. IV. Detailed Statement. V. General Conclusions. VI. Comparison with other Observers. Charts, and Tabular Statement. VII. References.

[1] This paper was presented to the University of Glasgow as a Thesis for the degree of M.D.

I. *Narrative of the Case.*

Mrs M'C——, æt. 53, Housewife, admitted to the Glasgow Royal Infirmary on the 26th April 1895, complaining of very severe pain in the right hypochondriac region, of 2 days' duration. She had experienced for many years back very poor appetite, but, so far as could be ascertained, had never had at any time anything of the nature of dyspepsia. She was habitually constipated, but had otherwise enjoyed good health.

Two days before admission she awoke at 3 A.M. with a severe pain in the right hypochondriac region. This was accompanied by vomiting of " bilious " material. Poultices were applied over seat of pain, but without avail, and she was sent into hospital. On admission she stated that her bowels had not moved for three days previously, although no fewer than ten enemata had been administered during that time. On admission, there was great pain complained of in right hypochondrium, the skin over which had been reddened by poulticing; after admission she had occasional bilious vomiting. A distinct tumour could be felt in the line of the gall-bladder, but somewhat lower down than usual.

The abdomen was opened in the right linea semilunaris, and a freely-movable sausage-shaped tumour, resembling a kidney, was pulled into the wound and fixed with a suture. A quantity of mucus-like fluid was drawn off from it by a trocar, after which the tumour was found to consist of a collection of stones in the sac of the gall-bladder. The bowel, on being examined, was not found to contain any of these concretions. After completing the suture of the bladder to the wound, a dressing was applied. Two days later, the sac was freely opened by incision, the gall-stones extracted, and a drainage-tube inserted through the opening. On the day following, there was a copious discharge of bile from the wound, while a large fæcal evacuation followed the administration of an enema of soap and water, castor oil and turpentine.

As regards the progress of the case, the woman continued in good health; no jaundice noted at any time; temperature normal; appetite somewhat poor and bowels constipated, requiring exhibition of medicine regularly. It was necessary to change the dressings on the fistula frequently, on account of their being saturated with discharge of bile. The fæces, however, were always normally coloured, although somewhat offensive. On one occasion the fistula was tightly plugged with gauze, and this was left in for twenty-four hours at least, without any accumulation of bile having taken place in the gall-bladder.

The patency of the ducts having been established beyond doubt, it was decided to close the fistula. This was done by inverting the rawed edges of gall-bladder and stitching the freshened skin-margin over that viscus. The wound healed by first intention and the patient went out well. A month or so later she reported herself as having kept well since dismissal.

II. *Limitation of the Inquiry.*

Towards the end of May, Dr. Fleming suggested to me the advisability of utilising the opportunity thus presented of analysing fresh human bile, and on the 6th of June the collecting of the discharge from the fistula was commenced. It was at first intended to make a complete analysis of the secretion, but it was found that this would involve more time than was available, and on talking the matter over with Professor M'Kendrick it was finally resolved to limit the inquiry to the determination of the bile-salts (Glycocholate and Taurocholate of Soda), the influence, if any, on the quantity secreted, of diet, time during the twenty-four hours, and temperature, and also as to any relation between the excretion of the salts and the amount of the urea excreted in the urine.

It was also determined to note the quantity of bile collected four-hourly, it being kept fully in mind, however, that there was a free vent into the intestine which would hinder any conclusions being drawn as to the *total* quantity excreted in the twenty-four hours.

III. *Methods.*

An attempt was made to collect the *bile* in the way described by Noël Paton (1), by means of an india-rubber tube connected with a Woulf's bottle; but this not proving successful, a modification was tried, by means of a balloon transfixed by the end of the tube, the former to be inflated when half way in the fistula, so as to assume an hour-glass shape. This was not found to be practicable, and finally the end of the tube was made bulbous by introducing a piece of glass tubing within its lumen. It was then passed into the fistula for a distance of three or four inches, and the tube retained in position by means of gauze strips dipped in collodion and made fast to skin of abdomen. Escape of bile alongside the tube was thus obviated. Silk threads were also used after the manner of shrouds in rigging. It was not found that the plugging action of the collodionised gauze was perfect, and it had to be renewed on several occasions.

The quantity collected was removed from the Woulf's bottle every four hours into a stoppered bottle. It was afterwards measured, and the estimation of the bile-salts made from sample from total daily (8 a.m.–8 p.m.) and total nightly (8 p.m.–8 a.m.) specimens. The physical appearances, colour, &c., of specimen were also noted. The reaction and specific gravity were taken irregularly, the latter being obtained by means of the common mercury-bulb urinometer.

The process adopted for the estimation of the bile-salts was as follows, and was taken from Sheridan Lea ([8]):—

A quantity of fresh bile, generally 25 c.c., was mixed with silver sand and evaporated on a sand-bath to a pulverisable mass. This was then extracted in a flask with strong boiling alcohol (rectified spirit), and the resulting green solution was filtered, decolorised with animal charcoal, and concentrated to a syrup. The syrup was then dissolved in a minimal quantity of absolute alcohol (if necessary, warmed), and precipitated with an excess of ether. The precipitate, consisting of glycocholate and taurocholate of soda, was collected on a weighed filter-paper, dried carefully, and weighed. No attempt was made to separate the one salt from the other.

The *Urine* was collected and measured (1) from 8 a.m.–8 p.m. and (2) from 8 p.m.–8 a.m. In each of these twelve-hourly quantities the specific gravity was observed and noted, and from a sample of total daily and total nightly quantity, estimation of urea was made by means of Gerrard's ureameter. The sex of the patient made it sometimes impracticable to obtain the whole quantity of urine passed. In these cases the percentage was estimated, but of course no conclusion could be drawn as to the quantity of urea excreted.

An account of diet, &c., was kept by the nurses in attendance on the patient.

IV. *Detailed Statement.*

Note.—The "day" of 24 hours dates from 8 A.M. of the day preceding.

June 6th. Quantity of bile collected :—

8 a.m. -12 noon	17 c.c.-	8 p.m. -12 mdnt.	19 c.c.
12 noon - 4 p.m.	45 ,,	12 mdnt.- 4 a.m.	15 ,,
4 p.m. - 8 p.m.	26·5 ,, —88·5 c.c.	4 a.m. - 8 a.m.	44 ,, —78 c.c.

The *colour* throughout was greenish. *Urine*, 8 a.m.-8 p.m., 15 oz., sp. gr. 1014, pale yellow. From 8 p.m.-8 a.m., 6 oz., sp. gr. 1020.

Diet.

8 a.m.	cocoa, 9 oz., ¾ slice bread, fish.	8 p.m.	soda water, 4 oz.
10.15 a.m.	whisky, ½ oz., water 3 oz.	9 p.m.	whisky, 1 oz., water 3 oz.
1 p.m.	soup, 12 oz., mince 4 oz.	4 a.m.	cocoa 10 oz., ½ slice bread and butter.
3 p.m.	soda water, 4 oz.	6·30 a.m.	whisky 1 oz., water 1 oz.
4 p.m.	tea, 12 oz., 1 slice bread.		

She had at 2 a.m., castor oil, ½ oz., and potass water, 1 oz.

The patient was very much excited about the proceedings, and complained of not having slept at all during the night. Castor oil was followed by a large motion consisting of dark-brown fæcal masses in fluid, and having an evil odour.

June 7th. Quantity of Bile.

8 a.m.	- 12 noon.	48 c.c.	*Colour*, greenish yellow.
12 noon	- 4 p.m.	9 ,,	lighter.
4 p.m.	- 8 p.m.	17 ,,	,,
8 p.m.	- 12 mdnt.	55 ,,	,,
12 mdnt.	- 4 a.m.	66 ,,	green and hazy.
4 a.m.	- 8 a.m.	36·5 ,,	greenish yellow, clear.
		231·5 c.c.	

Urine.—8 a.m. - 8 p.m. 14 oz., sp. gr. 1024.
8 p.m. - 8 a.m. 12 oz., sp. gr. 1022.

26 oz.

Diet, ordinary.

June 8th. Quantity of Bile.

8 a.m. - 12 noon	22 c.c.	*Colour*, yellow, greenish tint		·0450 grm. *Salts* in 25 c.c. = ·1800 grm. per 100 c.c.
12 noon - 4 p.m.	38 ,,	paler yellow		
4 p.m. - 8 p.m.	22 ,,	,, ,,		
8 p.m. - 12 mdnt.	63 ,,	darker, greenish, hazy		·0161 grm. *Salts* in 25 c.c. ·0644 grm. per 100 c.c.
12 mdnt. - 4 a.m.	18·5 ,,	lighter colour, hazy		
4 a.m. - 8 a.m.	50 ,,	very dark green		
	213·5 c.c.			

Urine.—8 a.m. - 8 p.m. 13 oz. sp. gr. 1024 *Urea* 3·6 %
8 p.m. - 8 a.m. 10 oz. sp. gr. 1025 ,, 3·5

23 oz.

Diet, ordinary.

Patient says she now feels quite comfortable as regards tubing, &c.

	June 9th.	*Quantity of Bile.*	
8 a.m. - 12 noon	49 c.c.	faint greenish tint	·0412 grm. *Salts* in 25 c.c. = ·1648 grm. per 100 c.c.
12 noon - 4 p.m.	42 ,,	,, ,,	
4 p.m. - 8 p.m.	49 ,,	very faint green	
8 p.m. - 12 mdnt.	45·5 ,,	golden yellow	.0750 grm. *Salts* in 25 c.c. = ·3000 grm. per 100 c.c.
12 mdnt. - 4 a.m.	42 ,,	darker ,, mucus	
4 a.m. - 8 a.m.	43·75 ,,	still darker, mucus	
	271·25 c.c.		

Urine.—8 a.m.-8 p.m. 9 oz. sp. gr. 1030 clear yellow, deposit of urates *Urea* 2·8 %
8 p.m.-8 a.m. 8 oz. sp. gr. 1015 ,, mucous sediment ,, 1·6

Diet, ordinary.

	June 10th.	*Quantity of Bile.*	
8 a.m. - 12 noon	51·5 c.c.	yellow, greenish tint	·1216 grm. *Salts* in 50 c.c. = ·2432 grm. per 100 c.c.
12 noon - 4 p.m.	51 ,,	lighter	
4 p.m. - 8 p.m.	65 ,,	greenish and opaque	
8 p.m. - 12 mdnt.	55 ,,	yellowish green	·1792 grm. *Salts* in 50 c.c. = ·3584 grm. per 100 c.c.
12 mdnt. - 4 a.m.	20·5 ,,	light yellow	
4 a.m. - 8 a.m.	42·5 ,,	clearer, yellow	
	285 c.c.		

Urine.—8 a.m. - 8 p.m. 15 oz. sp. gr. 1020 *Urea* 3·4 %
8 p.m. - 8 a.m. 15 oz. sp. gr. 1015 ,, 1·7

Diet, ordinary. Bowels moved after exhibition of Cascara. Motion dark and apparently normal.

	June 11th.	*Quantity of Bile.*	
8 a.m. - 12 noon	40 c.c.	greenish golden	·2441 grm. *Salts* in 50 c.c. = ·4882 grm. per 100 c.c.
12 noon - 4 p.m.	66 ,,	darker, hazy	
4 p.m. - 8 p.m.	36 ,,	golden greenish	
8 p.m. - 12 mdnt.	42 ,,	,, hazy	·0292 grm. *Salts* in 50 c.c. = ·0584 grm. per 100 c.c.
12 mdnt. - 4 a.m.	7·5 ,,	clear yellow	
4 a.m. - 8 a.m.	40 ,,	dark greenish, hazy	
	231·5 c.c.		

Urine.—8 a.m.-8 p.m. 9 oz., sp. gr. 1022 some lost (during purgation) *Urea* 2·5 %
8 p.m.-8 a.m. 8 oz., sp. gr. 1015 ,, ,, ,, 1·7

Diet, ordinary. Bowels still moving after exhibition of Cascara. Soft, dark-coloured motion, having bad odour.

	June 12th.	*Quantity of Bile.*	
8 a.m. – 12 noon	65 c.c.	orange hazy	·0517 grm. *Salts* in 50 c.c. = ·1034 grm. per 100 c.c.
12 noon – 4 p.m.	22 ,,	clear golden	
4 p.m. – 8 p.m.	42 ,,	golden, slightly hazy	
8 p.m. – 12 mdnt.	11·5 ,,	greenish, hazy	·0299 grm. *Salts* in 50 c.c. = ·0598 grm. per 100 c.c.
12 mdnt. – 4 a.m.	35 ,,	,, hazier	
4 a.m. – 8 a.m.	42 ,,	still darker green	
	217·5 c.c.		

Urine.—8 a.m. – 8 p.m. 9 oz., sp. gr. 1020 *Urea* 2·6 %
8 p.m. – 8 a.m. 12 oz., sp. gr. 1012 ,, 1·1

Diet, ordinary, but it is to be altered to-morrow, substituting, at dinner, farinaceous food for flesh-meat. Since yesterday the following has been taken, up to 8 a.m. this morning :—

8 a.m.	Cocoa, 14 oz., 1 slice of toast, fish.
12 noon.	Soda water, 2 oz.
1 p.m.	Soup, 14 oz., piece of chicken, ½ slice bread.
2 p.m.	Soda water, 2 oz.
4.30 p.m.	Tea, 8 oz., 1 slice bread.
9 p.m.	Whisky, 1 oz., water, 2 oz., and biscuit.
4 a.m.	Cocoa, 12 oz., 1 slice bread.
6.30 a.m.	Whisky, 1 oz., water, 1 oz.

	June 13th.	*Quantity of Bile.*	
8 a.m. – 12 noon	21 c.c.	greenish hazy	·0365 grm. *Salts* in 50 c.c. = ·0730 grm. per 100 c.c.
12 noon – 4 p.m.	28 ,,	golden, clearer	
4 p.m. – 8 p.m.	65 ,,	slightly greenish, hazy	
8 p.m. – 12 mdnt.	57 ,,	,, ,, ,,	·1410 grm. *Salts* in 50 c.c. = ·2820 grm. per 100 c.c.
12 mdnt. – 4 a.m.	41 ,,	dark greenish	
4 a.m. – 8 a.m.	45 ,,	,, ,,	
	257 c.c.		

Urine.—8 a.m. – 8 p.m. 22 oz., sp. gr. 1014 *Urea* 1·1 %
8 p.m. – 8 a.m. 25½ oz., sp. gr. 1012 ,, ·8 Deposit of urates.

Diet : The following represents dietary since 8 a.m. yesterday :—

8 a.m. Cocoa, 14 oz., 1 slice bread, fish
9 a.m. Water, 2 oz.
1 p.m. *Rice and milk*, 14 oz.
9 p.m. Whisky, 1 oz., water, 2 oz., biscuit.
4 a.m. Cocoa, 12 oz., toast, ½ slice.
6 a.m. Whisky, 1 oz., water, 1 oz.

	June 14th.	*Quantity of Bile.*	
8 a.m. – 12 noon.	41·5 c.c.	greenish yellow, hazy	·2695 grm. *Salts* in 25 c.c. = 1·0780 grm. per 100 c.c.
12 noon – 4 p.m.	31·5 ,,	clear golden yellow	
4 p.m. – 8 p.m.	15 ,,	,, ,,	
8 p.m. – 12 mdnt.	53 ,,	pale green, hazy	·3072 grm. *Salts* in 25 c.c. = 1·2288 grm. per 100 c.c.
12 mdnt. – 4 a.m.	54 ,,	darker green, hazy	
4 a.m. – 8 a.m.	46 ,,	still darker ,,	
	241 c.c.		

Urine.—8 a.m. – 8 p.m. 23 oz., sp. gr. 1012 *Urea* ·6 %
8 p.m. – 8 a.m. 8 oz., ,, 1012 ,, 1·3

Diet, as yesterday.

June 15th. Quantity of Bile.

8 a.m. – 12 noon.	34 c.c.	greenish orange, slight haze	·1684 grm. *Salts* in 25 c.c. = ·6736 grm. per 100 c.c.
12 noon – 4 p.m.	22 ,,	,, ,, ,,	
4 p.m. – 8 p.m.	28 ,,	,, ,, clearer	
8 p.m. – 12 mdnt.	42 ,,	,, ,, hazy	·2296 grm. *Salts* in 25 c.c. = ·9184 grm. per 100 c.c.
12 mdnt. – 4 a.m.	11 ,,	greener, hazy	
4 a.m. – 8 a.m.	30 ,,	Greener still. Very hazy	
	167 c.c.		

Urine.—8 a.m. – 8 p.m. 20 oz., sp. gr. 1015 *Urea* 1·7 %
8 p.m. – 8 a.m. 8 oz., sp. gr. 1012. Some lost during purgation.

Diet, as yesterday. At 2 a.m., 1 oz. castor oil administered.

June 16th. Quantity of Bile.

8 a.m. – 12 noon	17·5 c.c.	greenish tint, hazy	·3780 grm. *Salts* in 25 c.c. 1·5120 grm. per 100 c.c.
12 noon – 4 p.m.	17·5 ,,	,, ,,	
4 p.m. – 8 p.m.	40 ,,	orange, hazy	
8 p.m. – 12 mdnt.	3·5 ,,	yellow, hazy	·0250 grm. *Salts* in 25 c.c. = ·1000 grm. per 100 c.c.
12 mdnt. – 4 a.m.	33·25 ,,	light yellow, hazy	
4 a.m. – 8 a.m.	40 ,,	orange, hazy	
	151·75 c.c.		

Urine.—8 a.m. – 8 p.m. 12 oz., sp. gr. 1022 *Urea* 1·4 %
8 p.m. – 8 a.m. 15 oz., sp. gr. 1018 ,, 2·5

Diet, same as yesterday.

June 17th. Quantity of Bile.

8 a.m. – 12 noon	21 c.c.	clear golden	Bile thrown out by mistake before estimation made.
12 noon – 4 p.m.	27 ,,	golden, slight haze	
4 p.m. – 8 p.m.	32 ,,	,, clearer	
8 p.m. – 12 mdnt.	8 ,,	,, hazy	
12 mdnt. – 4 a.m.	20 ,,	bright, orange hazy	
4 a.m. – 8 a.m.	43 ,,	greenish ,,	
	151 c.c.		

Urine.—8 a.m. – 8 p.m. ? oz., sp. gr. 1025 urates deposited *Urea* 2·3 %
8 p.m. – 8 a.m. 8 oz., ,, 1022 ,, 3·3

Diet, resumption of ordinary mixed ; mince and soup to dinner.

June 18th. Quantity of Bile.

8 a.m. – 12 noon	30 c.c.	golden greenish hazy	·1722 grm. *Salts* in 25 c.c. = ·6888 grm. per 100 c.c.
12 noon – 4 p.m.	55 ,,	darker green ,,	
4 p.m. – 8 p.m.	21 ,,	glear golden yellow	
8 p.m. – 12 mdnt.	9 c.c.	golden hazy	·0956 grm. *Salts* in 25 c.c. = ·3824 grm. per 100 c.c.
12 mdnt. – 4 a.m.	7 ,,	,, ,,	
4 a.m. – 8 a.m.	16 ,,	,, ,,	
	138 c.c.		

Urine.—8 a.m. – 8 p.m. 14·5 oz., sp. gr. 1024 urates deposited *Urea* 3·5 %
8 p.m. – 8 a.m. 12 oz., ,, 1021 ,, 2·2

Diet, ordinary mixed.

	June 19th.	*Quantity of Bile.*	
8 a.m. - 12 noon	23· c.c.	orange, hazy	·2078 grm. *Salts* in 25 c.c. = ·8312 grm. per 100 c.c.
12 noon - 4 p.m.	46·5 ,,	,, clearer	
4 p.m. - 8 p.m.	17·5 ,,	,, ,,	
8 p.m. - 12 mdnt.	41·5 ,,	,, becoming hazy	·1652 grm. *Salts* in 25 c.c. = ·6608 grm. per 100 c.c.
12 mdnt. - 4 a.m.	46·5 ,,	dark green, opaque	
4 a.m. - 8 a.m.	41 ,,	,, ,, ,,	
	216 c.c.		

Urine.—8 a.m. - 8 p.m. 12 oz., sp. gr. 1024 *Urea* 1·8 %
8 p.m. - 8 a.m. 46 oz., ,, 1011 ,, ·6

Diet, ordinary mixed.

A saline aperient consisting of Sulphates of Magnesia (ʒiii) and Soda (ʒvi) given at 4 a.m., but vomited at 4.10 a.m. On our visiting the patient at 9 o'clock this morning, she is found greatly depressed and desiring to go home ; she says that salts have "never agreed with her." In bile-specimens taken during the night there is plentiful mucus, with blood corpuscles entangled in it. This may have come about from the mucous membrane of the gall-bladder having been injured by tube while the patient was vomiting. No action of the bowels having followed the saline, 5 grains of calomel were ordered to be taken to-night. Although there was no movement of bowels after the salts, she complained of great thirst.

	June 20th.	*Quantity of Bile.*	
8 a.m. - 12 noon.	13·5 c.c.	green, hazy	·2344 grm. *Salts* in 25 c.c. = ·9376 grm. per 100 c.c.
12 noon - 4 p.m.	26 ,,	golden, slightly hazy	
4 p.m. - 8 p.m.	13·5 ,,	,, ,,	
8 p.m. - 12 mdnt.	51 ,,	Bright golden, clear	Specimen lost during analysis.
12 mdnt. - 4 a.m.	15·5 ,,	,, hazy	
4 a.m. - 8 a.m.	24 ,,	,, ,,	
	143·5 c.c.		

Urine.—8 a.m. - 8 p.m., 24 oz., sp. gr. 1020 *Urea* 1·5 %
8 p.m. - 8 a.m. 20 oz., ,, 1010 ,, ·5 Some urine lost.

Diet, ordinary mixed. 5 grains of Calomel administered at 10 p.m. (last night). Bowels moved 4 times, the stools being natural in colour and not so offensive as on previous occasions. Unfortunately some urine lost, preventing total estimation of urea being made.

	June 21st.	*Quantity of Bile.*	
8 a.m. - 12 noon.	9 c.c.	orange, hazy	·1768 grm., *Salts* in 25 c.c. = ·7072 grm. per 100 c.c.
12 noon - 4 p.m.	22 ,,	,, clear	
4 p.m. - 8 p.m.	15 ,,	,, ,,	
8 p.m. - 12 mdnt.	8·5 ,,	,, ,,	·1290 grm., *Salts* in 12·5 c.c. = 1·0320 grm. per 100 c.c.
12 mdnt. - 4 a.m.	5 ,,	,, ,,	
4 a.m. - 8 a.m.	11 ,,	,, ,,	
	70·5 c.c.		

Urine.—8 a.m. - 8 p.m. 15 oz., sp. gr. 1020 *Urea* 2·3 %
8 p.m. - 8 a.m. 16·5 oz., sp. gr. 1012 ,, 1·1

Diet, ordinary mixed.

June 22nd. Quantity of Bile.

8 a.m. – 12 noon	14 c.c.	faint greenish, hazy	·1484 grm. *Salts* in 25 c.c. = ·5936 grm. per 100 c.c.
12 noon – 4 p.m.	22 ,,	yellowish, clearer	
4 p.m. – 8 p.m.	31 ,,	,, ,,	
8 p.m. – 12 mdnt.	46 ,,	,, clearer still	·1894 grm. *Salts* in 25 c.c. = ·7576 grm. per 100 c.c.
2 mdnt. – 4 a.m.	8 ,,	,, ,, ,,	
4 a.m. – 8 a.m.	46 ,,	dark-golden, clear	
	167 c.c.		

Urine.—8 a.m. – 8 p.m. 24 oz., sp. gr. 1018 *Urea* 1·5 %
8 p.m. – 8 a.m. 18·5 oz., ,, 1010 ,, ·5

Diet, ordinary mixed.

June 23rd. Quantity of Bile.

8 a.m. – 12 noon	14 c.c.	golden, hazy	·1500 grm. *Salts* in 25 c.c. = ·6000 grm. in 100 c.c.
12 noon – 4 p.m.	21·5 ,,	paler	
4 p.m. – 8 p.m.	22 ,,	,,	
8 p.m. – 12 mdnt.	38 ,,	golden, hazy	·2802 grm. *Salts* in 25 c.c. = 1·1208 grm. in 100 c.c.
12 mdnt. – 4 a.m.	10 ,,	,, ,,	
4 a.m. – 8 a.m.	36 ,,	dark greenish. Very hazy.	
	141·5 c.c.		

Urine.—8 a.m. – 8 p.m. 24 oz., sp. gr. 1015 *Urea* ·6 %
8 p.m. – 8 a.m. 9 oz., sp. gr. ,, ·7

Diet, ordinary mixed.

V. *General Conclusions.*

The following points present themselves for consideration and will be briefly noted :—

A. *Quantity of Bile.*

- (α) Secreted in 24 hours.
- (β) Relation to time of day.
- (γ) Relation to food { i. meal hours. ii. nature of food.
- (δ) Relation to drugs.
- (ε) ,, ,, quantity of urine.
- (ζ) ,, ,, temperature.

B. *Colour of Bile.* C. *Specific Gravity.* D. *Reaction.*

E. *Bile-Salts.*

- (α) Time of day, or night.
- (β) Relation to diet.
- (γ) ,, ,, drugs.
- (δ) Relation to Urea.
- (ε) ,, ,, temperature.

A. (*a*). *Quantity secreted in 24 hours.*

This varies within wide limits. The minimum quantity was collected on the 21st June, viz. 70·5 c.c.; while the maximum occurred on the 10th of same month, viz. 285·5 c.c. The average daily quantity over 18 days is 191·22 c.c.

Bearing in mind (p. 217) that there was reason to suppose a free escape into the intestine, the above figures of course are not indicative of the total secretion.

(*β*). *Relation to 4-hourly period of 24 hours at which collected.*

The greatest quantity collected in a 4-hourly period is seen below, for the different days :—

Date.	Quantity.	4-Hourly Period.
June 6,	45 c.c.	12 noon – 4 p.m.
,, 7,	66 ,,	12 mdnt.– 4 a.m.
,, 8,	63 ,,	8 p.m. –12 mdnt.
,, 9,	49 ,,	8 a.m. –12 noon.
,, 10,	65 ,,	4 p.m. – 8 p.m.
,, 11,	66 ,,	12 noon – 4 p.m.
,, 12,	65 ,,	8 a.m. –12 noon.
,, 13,	65 ,,	4 p.m. – 8 p.m.
,, 14,	54 ,,	12 mdnt.– 4 a.m.
,, 15,	42 ,,	8 p.m. –12 mdnt.
,, 16,	40 ,,	{ 4 p.m. – 8 p.m. 4 a.m. – 8 a.m.
,, 17,	43 ,,	4 a.m. – 8 a.m.
,, 18,	55 ,,	12 noon – 4 p.m.
,, 19,	46·5 ,,	{ 12 noon – 4 p.m. 12 mdnt.– 4 a.m.
,, 20,	51 ,,	8 p.m. –12 mdnt.
,, 21,	22 ,,	12 noon – 4 p.m.
,, 22,	46 ,,	{ 8 p.m. –12 mdnt. 4 a.m. – 8 a.m.
,, 23,	38 ,,	8 p.m. –12 mdnt.

From the figures in preceding pages the following *average* has been arrived at :—

8 a.m. – 12 noon	29·50 c.c.
12 noon – 4 p.m.	33·50 ,,
4 p.m. – 8 p.m.	30·90 ,,
8 p.m. – 12 mdnt.	36·02 ,,
12 mdnt. – 4 a.m.	25·31 ,,
4 a.m. – 8 a.m.	37·62 ,,
Average in 24 hours =	192·85 c.c.

Average maximum – 4–8 a.m.
,, minimum – 12–4 a.m.

These figures show the maximum quantity excreted during a period of 4 hours to be far from constant to any one period of the day. We have the daily maximum occurring from 12 noon–4 p.m. on five occasions, and for a similar number of times from 8 p.m.–12 midnight. On three occasions each the maximum is noted as occurring at the following periods: 12 midnt.–4 a.m., 4 p.m.–8 p.m., and 4 a.m.–8 a.m.; while from 8 a.m.–12 noon, we have the maximum flow on two occasions only.

In addition, it is found that on one occasion the maximum flow occurred; (1) from 4 p.m.–8 p.m. and 4 a.m.–8 a.m. on the same day; (2) on another at 12 noon–4 p.m. and 12 midnt.–4 a.m.; and (3) again at 8 p.m.–12 midnt. and 4 a.m.–8 a.m.

(γ). *Relation to taking of food.*

(i.) *Meal-hours: Breakfast*, 8 a.m. On five occasions maximum flow occurred from 12 noon–4 p.m., but on one of these an equal flow was observed from 12 midnt.–4 a.m. Maximum occurred twice from 8 a.m.–12 noon.

Dinner, 1 p.m. Again maximum noted as occurring on five occasions from 12 noon–4 p.m.

Tea, 4 p.m. Maximum on three occasions from 4 p.m.–8 p.m.; but on one of these there was an equal flow from 4 a.m.–8 a m. These observations do not bear out the existence of a relationship between the taking of food and the secretion of bile. See below, explanation offered at end of (δ.).

(ii.) *Nature of food:* According to the charts Nos. 1 and 3, there seems to be some falling off when reduced diet is being taken. This, however, is not at all marked when compared with the register following the resumption of the original diet.

(δ). *Drugs.*

(i.) At 2 a.m. on 6th June, *Castor Oil* $\frac{1}{2}$ oz. taken. From 12 midnt. to 4 a.m. 15 c.c. bile collected, while from 4–8 a.m., 44 c.c. and from 8 a.m.–12 noon, 48 c.c.

(ii.) At 11 p.m. on 11th June, *Cascara Sagrada* (Liq. Extr. ʒ i) administered. For each period of the 24-hours-day the quantity remained between 40 and 50 c.c. and no marked effect on the quantity seems to have followed the exhibition of this laxative.

(iii.) At 2 a.m. on the 15th, *Castor Oil* 1 oz. administered. For the following 24 hours, the quantities of bile seem to be somewhat below the usual, keeping for the most part under 40 c.c., and at 12 midnight dropping to 3·5 c.c.

(iv.) *Saline Aperient* (Magnes. Sulph. ʒ iii Sod. Sulphat. ʒ vi) given at 4 a.m. on 19th. From 8 a.m.–8 p.m. there was a decided drop in the quantity collected. At 12 midnight it had risen to 50 c.c. (*Calomel* gr. v having been administered at 10 p.m.). She vomited the salts about 10 minutes after having taken them. The quantities collected were very low during the 32 hours following the administration of the calomel, being for the most part below 20 c.c. They then began to creep up, ranging about the 40's.

The explanation offered of the fall in quantity after the administration of the above drugs (with the exception of Cascara) is, that more of the bile flowed into the active intestine than when the viscera were in a state of rest. Perhaps this explanation may account for absence of apparent relationship between bile-flow and taking of food, noted above.

(ε). *Urine.*

On reference to Chart No. 3, it will be seen, so far as is shown—the urine having been lost occasionally, as after purgation—that there is a relation between the quantity of this secretion and that of the bile. When the bile-register keeps high and more or less uniform, the urine keeps low and uniform. When, however, towards the end of the chart, the bile-tracing comes down, that of the urine jumps up. It is felt that the observations on this point are too scanty to be of much worth; nevertheless it is thought well to record them.

(ζ). *Temperature.*

We lastly come to consider the relation, if any, between the patient's body-temperature and the quantity of bile collected.

Throughout the time during which the observation was being carried on the temperature showed very little oscillation, and any there is can hardly be said to bear any relation to the bile-curve.

B. *Colour of the Bile.*

This varies much, both in the 24 hours and from day to day. It seems, however, to be of dark greenish tint from 12–4 a.m. and 4 a.m.–8 a.m. as a rule, although sometimes the day specimens show this colour, while those collected at night are golden-yellow and clear.

Drugs seem to influence this:—Cascara, 11 p.m. on 9th June. Darkening of colour of night specimens to greenish hue, to be followed in a day or so by orange-yellow bile, after which the greenish colour is again observed.

On the 15th June, Castor Oil followed by greenish bile. On the 16th, the bile is mostly orange or golden-yellow.

After salts on the 19th the colour is dark green and opaque, while after Calomel on evening of 19th the bile is golden and clear on to the 22nd June. By the 23rd June, it is observed to be returning to general condition of "dark greenish, hazy" in the morning.

C. *Specific Gravity of Bile.*

This was only irregularly taken, but the following results were obtained :—

Average of 8 day-specimens	=	1011·75.
" " 6 night- "	=	1012·50.

So far as shown, drugs had no influence on the specific gravity. There is no relation between the quantity of bile collected and the specific gravity.

D. *Reaction of Bile.*

Tested on eighteen occasions and found always to be faintly alkaline.

E. *Bile-salts* (*Glycocholate and Taurocholate of Soda.*

As will be seen on referring to Chart No. 2, the quantity of salts excreted from fistula varies within wide limits.

(*a*). *Influence of time of day or night :—*

Average for day	=	0·4840 grm.	(0·5249 grm. per 100 c.c. bile).
" " night	=	0·4957 grm.	(0·5231 grm. per " "

(*β*). *Relation to food* (referring to *diet*).

Up to 13th June, the patient was taking ordinary mixed diet (as on p. 221). On that date farinaceous food was substituted for the ordinary dinner of flesh-meat. On the 13th, morning-salts = ·07 grm., evening ditto = ·4 grm., while on 14th the morning-salts = ·94 grm., evening = 1·86 grm. On the morning of 15th, they were down to ·56 grm., evening ·75 grm.

(Castor Oil ℥ i was taken at 2 a.m. on 15th). On 16th, salts of morning specimen = 1·13 grm., while on the evening of this day they fell to ·07 grm.

The original mixed diet was resumed on the following day, but by some mistake the specimens of bile were thrown out before having been analysed.

On the 18th, morning = ·72 grm.; evening = ·12 grm.
" " 19 " " = ·74 grm. " = ·85 grm.

At 4 a.m. on 19th, Saline administered (Sulph. of Magnesia ʒ iii and of Soda ʒ vi) on account of constipation. The patient received also at 10 p.m. 5 grs. Calomel. The analysis for 20th (including from 8 a.m. 19th) is as follows:—

Morning = ·49 grm. The evening specimen lost during analysis owing to an accident to the apparatus. The Calomel was administered on account of the salts having been vomited and was followed by a lively catharsis. Analysis for 21st June was as follows:—morning = ·32 grm.; evening = ·25 grm.

There was slight rise on succeeding day to ·39 and ·75 for morning and evening respectively. The 23rd = morning ·34 grm., evening ·94 grm.

From the above details it seems that the withdrawal of flesh-meat from the dietary is followed by increase in the quantity of the bile-salts, while on resumption of flesh-diet there is a fall. It is unfortunate that only the quantity for day succeeding and not that for day of resumption is determined. There is, towards the close of chart, a tendency to creep up.

(γ). *Drugs.*

The administration of Ol. Ricini is followed by an increase and subsequent decrease in quantity of the salts. The saline seems to have had but little effect on the salts (bile), while the effect of the Calomel cannot be ascertained. Judging from other parts of the chart, the fall on the 21st might indicate a rise on the 20th.

(δ). *Relationship to Urea.*

This is shown in a marked way in Chart No. 2, in which the tracings of urea and bile-salts are compared. As the quantity of salts rises, there is almost invariably a fall in urea, while the converse also holds good. When the rise of salts follows the modification of diet, the urea is seen to fall. The effect of drugs on this relationship cannot be seen on account of the patient's sex.

While it is noted that on last day of observation the bile-salts show a tendency to creep up, this is checked by the fall in the excretion of the urea.

When the *percentage* of salts is considered, similar results obtain.

(ε). *Temperature.*

Same remarks apply here as on p. 227, where the temperature-notes are compared with quantity of bile secreted.

N.B.—The bile decomposed readily during hot weather.

Summary.

1. Quantity of bile collected varies much.

2. The variation is not regular for any period of the day, the occurrence of the maximum being very variable. The average maximum occurs at 4–8 a.m.; minimum 12–4 a.m.

3. The variation shows no relation to meal-hours.

4. Effect of change of diet is doubtful.

5. The various purgatives employed (with exception of Cascara) are followed by diminished discharge from the fistula. Does more of the bile pass into the active intestine?

6. Quantity of bile discharged varies inversely as that of the urine.

7. As a rule, bile collected during the night-hours is of a dark greenish tint.

8. Greenish colour follows exhibition of purgatives, and is succeeded by change to golden-yellow.

9. Specific gravity low, but higher at night than through the day.

10. Reaction, so far as taken, faintly alkaline.

11. Average salts slightly lower by day than by night.

12. Farinaceous food followed by increase of salts. On resumption of flesh-meat, salts do not drop to former level.

13. Effect of drugs on salts not satisfactorily determined.

14. There is very distinct inverse relation of salts to excretion of urea.

15. Antisepticity of bile low.

VI. *Comparison with other Observers.*

The variation in quantity excreted is mentioned by others. Our observations as to the average minimum and maximum do not agree with those of Paton and Balfour (1):—

Paton and Balfour.		Present Observations.
8 a.m. - 12 noon	106·0 c.c.	29·50 c.c.
12 noon - 4 p.m.	140·5 ,,	33·50 ,,
4 p.m. - 8 p.m.	102·0 ,,	30·90 ,,
8 p.m. - 12 mdnt.	100·6 ,,	36·02 ,,
12 mdnt. - 4 a.m.	88·5 ,,	25·31 ,,
4 a.m. - 8 a.m.	116·0 ,,	37·62 ,,

Copeman and Winston (2) find rate of secretion lowest at 5 a.m., highest at 12 noon, and this they attribute to the taking of food. The researches of Yeo and Herroun (3) show no increase after meals; they also say that amount secreted during day is same as that during night. They are willing to believe, however, that while this result may be obtained in hospital, where meals are frequent and moderate, yet a different state might obtain where meals were larger and taken at longer intervals. Mayo Robson (4), on the other hand, finds a rise in quantity at night. He also finds change of diet not followed by any great alteration in the quantity of the bile secreted, and his results point to a diminution in quantity following the administration of cholagogues, agreeing with our experience with purgatives (?).

Specific gravity is in our case in accordance with the results of others, being about 1011. Jacobsen (quoted by Halliburton [5]) draws attention to the difference between fistula-bile and gall-bladder-bile in this respect. We find it higher at night, and in this agree with Paton and Balfour. These observers, and also Mayo Robson, agree with us as to increased secretion of bile-salts during the night. As will be seen below, however, our percentage is higher for day than night. The following table gives a comparison of different observations, and is taken from Paton and Balfour's paper.

	Jacobsen.	Yeo and Herroun.	Copeman and Winston.	Robson.	Paton and Balfour.		Present Case.
Sod. Glycocholate, .	1·01	·165	·628	·751	·356	·349	·524
Sod. Taurocholate, .	...	·055	...	·009	·049		

Paton and Balfour.		Present Case.	
8 a.m.–8 p.m.	8 p.m.–8 a.m.	8 a.m.–8 p.m.	8 p.m.–8 a.m.
·2426	·4571	·5249	·5231
·349		·524	

As regards general metabolism, we find with ordinary mixed diet less salts formed than with farinaceous modification. This is also borne out in comparing with the urea excreted, and this seems to be in agreement with the results of Kunkel and Spirs (quoted by Bunge [6]), who show that only a small part of nitrogen and sulphur resulting from proteid metabolism appears in bile. Mayo Robson and Paton ([7]) and Balfour agree as to excrementitious nature of the bile; and Zweifel (quoted by Bunge) declares that the bile must to a certain extent be excretory, seeing that it is formed during the third month of embryonic life, whereas secretions from other glands for intestinal tract begin after birth, on taking of food.

Most are agreed on the question of the low antisepticity of bile. (See Tables, p. 234.)

Note.—Since writing the above, I have had an opportunity of observing another case of biliary fistula. The patient was operated on by Dr Henry Rutherfurd for gallstones. The gall-ducts were patent, but a biliary fistula existed for some time after the operation, and from this considerable quantities of bile were passed. It was observed that the discharge of bile was increased very much by exhibition of Seidlitz powder, or Colocynth pill, a matter of frequent occurrence on account of constipation.

The increase was such as to require additional dressings to be applied over the fistula.

VII. *References.*

(1.) *Laboratory Reports, Royal College of Physicians, Edinburgh*, vol. iii., 1891.

(2.) *Journal of Physiology*, vol. x. p. 213, 1889.

(3.) „ „ vol. v. p. 116, 1884.

(4.) *Proc. Royal Society*, vol. xlvii. p. 499, 1890.

(5.) Halliburton, *Text-book of Chemical Physiology and Pathology*, 1889, p. 675.

(6.) *Physiological and Pathological Chemistry*, Bunge, trans. by Wooldridge, 1890, p. 214.

(7.) *Laboratory Reports, Royal College of Physicians, Edinburgh*, vol. iv., 1892.

(8.) *Foster's Physiology*. Appendix. Sheridan Lea. p. 211.

[Tabular Statement.

TABULAR STATEMENT.

Date.	Bile. Hour.	Bile. Quantity in c.c.	Bile. Specific Gravity.	Bile. Salts. Per-centage.	Bile. Salts. Total in Grammes.	Urine. Hour.	Urine. Quantity in oz.	Urine. Specific Gravity.	Urine. Urea. Per-centage.	Urine. Urea. Total in Grammes.	Urine. Temperature ° F.	Remarks.
1895. June 6.	8 a.m. -12 noon	17	..									The percentage of salts of bile is given as grm. per 100 c.c. The *total salts* means' *total excreted from fistula.*
	12 noon - 4 p.m.	45	..	..	..	8 a.m. - 8 p.m.	15	1014	..	..	..	
	4 p.m. - 8 p.m.	26·5	..									
	8 p.m. -12 mdnt.	19	..									
	12 mdnt.- 4 a.m.	15	..	..	..	8 p.m. - 8 a.m.	6	1020	..	..	..	
	4 a.m. - 8 a.m.	44	..									
		166·5	..	..	..		21	..	..	..		
" 7.	8 a.m. -12 noon	48	..									
	12 noon - 4 p.m.	9	..	..	..	8 a.m. - 8 p.m.	14	1024	..	..	..	
	4 p.m. - 8 p.m.	17	..									
	8 p.m. -12 mdnt.	55	..									
	12 mdnt.- 4 a.m.	66	..	..	..	8 p.m. - 8 a.m.	12	1022	..	..	..	
	4 a.m. - 8 a.m.	36·5	..									
		231·5	..	..	..		26	..	..	..		
" 8.	8 a.m. -12 noon	22	..									
	12 noon - 4 p.m.	38	..	·1800	·14	8 a.m. - 8 p.m.	13	1024	3·6	13·25	M. 97·8	
	4 p.m. - 8 p.m.	22	..									
	8 p.m. -12 mdnt.	63	..									
	12 mdnt.- 4 a.m.	18·5	..	·0644	·07	8 p.m. - 8 a.m.	10	1025	3·5	10·06	E. 98	
	4 a.m. - 8 a.m.	50	..									
		213·5	..	..	·21		23	..	..	23·31		
" 9.	8 a.m. -12 noon	49	..									At 11 p.m. Cascara Sagrada (ʒi Liq. Extract).
	12 noon - 4 p.m.	42	..	·1648	·22	8 a.m. - 8 p.m.	9	1030	2·8	7·15	M. 98	
	4 p.m. - 8 p.m.	49	..									
	8 p.m. -12 mdnt.	45·5	..									
	12 mdnt.- 4 a.m.	42	..	·3000	·39	8 p.m. - 8 a.m.	8	1015	1·6	3·63	E. 98·4	
	4 a.m. - 8 a.m.	43·75	..									
		271·25	..	..	·61		17	..	..	10·78		

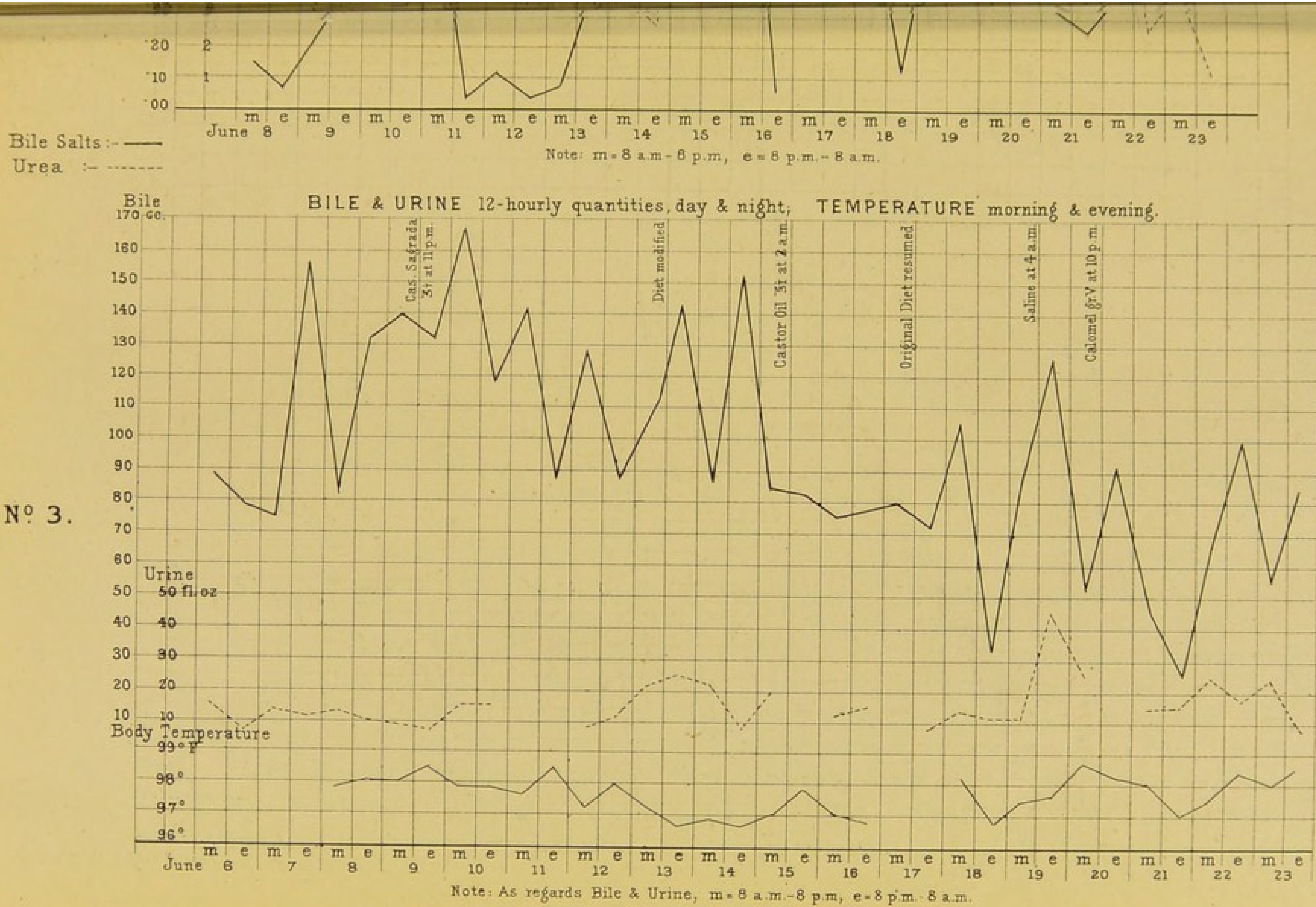
1895. June 10.	8 a.m. -12 noon 12 noon - 4 p.m. 4 p.m. - 8 p.m.	51·5 51 65	.. .. ..	·2432	·40	8 a.m. - 8 p.m.	15	1020	3·4	14·48	M. 97·8	Motions passed, dark brown colour, bad odour, apparently normal.
	8 p.m. -12 mdnt. 12 mdnt.- 4 a.m. 4 a.m. - 8 a.m.	55 20·5 42·5	.. .. ..	·3584	·41	8 p.m. - 8 a.m.	15	1015	1·7	7·24	E. 97·8	
		285·5	..	..	·81		30	..	..	21·72		
" 11.	8 a.m. -12 noon 12 noon - 4 p.m. 4 p.m. - 8 p.m.	40 66 36	.. .. ..	·4882	·68	8 a.m. - 8 p.m.	9*	1022	2·5	..	M. 97·6	* Some lost.
	8 p.m. -12 mdnt. 12 mdnt.- 4 a.m. 4 a.m. - 8 a.m.	42 7·5 40	.. .. ..	0584	·04	8 p.m. - 8 a.m.	8*	1015	1·9	..	E. 98·4	* " "
		231·5	..	..	·72		17	..	..	..		
" 12.	8 a.m. -12 noon 12 noon - 4 p.m. 4 p.m. - 8 p.m.	65 22 42	.. .. ..	·1034	·12	8 a.m. - 8 p.m.	9	1020	2·6	6·64	M. 97·2	
	8 p.m. -12 mdnt. 12 mdnt.- 4 a.m. 4 a.m. - 8 a.m.	11·5 35 42	.. .. ..	·0598	·04	8 p.m. - 8 a.m.	12	1012	1·1	3·74	E. 98	
		217·5	..	..	·16		21	..	..	10·38		
" 13.	8 a.m. -12 noon 12 noon - 4 p.m. 4 p.m. - 8 p.m.	21 28 65	.. .. ..	·0730	·07	8 a.m. - 8 p.m.	22	1014	1·1	6·87	M. 97·2	Diet modified.
	8 p.m. -12 mdnt. 12 mdnt.- 4 a.m. 4 a.m. - 8 a.m.	57 41 45	.. .. ..	·2820	·40	8 p.m. - 8 a.m.	25·5	1012	·8	5·79	E. 96·6	
		257	..	..	·47		47·5	..	..	12·66		
" 14.	8 a.m. -12 noon 12 noon - 4 p.m. 4 p.m. - 8 p.m.	41·5 31·5 15	.. .. ..	1·0780	·94	8 a.m. - 8 p.m.	23	1012	·6	3·91	M. 96·8	
	8 p.m. -12 mdnt. 12 mdnt.- 4 a.m. 4 a.m. - 8 a.m.	53 54 46	.. .. ..	1·2288	1·86	8 p.m. - 8 a.m.	8	1012	1·3	2·95	E. 96·6	
		241	..	..	2·80		31	..	..	6·86		

TABULAR STATEMENT—*continued.*

Date.	Bile. Hour.	Bile. Quantity in c.c.	Bile. Specific Gravity.	Bile. Salts. Per-centage.	Bile. Salts. Total in Grammes.	Urine. Hour.	Urine. Quantity in oz.	Urine. Specific Gravity.	Urine. Urea. Per-centage.	Urine. Urea. Total in Grammes.	Urine. Temperature ° F.	Remarks.
1895. June 15.	8 a.m. –12 noon	34	1011	·6736	·56	8 a.m. – 8 p.m.	20	1015	1·7	9·65	M. 97	Ol. Ricini (℥i) at 2 a.m.
	12 noon – 4 p.m.	22										
	4 p.m. – 8 p.m.	28										
	8 p.m. –12 mdnt.	42	1013	·9184	·75	8 p.m. – 8 a.m.	8*	1012	2	..	E. 97·8	* Some lost.
	12 mdnt.– 4 a.m.	11										
	4 a.m. – 8 a.m.	30										
		167	..	..	1·31		..	..	..	..		
,, 16.	8 a.m. –12 noon	17·5	1012	1·5120	1·13	8 a.m. – 8 p.m.	12	1022	1·4	4·77	M. 97	
	12 noon – 4 p.m.	17·5										
	4 p.m. – 8 p.m.	40·										
	8 p.m. –12 mdnt.	3·5	1014	·1000	·07	8 p.m. – 8 a.m.	15	1018	2	8·51	E. 96·8	
	12 mdnt.– 4 a.m.	33·25										
	4 a.m. – 8 a.m.	40										
		151·75	..	..	1·20		..	..	..	13·28		
,, 17.	8 a.m. –12 noon	21	1011	..	..	8 a.m. – 8 p.m.	..	1025	2·3	..	..	
	12 noon – 4 p.m.	27										
	4 p.m. – 8 p.m.	32										
	8 p.m. –12 mdnt.	8	1012	..	..	8 p.m. – 8 a.m.	8	1022	3·3	7·50	..	Original diet resumed.
	12 mdnt.– 4 a.m.	20										
	4 a.m. – 8 a.m.	43										
		131·	..	..	..		..	..	..	..		
,, 18.	8 a.m. –12 noon	30	1014	·6888	·72	8 a.m. – 8 p.m.	14·5	1024	3·0	12·35	M. 98·2	
	12 noon – 4 p.m.	55										
	4 p.m. – 8 p.m.	21										
	8 p.m. –12 mdnt.	9	..	·3824	·12	8 p.m. – 8 a.m.	12	1021	2·2	7·5	E. 96·8	
	12 mdnt.– 4 a.m.	7										
	4 a.m. – 8 a.m.	16·5										
		138·5	..	..	·84		26·5	..	..	19·85		

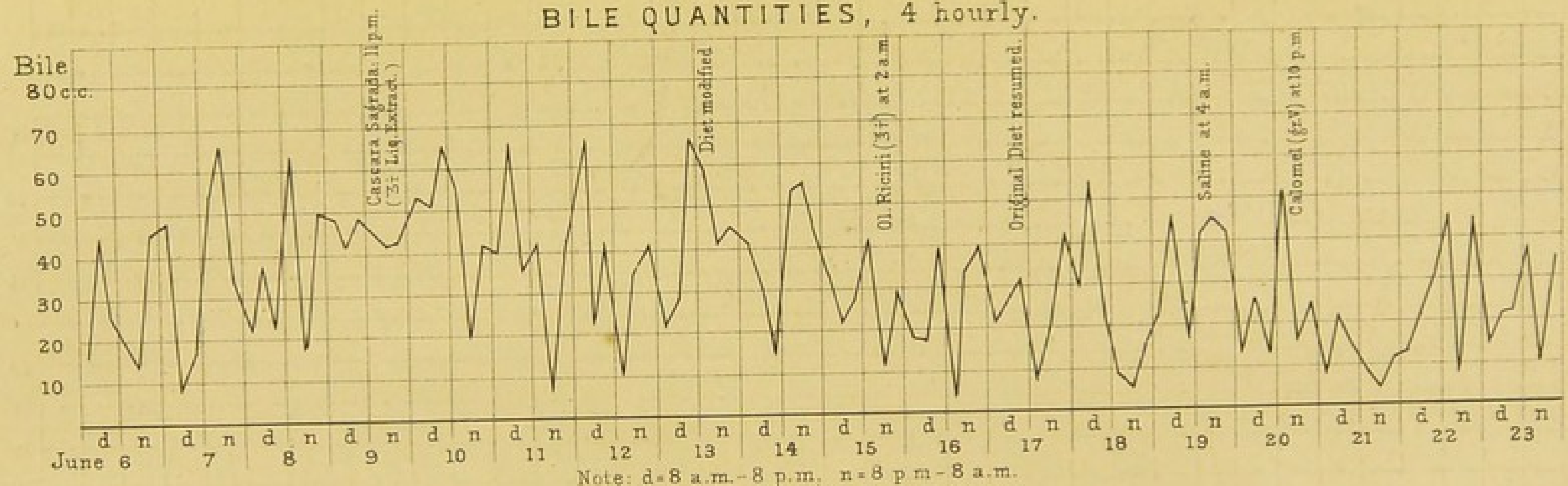
1895. June 19.	8 a.m. -12 noon	23	1013	·8312	·74	8 a.m. - 8 p.m.	12	1024	1·8	6·13	M. 97·4	Sod. sulph. (ʒvi) and Magn. sulph. (ʒiii) at 4 a.m.
	12 noon - 4 p.m.	46·5										
	4 p.m. - 8 p.m.	17·5										
	8 p.m. -12 mdnt.	41·5	1012	·6608	·85	8 p.m. - 8 a.m.	46	1011	·6	7·84	E. 97·6	
	12 mdnt.- 4 a.m.	46·5										
	4 a.m. - 8 a.m.	41										
		216	..	..	1·59		58	..	..	13·97		
,, 20.	8 a.m. -12 noon	13·5	1012	·9376	·49	8 a.m. - 8 p.m.	24	1020	1·5	10·22	M. 98·6	Calomel (gr. v.) at 10 p.m.
	12 noon - 4 p.m.	26										
	4 p.m. - 8 p.m.	13·5										
	8 p.m. -12 mdnt.	51	1013	*	..	8 p.m. - 8 a.m.	20·†	1010	·5	..	E. 98·2	* Lost in analysis. † Some urine lost.
	12 mdnt.- 4 a.m.	15·5										
	4 a.m. - 8 a.m.	24										
		143·5	..	..	..		..	..	..	..		
,, 21.	8 a.m. -12 noon	9	1011	·7072	·32	8 a.m. - 8 p.m.	15	1020	2·3	9·79	M. 98	
	12 noon - 4 p.m.	22										
	4 p.m. - 8 p.m.	15										
	8 p.m. -12 mdnt.	8·5	..	1·0320	·25	8 p.m. - 8 a.m.	16·5	1012	1·1	5·15	E. 97	
	12 mdnt.- 4 a.m.	5										
	4 a.m. - 8 a.m.	11										
		70·5	..	..	·57		..	..	..	14·94		
,, 22.	8 a.m. -12 noon	14	1011	·5936	·39	8 a.m. - 8 p.m.	24	1018	1·5	10·22	M. 97·4	
	12 noon - 4 p.m.	22										
	4 p.m. - 8 p.m.	31										
	8 p.m. -12 mdnt.	46	1013	·7576	·75	8 p.m. - 8 a.m.	18·5	1010	·5	2·62	E. 98·4	
	12 mdnt.- 4 a.m.	8										
	4 a.m. - 8 a.m.	46										
		167	..	..	1·14		..	..	..	12·84		
,, 23.	8 a.m. -12 noon	14	..	·6000	·34	8 a.m. - 8 p.m.	24	1015	·6	4·09	M. 98	
	12 noon - 4 p.m.	21·5										
	4 p.m. - 8 p.m.	22										
	8 p.m. -12 mdnt.	38	..	1·1208	·94	8 p.m. - 8 a.m.	9	..	·5	1·27	E. 98·4	
	12 mdnt.- 4 a.m	10										
	4 a.m. - 8 a.m.	36										
		141·5	..	..	1·28		..	..	..	5·36		

No. 3.

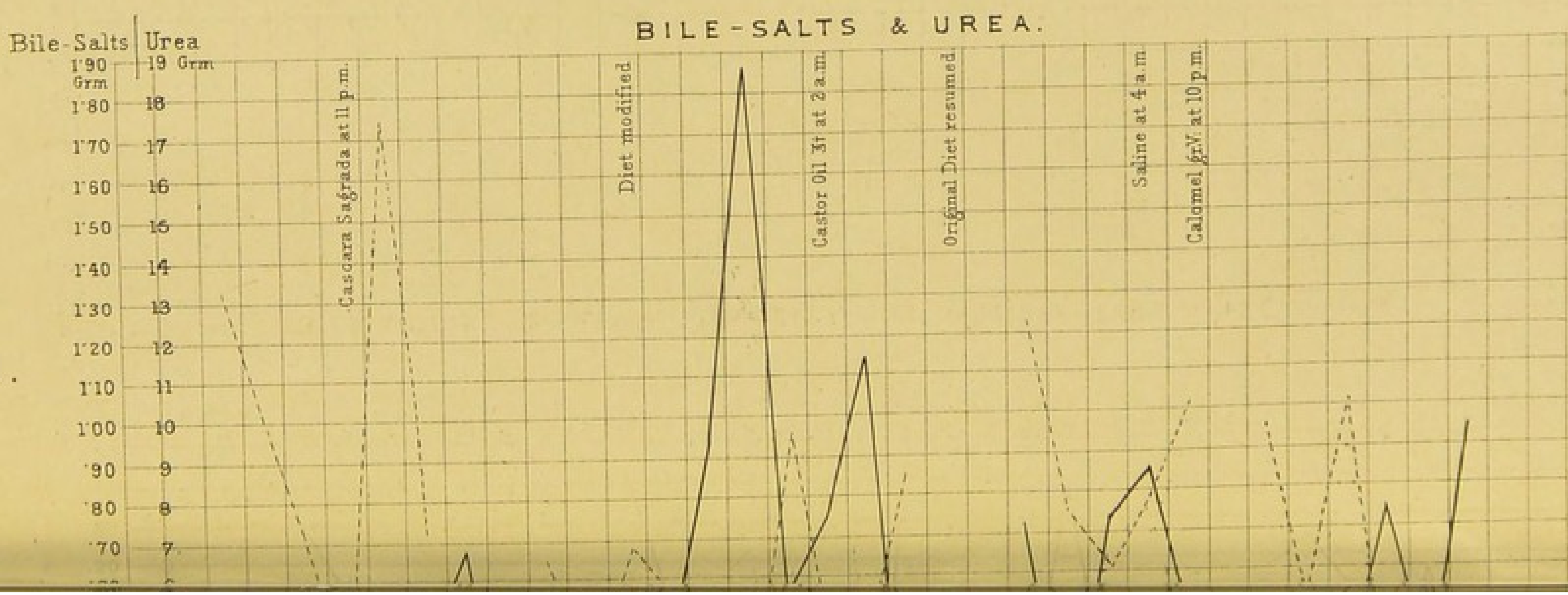


F. Huth, Lith. Edin.

Nº 1.


BILE QUANTITIES, 4 hourly.
Bile 80 c.c.
70
60
50
40
30
20
10
June 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
d n
Cascara Sagrada: 11 p.m. (ʒi Liq. Extract.)
Diet modified
Ol. Ricini (ʒi) at 2 a.m.
Original Diet resumed.
Saline at 4 a.m.
Calomel (gr.V) at 10 p.m.
Note: d=8 a.m.–8 p.m. n=8 p.m.–8 a.m.

Nº 2.


BILE-SALTS & UREA.
Bile-Salts 1·90 Grm
Urea 19 Grm
1·80 18
1·70 17
1·60 16
1·50 15
1·40 14
1·30 13
1·20 12
1·10 11
1·00 10
·90 9
·80 8
·70 7
Cascara Sagrada at 11 p.m.
Diet modified
Castor Oil ʒi at 2 a.m.
Original Diet resumed.
Saline at 4 a.m.
Calomel gr.V. at 10 p.m.

NOTES ON CERTAIN PHYSICAL AND PHYSIOLOGICAL MEASUREMENTS AND ESTIMATES. By JOHN G. M'KENDRICK, M.D., *Professor of Physiology in the University of Glasgow.*

1.—Units { Fractions of an inch.
Millimetre $= \frac{1}{25}$th of an inch.
Micron $= \frac{1}{1000}$ of 1 mm. $= \frac{1}{1000}$ of $\frac{1}{25} = \frac{1}{25,000}$th inch.
Micron $= \mu$.

2.—Diameter of a *molecule* from $\frac{1}{1,000,000}$ to $\frac{10}{1,000,000}$ of a millimetre, or $\frac{1}{25,000,000}$ to $\frac{10}{25,000,000}$ of an inch.
Take diameter at $\frac{1}{2,000,000}$ millimetre or $\frac{1}{50,000,000}$ inch.

3.—Suppose each *biophor* (vital unit of Weismann) to be cubical, and to contain 1000 molecules, that is ten in a row, or $10 \times 10 \times 10 = 1000$. *Then the biophor would measure* 10 molecules in length, or $\frac{1}{2,000,000} \times 10 = \frac{10}{2,000,000}$ or $\frac{1}{200,000}$ mm.

4.—200 biophors would therefore measure $\frac{200}{200,000}$ or $\frac{1}{1000}$ millimetre or 1μ, (micron), or the $\frac{1}{25,000}$ of an inch.

5.—Imagine a cube, one side of which was $1\ \mu$ or $\frac{1}{25,000}$th inch, it would contain $200 \times 200 \times 200 = 8,000,000$ biophors.

6.—A human red blood corpuscle measures about 7·7 μ in diameter and 1·6 μ in thickness: suppose it to be cubed it would contain 3,652,000,000 biophors. As it is not a cube but only a disk 1·6 μ in thickness, it will contain considerably fewer. If we take it as a disk of uniform thickness (1·6 μ) and not biconcave, as it really is, the number of biophors would be 416,000,000.

7.—Smallest particle of matter that can be seen with highest microscopic powers is $\frac{1}{20,000}$ millimetre or $\frac{1}{500,000}$th of an inch.

8.—Each biophor is $\frac{1}{200,000}$ mm. in diameter, so there would be 10 in the $\frac{1}{20,000}$ millimetre, or 1000 in the *cube.*

9.—Average diameter of molecule $= \frac{1}{2,000,000}$ mm.

10.—Smallest visible particle $= \frac{1}{20,000}$ mm. Then there would be in the side of the cube, in a row 100 such molecules, or in the cube $100 \times 100 \times 100 = 1,000,000$ molecules.

11.—A *molecule* of organised matter contains about 50 elementary *atoms.* So that the 1,000,000 molecules in groups of about 50 would number $\frac{1,000,000}{50} = 20,000$ organic particles.

12.—Thus a cube $\frac{1}{20,000}$ mm. would contain about 20,000 organic particles.

13.—Suppose one-half to be water, then there would remain 10,000 organic particles. That is 22 in a row. Each would then be about $\frac{1}{440,000}$ mm.

14.—The organic *molecule* must be 5 times larger at least than a molecule of H.

Molecule of H.	*Organic Molecule.*
$\frac{1}{2.000.000}$ mm.	$\frac{1}{440.000}$ mm.

15.—Smallest visible cube would contain in a row

100 molecules of H.	and	about 22 molecules of organised matter.

16.—Now as 200 biophors $= 1\mu = \frac{1}{1000}$ mm.

Then 1 biophor $= \frac{1}{200.000}$ mm. in diameter.

17.—That is to say the smallest particle of matter visible to the highest microscopic powers,

$\frac{1}{20.000}$ mm.—is $\left\{\begin{array}{l}\text{10 times the diameter or}\\ \text{1000 times the volume}\end{array}\right\}$ of the ultimate vital unit—the biophor $= \frac{1}{200.000}$ mm.

18.—Diameter of a molecule of H $= \frac{1}{50.000.000}$ inch, or $\frac{1}{2.000.000}$ mm.

19.—Smallest *particle* that can be seen microscopically is $\frac{1}{500.000}$ inch, or $\frac{1}{20.000}$ mm.

20.—Smallest ultimate vital unit (biophor) is . . . . . . $\frac{1}{5.000.000}$ inch, or $\frac{1}{200.000}$ mm.

21.—Smallest particle (visible cube) that can be microscopically seen may contain . . . 20,000 organic particles + water.

22.—Smallest ultimate vital unit (biophor) may contain 20 organic particles.

23.—Germinal vesicle is about $\frac{1}{500}$ inch in diameter—or $\frac{1}{20}$th mm.

24.—Germinal vesicle may contain 1,000,000,000,000 biophors.

25.—Head of sperm cell is about $\frac{1}{5000}$ inch in diameter, or $\frac{1}{200}$ mm.

26.—Sperm cell element may contain 1,000,000,000 biophors.

27.—Smallest thing that can be seen with naked eye, $\frac{1}{600}$ inch, or $\frac{1}{24}$ of a mm. *The retinal image at distance of 1 inch from eye would be $\frac{1}{12.500}$ inch, or about 4 wave-lengths of light.*

28.—Germinal vesicle is $\frac{1}{500}$ inch, or $\frac{1}{20}$ of a mm.

29.—Sperm cell is $\frac{1}{5000}$ inch, or $\frac{1}{200}$ of a mm.

30.—Wave-length of green light is $\frac{1}{50.000}$ inch, or $\frac{1}{2000}$ of a mm.

31.—Smallest thing that can be seen with microscope is $\frac{1}{500.000}$ inch, or $\frac{1}{20.000}$ of a mm., or $\frac{1}{10}$th of a wave-length of light.

32.—Ultimate vital unit (biophor) is $\frac{1}{5.000.000}$ inch, or $\frac{1}{200.000}$ of a mm., or $\frac{1}{100}$th of a wave-length of light.

33.—Molecule of organised matter, like albumen, is $\frac{1}{440.000}$ mm., or $\frac{1}{11.000.000}$ inch.

34.—Molecule of hydrogen is $\frac{1}{50.000.000}$ inch, $\frac{1}{2.000.000}$ of a mm., or $\frac{1}{1000}$th of a wave-length of light.

35.—Average wave-length of light, $\frac{1}{50.000}$ inch.

36.—Velocity of light in round numbers :—186,000 miles per second; there are about 62,208 inches per mile; 186,000 × 62,208 = 11,570,680,000 inches per second. 11,570,680,000 ÷ 1/50,000 = 11,570,680,000 × 50,000 = 578,534,000,000,000 vibr. per second falling on retina.

37.—Diameter of a single retinal rod or cone is about $\frac{1}{8000}$th inch.

38.—Length of shortest vibrating hair in the ear, $\frac{1}{1400}$ inch. Diameter about $\frac{1}{4}$ of $\frac{1}{1400} = \frac{1}{5600}$ inch.

39.—Rod or cone $= \frac{1}{8000}$ inch, or $\frac{1}{320}$ mm. Suppose a cube. It might contain 240,000,000 biophors. As the rod or cone is prismatic or cylindrical in shape, the number of biophors—bodies possibly differing as to sensitiveness to light—may be two or three times greater. Groups of such elements of the rod or cone may be differently affected by various wave-lengths.