

Thesis

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The Bile-salts (Glyco- + Taurocholate of Soda) in their Relation to the Excretion of Urea, &c &c.

by G. H. Edington, M.B., Glasg.

The following observations are the result of a research undertaken at the suggestion of W. J. Fleming, Esq, M.D. Surgeon to the Glasgow Royal Infirmary, from a patient in whose hands the material was obtained.

The investigation was carried out in the Physiological Laboratory of the University by the kind permission of Professor McKendrick, & was determined on in view of the small number of observations made during life on the composition of the 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 & also the patient's anxiety to have the fistula closed — these did not exceed 30 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 + Taurocholate of Soda) & that of Urea.

I wish here to express my sincere thanks to Mr Fleming for the opportunities placed at my disposal in his hands, & for the assistance he so freely rendered me in every way, & I have also to thank Prof. McKendrick for his kind permission to work in the Physiological Laboratory, & for the many practical hints he gave me while conducting the Experiments.

The paper is divided under the following headings:—

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VII. References.

I Narrative of the case:

Mrs. McL., aet. 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 suffered for many years back from 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 was awakened 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, & she was sent into hospital. On admission she stated that the bowels had not moved for 3 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 gallbladder, but somewhat lower down than usual.

The abdomen was opened in the ~~middle line~~ right semilunar line, & a freely-movable, sausage-shaped tumour, resembling kidney was pulled into the wound & fixed with suture. A quantity of mucous-like fluid was drawn off by a trocar, after which there was found to be a collection of stones in the sac of the gallbladder. The bowel on being examined, it was not found to contain any of these concretions. After completing the suturing of the bladder to the wound, a dressing was applied. Two days later the sac was opened by incision, the gall stones extracted & a drainage tube inserted through the opening. On the day following, there was a copious discharge of bile from the wound, while a large faecal evacuation followed the administration of an enema of soap water, Castor oil & 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 & 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 the discharge of bile. The faeces, however, were always normally coloured, although somewhat offensive. On one occasion the fistula was tightly plugged with faeces & this was left in

for 24 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 raw edges of gall bladder & stitching the freshened skin-margin over that viscus. The wound healed by first intention & 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, & 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 Mackendrick it was finally resolved to limit the inquiry to the determination of the bile-salts (Glycocholate & Taurocholate of Soda), the influence, if any, on the quantity secreted, of diet, time during the 24 hours, & temperature, & also as to any relation between the percentage of the salts & the amount of 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 24 hours.

III. Methods.

It was determined to collect the bile in the way described by Noël Paton ¹ by means of an india rubber tube connected with a ^{Woulfe's} wolff's bottle, but this ^{was} 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 halfway in so as to assume an hourglass shape. This was not found to be practicable, & finally the end of the tube was made bulbous by introducing a piece of glass tubing within its lumen. This was then passed into the fistula for a distance of 3 or 4 inches, & the tube retained in position by means of gauze strips dipped in collodion & made fast to skin of abdomen. ^(Escape of bile alongside the tube was thus avoided.) Silk threads were also used after the manner of shrouds in rigging. It was not found that the plugging action of the collodion.

igid gauze was perfect, it had to be renewed on several occasions.

The quantity collected was removed from the Wolff's bottle every 4 hrs into a stoppered bottle. This was afterwards measured, + the estimation of the bile-salts made from the total daily (8 AM to 8 PM) + total nightly (8 PM - 8 AM) specimens. The physical appearances, colour etc, of specimens were also noted. The reaction, + specific gravity were taken irregularly, the latter being obtained by means of the common mercury-bull urinometer.

The process^{adopted} for the estimation of the Bile-Salts was as follows + was taken from Sheridan-Lea (5) :-

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

The urine was collected + measured (1) from 8 AM to 8 PM + (2) from 8 PM - 8 AM. In each of these 12-hourly quantities the specific gravity was observed + noted, + from a sample of total daily + total nightly quantity, estimation of urea was made, by means of Gerard'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, etc was kept by the nurses in attendance on the patient.

IV Detailed Statement.

Note: The "day" of 24 hours dates from 8 AM. of the day preceding.

June 6th Quantity of Bile collected :-

8 am - 12 noon	17 cc.	8 pm - 12 midnt.	19 cc
12 noon - 4 pm	45 cc	12 midnt. - 4 am.	15 cc
4 pm - 8 pm	26.5 cc	4 am - 8 am	44 cc
	<u>88.5 cc</u>		<u>78 cc</u>

June 6th contd. The colour throughout was greenish. The urine: 8 am - 8 pm. 15 oz.

Sp. gr. 1014, colour pale yellow. From 8 pm - 8 am 6 oz. sp. gr. 1020.

Diet:-

Cocoa 9 oz.	3/4 slice of bread, + fish	at	8 am.
Whisky 1/2 oz.	Water 3 oz.	-	10.15 am.
Soup 12 oz.	Mince 4 oz.		1 pm.
Soda water 4 oz.			3 pm
Tea 12 oz.	1 slice bread		4 pm
Soda water 4 oz.			8 pm
Whisky 1 oz.	Water 3 oz.		9 pm.
Cocoa Cocoa 10 oz.	1/4 slice bread, + butter		4 am
Whisky 1 oz.	Water 1 oz.		6.30 am.

She had at 2 am. Castor oil 1/2 oz + Potash water 1 oz.

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

June 7th Quantity of bile:-

8 am. to 12 noon	48 cc	Colour.	Greenish yellow
12 noon - 4 pm.	9 cc		lighter.
4 pm - 8 pm	17 cc		"
8 pm - 12 midnight.	55 cc		"
12 mid. - 4 am	66 cc		green + hazy.
4 am. - 8 am	36.5 cc.		Greenish yellow: clear.
	231.5 cc.		

Urine: 8 am - 8 pm 14 oz. sg. 1024.
 8 pm - 8 am 12 oz. sg. 1022.
 26 oz.

Diet ordinary.

June 8th Quantity of bile:-

8 am - 12 noon	22 cc	Color	Yellow: greenish tint	} .0450 gram. Salts in 25 cc.
12 noon - 4 pm	38		Pale yellow	
4 pm - 8 pm	22		"	} = .1800 gram per 100 cc.
8 pm - 12 mid	63		Darker, greenish, hazy	
12 mid - 4 am	18.5		Lighter color, hazy	} .0161 gram. Salts in 25 cc
4 am - 8 am	58		Very dark green	
	213.5 cc.			} = .0644 gram. per 100 cc.

June 8 (cont) Urine: 8am - 8pm 13oz. S.g. 1024. % Urea 3.6.
 8pm - 8am 10oz. S.g. 1025. " " 3.5.
 23oz.

Diet. Ordinary.

Patient says she now feels quite comfortable as regards tubing etc.

June 9th Quantity of bile:

8 am - 12 noon	49 cc	faint greenish tint	} 0.412 gramme Salts in 25 cc. = 1.648 gram per 100 cc.
12 noon - 4 pm	42 "	" " "	
4 pm - 8 pm	49 "	Very faint green	
8 pm - 12 mid.	45.5 "	Golden yellow	} 0.750 gramme Salts in 25 cc. = 3.000 gramme per 100 cc.
12 mid. - 4 am	42 "	darker - " - mucus	
4 am - 8 am	43.75 "	Still darker, mucus	
271.25 cc.			

Urine 8am - 8pm 9oz. sp. gr. 1030. Clear yellow, with deposit of mucus. % 2.8.
 8pm - 8am 8oz. sp. gr. 1015 " " mucous sediment. " " 1.6.

Diet ordinary.

June 10th Quantity of bile:

8 am - 12 noon	57.5 cc	yellow, greenish tint	} 1.216 gramme Salts in 50 cc. = 2.432 gramme per 100 cc.
12 noon - 4 pm	57 "	lighter.	
4 pm - 8 pm	65 "	greenish + opaque	
8 pm - 12 midnt!	53 "	Yellowish green	} 1.792 gramme Salts in 50 cc. = 3.584 gramme per 100 cc.
12 midnt. - 4 am	20.5 "	Light yellow.	
4 am - 8 am	42.5 "	Clearer, yellow.	
285 cc.			

Urine 8am - 8pm 15oz Sg. 1020 Urea % 3.4
 8pm - 8am 15oz. Sg. 1015 " " 1.7.

Diet ordinary. Bowels moved after exhibition of Ascaris: motion dark + apparently normal.

June 11th Quantity of bile:

8 am - 12 noon	40 cc	Greenish golden.	} 2.441 gramme Salts in 50 cc. = 4.882 gramme per 100 cc.
12 noon - 4 pm	66 "	darker, hazy.	
4 pm - 8 pm	36 "	Golden greenish.	
8 pm - 12 midnt.	42 "	" hazy.	} 0.292 gramme Salts in 50 cc. = 0.584 gramme per 100 cc.
12 midnt. - 4 am	7.5 "	Clear yellow	
4 am - 8 am	40 "	Dark greenish, hazy	
231.5			

Innell (Contd.) Urine 8am - 8pm 9oz. 1022 sp. Some lost: pringative having been taken 1% 2.5
 8pm - 8am 8oz. 1015 " " " " " " 1.7.

Diet ordinary. Bowels still moving after exhibition of ascaras. Soft, dark colored, motions, having bad odour.

June 12th, Quantity of bile:

8am - 12 noon	65 cc.	Orange, hazy	} .0577 Gram. Salts in 50 cc. = .1034 Gramme per 100 cc.
12 noon - 4 pm	22 "	Clear Golden	
4 pm - 8 pm	42 "	Golden: slightly hazy	} .0299 Gramme Salts in 50 cc. = .0598 Grammes per 100 cc.
8 pm - 12 midnt.	11.5 "	Greenish, hazy	
12 midnt - 4 am	35 "	" hazier	} .0598 Grammes per 100 cc.
4 am - 8 am	42 "	Still dark green	
2 17.5 cc.			

Urine 8am - 8pm 9oz. Sp. gr. 1020. Urea % 2.6
 8pm - 8am 12oz. " " 1012 " " 1.1

Diet ordinary, but is to be altered tomorrow, substituting farinaceous food for flesh meat at dinner. Since yesterday the following has been eaten up to 8am this morning:-

- Cocoa 14 oz., 1 slice toast, + fish at 8 am
- Sodalwater 2oz. " 12 noon
- Soup 14oz. Pieces of chicken 1/2 slice bread " 1 pm.
- Sodalwater 2oz. " 2 pm
- Tea 8oz. 1 slice of bread " 4.30 pm
- Whisky 1oz. Water 2oz + biscuit " 9 pm.
- Cocoa 12oz. 1 slice bread " 4 am
- Whisky 1oz. Water 1oz. " 6.30 am

June 13th Quantity of bile:

8am - 12 noon	21 cc.	Greenish, hazy.	} .0365 Gramme Salts in 50 cc. = .0730 Gramme per 100 cc.
12 noon - 4 pm	28 cc	Golden: clearer	
4 pm - 8 pm	65 "	Slightly greenish, hazy.	} .1410 Gramme Salts in 50 cc. = .2820 Gramme per 100 cc.
8 pm - 12 midnt.	57 "	" " "	
12 midnt. - 4 am	41 "	Dark greenish "	} .2820 Gramme per 100 cc.
4 am - 8 am	45 "	" " "	
2 57			

Urine 8am - 8pm 22 oz. sp gr. 1014 Urea % 1.1
 8pm - 8am 25 1/2 oz. " " 1012 " " .8 Deposit of urates.

June 13 (cont.) Diet. The following represents dietary since 8 am yesterday:-

- Cocoa 14 oz., 1 slice bread, fish at 8 am.
- Water 2 oz. " 9 am
- Rice + milk 14 oz. " 1 pm
- Whisky 1 oz. Water 2 oz. Biscuit. " 9 pm
- Cocoa 12 oz. 1/2 slice toast " 4 am
- Whisky 1 oz. Water 1 oz. " 6 am.

June 14 Quantity of Urine:

8 am - 12 noon	4.5	greenish yellow, hazy	} 2695 Gramme <u>Salts</u> in 25 cc. = 10780 Gramme per 100 cc
12 noon - 4 pm	3.5	Clear golden yellow.	
4 pm - 8 pm	15	" " "	
8 pm - 12 midnt.	5.3	pale green, hazy	} 3072 Gramme <u>Salts</u> in 25 cc. = 12288 Gramme per 100 cc.
12 midnt. - 4 am	5.4	Dark green "	
4 am - 8 am	4.6	Still darker "	
241 cc.			

Urine: 8 am - 8 pm 23 oz. 1012 Urea % 6
 8 pm - 8 am 8 oz. " 1012 " " 1.3

Diet as yesterday.

June 15 Quantity of Urine:

8 am - 12 noon	34 cc	greenish orange, slight haz.	} 1684 gm. <u>Salts</u> in 25 cc. = 6736 gm per 100 cc.
12 noon - 4 pm	22	" " "	
4 pm - 8 pm	28	" " clearer	
8 pm - 12 midnt.	42	" " hazy	} 2296 gm. <u>Salts</u> in 25 cc. = 9184 gm. per 100 cc.
12 midnt. - 4 am	11	Greener, hazy	
4 am - 8 am	30	Greener still, very hazy.	
167 cc.			

Urine 8 am - 8 pm 20 oz. 1015 Urea % 1.7
 8 pm - 8 am 8 oz. 1012 Somelost when bowels being moved.

Diet as yesterday.

At 2 am. 103 Castor oil administered.

June 16th Quantity of Urine:

8 am - 12 noon	17.5	Greenish tint, hazy.	} = 3.780 grammes Salts in 25 cc	
12 noon - 4 pm	17.5	" " "		} = 1.5120 grammes in 100 cc.
4 pm - 8 pm	40	Orange - hazy		
8 pm - 12 midnt.	3.5	Yellow, hazy	} = 0.250 grammes Salts in 25 cc	
12 midnt. - 4 am	33.25	Light yellow, hazy		} = 1.000 Grammes in 100 cc.
4 am - 8 am	40	Orange, hazy		
<u>151.75 cc.</u>				

Urine 8 am - 8 pm 12 oz. sg. 1022. Urea % 1.4.
 8 pm - 8 am 15 oz. sg. 1018 " " 2.5,

Diet same as yesterday.

June 17th Quantity of Urine:

8 am - 12 noon	21 cc	Clear golden.	} Unfortunately the urine for to-day was thrown out before the Estimation had been made.
12 noon - 4 pm	27	Golden, slight haze.	
4 pm - 8 pm	32	" clearer	
8 pm - 12 midnt.	8	" hazy	
12 midnt. - 4 am	20	Bright orange "	
4 am - 8 am	<u>43</u>	Greenish "	
<u>151 cc</u>			

Urine: 8 am - 8 pm ? oz. S.g. 1025. Urates deposited 2.3% Urea
 8 pm - 8 am 8 oz. " " 1022 3.3% "

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

June 18th Quantity of Urine:

8 am - 12 noon	30 cc	Golden greenish; hazy	} = 1.722 gm. Salts in 25 cc	
12 noon - 4 pm	55 cc	dark green -		} = 6.888 gm. in 100 cc.
4 pm - 8 pm	21	Clear golden yellow.		
8 pm - 12 midnt.	9	Golden, hazy	} = 0.956 gm. Salts in 25 cc.	
12 midnt. - 4 am	7	" "		} = 3.824 gm. per 100 cc.
4 am - 8 am	<u>16</u>	" "		
<u>138 cc</u>				

Urine 8 am - 8 pm 14.5 oz. sg. 1024. Urea % 3.5. Urates deposited
 8 pm - 8 am 12 oz. sg. 1021 " " 2.2.

Diet ordinary mixed.

June 19th Quantity of bile:

8 am - 12 noon	23 cc.	Orange, hazy.	} 2078 gm. Salts in 25 cc.
12 noon - 4 pm	46.5 cc	" clearer	
4 pm - 8 pm	17.5 "	" "	
8 pm - 12 midnt.	41.5 "	" Getting hazy	} 1652 gm. Salts in 25 cc.
12 midnt - 4 am	46.5 "	Dark green & opaque	
4 am - 8 am	41 "	" " "	
	<u>216 cc.</u>		

Urine: 8 am - 8 pm 12 oz. sp. 1024 Urea % 1.8
 8 pm - 8 am 46 oz. " 1011 " " .6

Diet, ordinary mixed.

A saline aperient consisting of Sulphate of magnesia (3iii) + Soda (3vi) given at 4 am., but was vomited at 4.10 am. On our visiting the patient at 9 o'clock this morning, she is found greatly depressed & wanting 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-corpuses entangled in it. This may have come from the mucous membrane of the full bladder having been injured by tube while the patient was vomiting. No action of 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 am - 12 noon	13.5 cc	Green, hazy	} 2344 gm. Salts in 25 cc.
12 noon - 4 pm	26 "	Golden, slightly hazy	
4 pm - 8 pm	13.5 "	" " "	
8 pm - 12 midnt.	57 "	Bright golden, Clear.	} Specimen lost during analysis.
12 midnt. - 4 am	15.5 "	" " hazy	
4 am - 8 am	24 "	" " "	
	<u>143.5</u>		

Urine: 8 am 8 pm 24 oz. sp. 1020 Urea % 1.5
 8 pm 8 am 20^{*} oz. sp 1010 Urea % .57. * Some of urine lost.

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

June 21st Quantity of bile:

8am - 12 noon.	9 cc.	orange, hazy	} 1.768 gm. Salts in 25 cc.
12 noon - 4 pm	22 "	" clear	
4 pm - 8 pm	15 "	" "	} = 1.9072 gm in 100 cc.
8 pm - 12 midnt.	8.5 "	" "	
12 midnt. - 4 am	5 "	" "	} 1.290 gm. Salts in 12.5 cc
4 am - 8 am	11 "	" "	
<u>70.5 cc.</u>			= 1.0320 gm. in 100 cc.

Urine 8am - 8pm 1503. sg. 1020 Urea % 2.3
 8pm - 8am 16.503. sg. 1012 " " 1.1

Diet ordinary mixed.

June 22nd Quantity of bile:

8am - 12 noon.	14 cc	Faint greenish, hazy.	} 1.484 gm. Salts in 25 cc.
12 noon - 4 pm	22 "	Yellowish, clearer	
4 pm - 8 pm	31 "	" "	} = 1.5936 gm. in 100 cc.
8 pm - 12 midnt.	46 "	" Clearer still	
12 midnt - 4 am	8 "	" " "	} 1.894 gm. Salts in 25 cc
4 am - 8 am	16 "	Dark golden, clear	
<u>167 cc.</u>			= 1.7576 gram in 100 cc.

Urine: 8am - 8pm 2403. sg. 1018 Urea % 1.5
 8pm - 8am 18.503. sg. 1010 " " .5

Diet: ordinary mixed.

June 23rd Quantity of bile:

8am - 12 noon	14 cc	golden, hazy.	} 1.500 gm Salts in 25 cc
12 noon - 4 pm	21.5 "	paler.	
4 pm - 8 pm	22 "	" -	} = 1.6000 gm in 100 cc
8 pm - 12 midnt.	38 "	golden, hazy.	
12 midnt. - 4 am	10 "	" "	} 2.802 gm. Salts in 25 cc
4 am - 8 am	36 "	dark greenish, very hazy	
<u>141.5 cc.</u>			= 1.1208 gm. in 100 cc.

Urine 8am - 8pm 2403. sg. 1015 Urea % .6
 8pm - 8am 903. " " .7

Diet ordinary mixed.

V. General Conclusions:

The following points present themselves for consideration, & will be briefly noted :-

A. Quantity of Bile	(a) Secreted in 24 hours.	p. 13.
	(b) Relation to time of day	p. 13.
	(c) Relation to food { i meal hours	p. 14.
	ii nature of food	p. 14.
	(d) Relation to drugs.	p. 14.
	(e) Relation to quantity of urine.	p. 15.
	(f) Relation to Temperature.	p. 15.
B. Colour of Bile.		p. 15.
C. Specific Gravity.		p. 16.
D. Reaction.		p. 16.
E. Bile Salts.	(a) Time of day or night.	p. 16.
	(b) Relation to diet.	p. 16.
	(c) Relation to drugs.	p. 17.
	(d) Relation to Urea	p. 17.
	(e) Temperature.	p. 17.
Summary.		p. 18.

A (a) Quantity secreted in 24 hrs. :

This varies between wide limits. The minimum quantity was collected on the 21st June, viz. 70.5 cc, while the maximum occurred on the 10th of same month, viz. :- 285.5 cc. The average daily quantity over 18 days, is 191.22 cc.

Bearing in mind (p.3.) that there was reason to suppose a free escape into the intestine, the above figures of course are not indicative of the total secretion.

B) Relation to 4 hourly period of 24 hrs. at which collected :

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

June 6 th	45 cc.	12 noon - 4 pm
" 7 th	66	12 midnt. - 4 am
" 8 th	63	8 pm - 12 midnt.
" 9 th	49	8 am - 12 noon
" 10 th	65	4 pm - 8 pm
" 11 th	66	12 noon - 4 pm
" 12 th	65	8 am - 12 noon
" 13 th	65	4 pm - 8 pm
" 14 th	54	12 midnt. - 4 am
" 15 th	42	8 pm - 12 midnt.
" 16 th	40	4 pm - 8 pm 4 am - 8 am
" 17 th	43	4 am - 8 am
" 18 th	55	12 noon - 4 pm
" 19 th	46.5	12 noon - 4 pm 12 midnt. - 4 am
" 20 th	57	8 pm - 12 midnt.
" 21 st	22	12 noon - 4 pm
" 22 nd	46	8 pm - 12 midnt. 4 am - 8 am
" 23 rd	38	8 pm - 12 midnt.

in preceding pages
From these figures the following
Average has been arrived at :-

8 am. - 12 noon	29.50 cc
12 - 4 pm	33.50 .
4 - 8 pm	30.90 .
8 - 12 midnt.	36.02 .
12 - 4 am	25.31 .
4 - 8 am	37.62 .
<u>Average in 24 hrs.</u>	<u>192.85 cc.</u>

Average maximum - 4-8 am
" minimum - 12-4 am

These figures show the maximum quantity secreted 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 pm on 5 occasions, & for a similar number of times from 8 pm. to 12 midnt. On 3 occasions each the maximum noted as occurring at the following periods: 12 midnt. to 4 am, 4 pm - 8 pm, & 4 am - 8 am, while from 8 am - 12 noon, we have the maximum flow on 2 occasions only.

In addition, it is found that (6x) on one occasion the maximum flowed occurred 4 pm - 8 pm & 4 am - 8 am on the same day.

- (B) On another at 12 noon to 4 pm, + 12 midnt - 4 am,
 (C) And again, at 8 pm to 12 midnt. + 4 am - 8 am.

(C.) Relation to taking of food:

(i) Meal hours: Breakfast: 8 am. On 5 occasions maximum flow occurred from 12 noon to 4 pm, but on one of these, an equal flow was observed from 12 midnight to 4 am. Maximum occurred twice from 8 am to 12 noon.

Dinner: 1 pm. Again, maximum noted as occurring from 12 noon to 4 pm. on 5 occasions.

Tea: 4 pm. Maximum on 3 occasions from 4 pm - 8 pm, but on one of these there was an equal flow from 4 am to 8 am. These observations do not bear out the existence of a relationship between the taking of food + the secretion of bile.

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

(d.) Drugs:

(i) At 2 am. on 6th June, Caster oil, $\frac{1}{2}$ oz, taken. From 12 midnt. to 4 am 15 cc. bile collected, while from 4 - 8 am, 44 cc, from 8 am to 12 noon, 48 cc.

(ii) At 11 pm on 8th June, Cascara sagrada (Liq. Extract. 3i) administered. For each period of this 24-hours-day the quantity remained between 40 + 50 cc & no marked effect in quantity, seems to have followed the exhibition of this laxative.

(iii) At 2 am. on the 15th Caster oil 1 oz, administered. On the following 24 hrs. the quantity of bile seems to be somewhat below the usual, keeping for the most part under 40 cc + at 12 midnt dropping to 3.5 cc.

(iv) Saline aperient (Magnes. Sulph. 3iii, Sod. Sulphas 3vi) given at 4 am. on the 19th. From 8 am - 8 pm there was a decided drop in the quantity collected. At 12 midnt it had risen to 50 cc. (Calomel grs. V having been administered at 10 pm). 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 cc. 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 it passed into the active intestine than when the viscera were in a state of rest.

(e.) Urine :-

On reference to Chart No 3, it will be seen so far as is shown — the urine having been lost occasionally, as after purgatives —, that there is a relation between the quantity of this secretion & that of bile. Where the bile-register keeps high, & more or less uniform, the urine keeps low & 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.

(f.) Temperature :

We lastly come to consider the relation, if any, between the patient's body-temperature & the quantity of bile ~~secreted~~ collected. Throughout the time during which the observation was being carried on the temperature showed very little oscillation, & any there is can hardly be said to bear any relation to the bile-curve.

B. Colour of Bile :

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

Drugs seem to influence this :- Cascara, 11 p.m. on 9th June. Darkening of colour of night-specimens to greenish, to be followed in a day or so by orange yellow bile, after which the greenish color is 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 color is dark green & opaque. While after Calomel on evening of 19th the bile is golden & clear, on to the 22nd of June. By the 23rd, returning to general condition of dark greenish, hazy in the morning.

ministers on account of the Salts having been vomited, & was followed by a lively catharsis. Analysis for 21st is as follows:-

Morning = .32 gm. Evening = .25 gm.

There is slight ^{rise} fall on succeeding day to .39 + .75 for morning & evening respectively. The 23rd = morning, .34 gm. Evening .94 gm.

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

(c) Drugs:-

The administration of Ol. Ricini is followed by an increase & subsequent decrease in the quantity of the Salts, although when looking at percentages, there is a decrease followed by increase. The saline seems to have had but little effect on the Salts, while unfortunately that of Calomel cannot be ascertained. Judging from other parts of the chart, the fall on the 21st might indicate a rise on the 20th.

(d) Relationship to Urea:-

This is shown in a marked way in Chart No. 2, in which the tracings of urea & bile salts are compared. As the ~~percentage~~ ^{percentage} of Salts rises, there is almost invariably a fall in urea, while the converse is true also. 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 total gly. of salts is considered, similar results obtain.

(e) Temperature:

Same remarks apply here as on p. 15, when the temperature notes are compared with quantity of bile excreted.

N.B. Bile decomposed easily 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 Am, minimum 12-4 Am.
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 a diminished discharge from the fistula. Does none 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, & is succeeded by change to golden-yellow.
9. Specific fairly 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 an increase of salts. On resumption of flesh meat, the salts do not drop to former level.
13. Effect of drugs on salts is not satisfactorily determined.
14. There is very distinct inverse relation of salts to excretion of urea.
15. Antisepticity low.

VI Comparison with other observers.

The variation in quantity excreted is mentioned by others. Our observations as to

① Average maximum & minimum do not agree with those of Paton & Balfour. ①

	<u>Paton & Balfour.</u>	<u>Present observations.</u>
8 am 12	106.0 cc	29.50
12 - 4 pm	140.5 .	33.50
4 - 8 pm	102.0 .	30.90
8 - 12	100.6 .	36.02
12 - 4 am	88.5 .	25.31
4 - 8 am	116. .	37.62

② Copeman & Winston ② find rate of secretion least at 5 am, & greatest at 12 noon & this they attribute to the taking of food. The researches of Yso & 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

③

may be obtained in Hospital where meals are frequent + moderate, yet a different state might obtain where meals were larger + 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 bile secreted, + his results point to a diminution in quantity following the administration of Chologogues, agreeing with our experience with purgatives.

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

	Jacobsen	Yeo + Herroon	Copeman + Winston	Robson.	Paton + Balfour	Present Case.
Sod. Glycochol.	1.01	.165	} .628	.751	.356	} .524.
" Jaurochol.	-	.055		.009	.049	

Paton + Balfour.		Present Case	
8am - 8pm	8pm - 8am	8am - 8pm	8pm - 8am
.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 on comparing with the urea excreted, + this seems to be in agreement with the results of Hunkel + Spiro⁽⁶⁾ (quoted by Bunge) who show that only a small part of Nitrogen + Sulphur resulting from proteid metabolism appears in bile. Mayo Robson, + Paton⁽⁷⁾ + Balfour agree as to excrementitious nature of the bile, + Zweifel (quoted by Bunge) declares that the bile must to a certain extent be excretory, seeing that it is formed during the 3rd month of embryonic life, whereas secretions from other glands for intestinal tract begin after birth, on taking of food.

Most are agreed on the low antisepticity of bile.

		Bile				Urine				Remarks			
Date	Hour	Styp. cc.	Sp. gr.	Salts		Hour	Styp.	Sp. gr.	Urea				
				Pa cent	Total				Pa cent		Total		
1895 June 10	8am 12	57.5		2432	.40	8am 8pm	15	1020	3.4	14.48	M 978	Factions passed, dark brown color bad odor, apparently normal.	
	12 4pm	51				8pm 8am	15	1015	1.7	7.24	F 978		
	4pm 8pm	65					30			21.72			
	8pm 12	53					8am 8pm	9*	1022	2.5	-		M 976
	12 4am	20.5					8pm 8am	8*	1015	1.9	-		F 984
	4am 8am	42.5											
		285.5			.81								
11	8am 12	40		4882	.68	8am 8pm	9*	1022	2.5	-	M 976	* Some lost	
	12 4pm	66				8pm 8am	8*	1015	1.9	-	F 984		
	4pm 8pm	36					17						
	8pm 12	42											
	12 4am	7.5											
	4am 8am	40			.04								
		231.5			.72								
12	8am 12	65		1034	.12	8am 8pm	9	1020	2.6	6.64	M 972	Diet modified.	
	12 4pm	22				8pm 8am	12	1012	1.1	3.74	F 98		
	4pm 8pm	42					21			10.38			
	8pm 12	11.5											
	12 4am	35											
	4am 8am	42			.0598								
		217.5			.16								
13	8am 12	21		.0730	.07	8am 8pm	22	1014	1.1	6.87	M 972		
	12 4pm	28				8pm 8am	25.5	1012	.8	5.79	F 966		
	4pm 8pm	65					47.5			12.66			
	8pm 12	57											
	12 4am	41											
	4am 8am	45			.47								
		257			.47								

Date	Bile		Salts		Hour	Qty	Sp. gr.	Urea		Temp. (°C)	Remarks.	
	Hour	Qty in cc	Sp. gr.	Per cent				Total	Per cent			Total
1895 June 14	8-12 12-4pm 4p-8pm 8pm-12 12-4am 4-8am	41.5 31.5 15.0 53.0 54.0 46.0		1.0780	94	Sam Spm	23	1012	6	3.91	M 968	
			1.2288	1.86		Spm Sam	8	1012	1.3	2.95	F 966	
		2.41		2.80			31			6.86		
15	8am-12 12-4pm 4-8pm 8-12 noon 12-4am 4-8am	34 22 28 42 11 30	1011	.6736	.56	Sam Spm	20	1015	1.7	9.65	M 997	Castor Oil (3i) at 2 am.
			1013	.9184	.75	Spm Sam	8*	1012	2	4.54	F 998	* Some lost.
		1.67		1.31						14.19		
16	8-12 12-4pm 4-8pm 8-12 12-4am 4am-8am	17.5 17.5 40.0 38 33.25 40.0	1012	1.5720	1.13	Sam Spm	12	1022	1.4	4.77	M 997	
			1014	1.000	.07	Spm Sam	15	1018	2	8.57	F 968	
		1.57.75		1.20						13.28		
17	8-12 12-4pm 4p-8pm 8-12 12-4am 4am-8am	21.0 27.0 32.0 8.0 20.0 43.0	1011	-	*	Sam Spm	-	1025	2.3	-	-	* Bile thrown out by mistake, before analysis.
			1012	-	-	Spm Sam	8	1022	3.3	7.50	-	Original diet resumed.
		131.0		-	-					-		

Date	Bile					Urine					Remarks	
	Hour	Alp. i. ce.	Sp. gr.	Salts		Hour	Qty	Sp. gr.	Urea			Temperature
				Per cent	Total				Per cent	Total		
1895 June 18 th	8am-12	20	1014	.6888	.72	8am-8pm	14.5	1024	3.0	12.35	M	98.2
	12-4pm	53										
	4-8pm	21										
	8-12	9										
	12-4am	7										
	4-8am	16.5										
		138.5			.84		26.5			19.85		
19 th	8am-12	23	1013	.8312	.74	8am-8pm	12	1024	1.8	6.13	M	97.4
	12-4pm	46.5										
	4-8pm	17.5										
	8-12	41.5										
	12-4am	46.5										
	4-8am	41				46	1011	.6	7.84	R	97.6	
		246.0			1.59		58			13.97		
20 th	8am-12	13.5	1012	.9376	.49	8am-8pm	24	1020	1.5	10.22	M	98.6
	12-4pm	26.0										
	4-8pm	13.5										
	8-12	57.0										
	12-4am	15.5										
	4-8am	24.0					1010	.5	-	F	98.2	
		143.5			-					-		
21 st	8am-12	9.0	1011	.7072	.32	8am-8pm	15	1020	2.3	9.79	M	98
	12-4pm	22.0										
	4-8pm	15.0										
	8-12	8.5										
	12-4am	5.0										
	4am-8am	11.0				16.5	1012	1.1	5.15	R	97	
		70.5			1.0320							
					.57					14.94		

Sulphate of Soda (3rd) Magnesia (3rd) at 4 am.

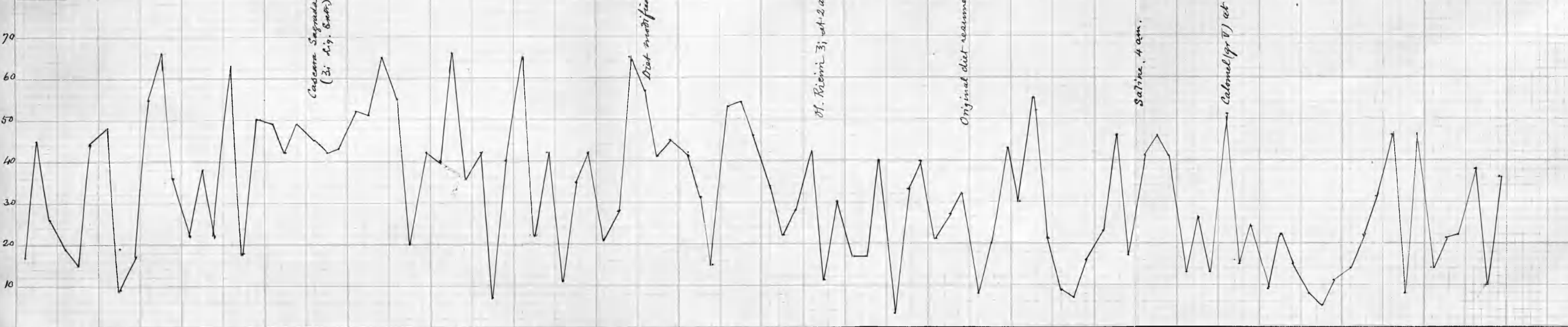
Calomel (gr V) at 10 pm.

*: Lat in analysis.
 **: Some urine lost

Date	Bile				Urine				Remarks	
	Hour	Qty. cc.	Sf. gr.	Salts	Hour	Qty.	Sf. gr.	Urea		
			Per cent	Total				Per cent	Total	
1895	8-12	14			San 8pm	24	1018	1.5	10.22	974
June 22	12-4 pm	22	1011	.5736	.39	24	1018	1.5	10.22	M 974
	4-8 pm	31								
	8-12	46								
	12-4 am	8								
	4-8 am	46	1013	.7576	.75	San 8 am	185	1010	2.62	F 984
		167							12.84	
23	8-12	14.0	1015	.6000	.34	San 8 pm	24	.6	4.09	M 98.
	12-4 pm	21.5								
	4-8 pm	22.0								
	8-12	35.0								
	12-4 am	10.0								
	4-8 am	36.0	1.1208	.94	8 pm San	9	.5	1.27	F 984	
		141.5		1.28					5.36	

Bile Quantities: - 4-hourly.

cc Bile



Casenum Sagrada
(3i dig. 60gr)
11 pm.

Diet modified

St. Riemi 3i at 2 am

Original diet resumed

Saline, 4 am.

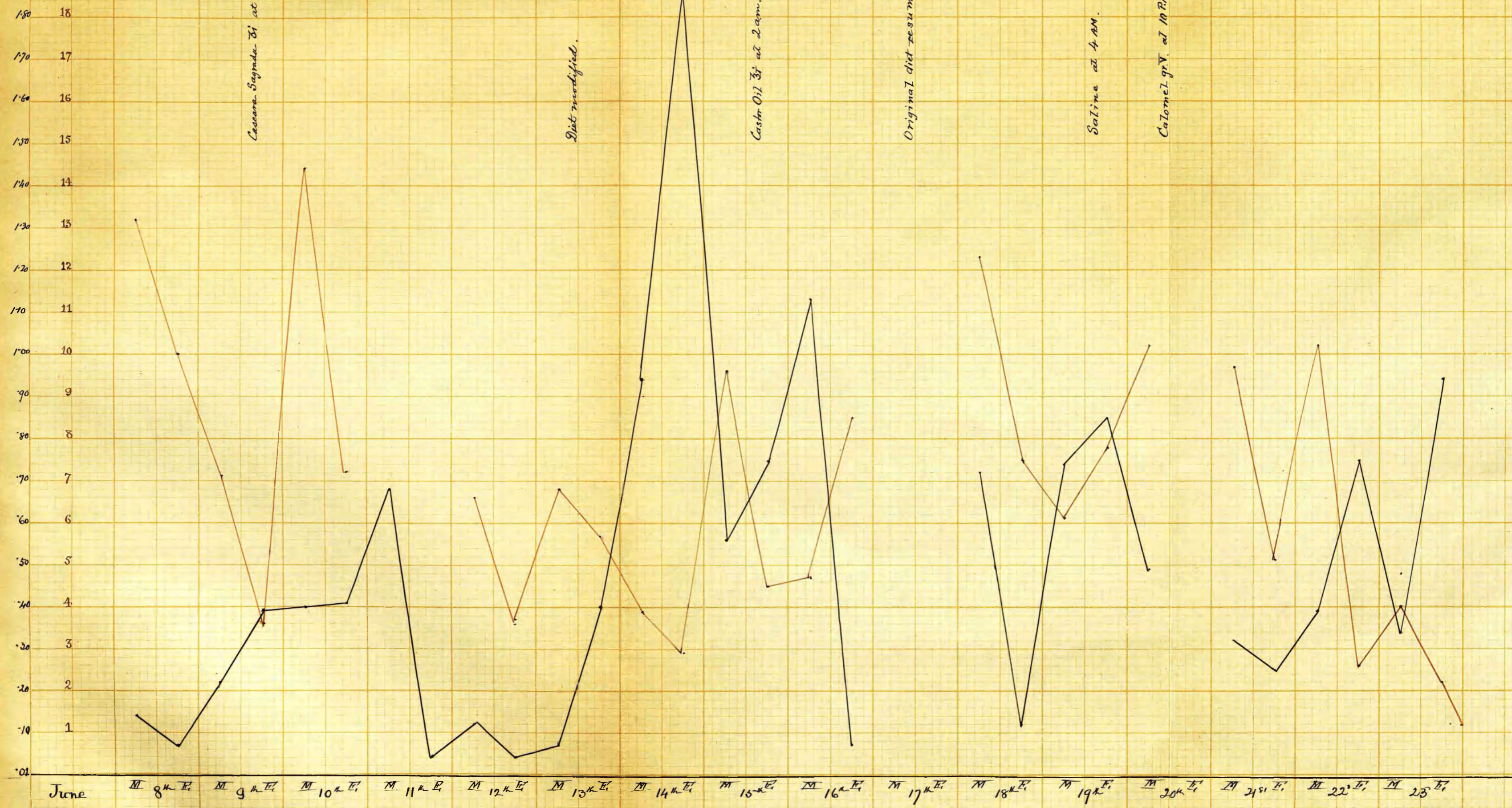
Calomel (gr V) at 10 pm.

June 6^d n 7ⁿ 8ⁿ 9ⁿ 10ⁿ 11ⁿ 12ⁿ 13ⁿ 14ⁿ 15ⁿ 16ⁿ 17ⁿ 18ⁿ 19ⁿ 20ⁿ 21ⁿ 22ⁿ 23ⁿ

Note { d = 8 am - 8 pm
 n = 8 pm - 8 am

Bile - Salts & Urea.

196 Grm. Urea.
Bile Salts.



Caecora Sagnata Bi at 11 pm.

Diet modified.

Castor Oil 3i at 2 am.

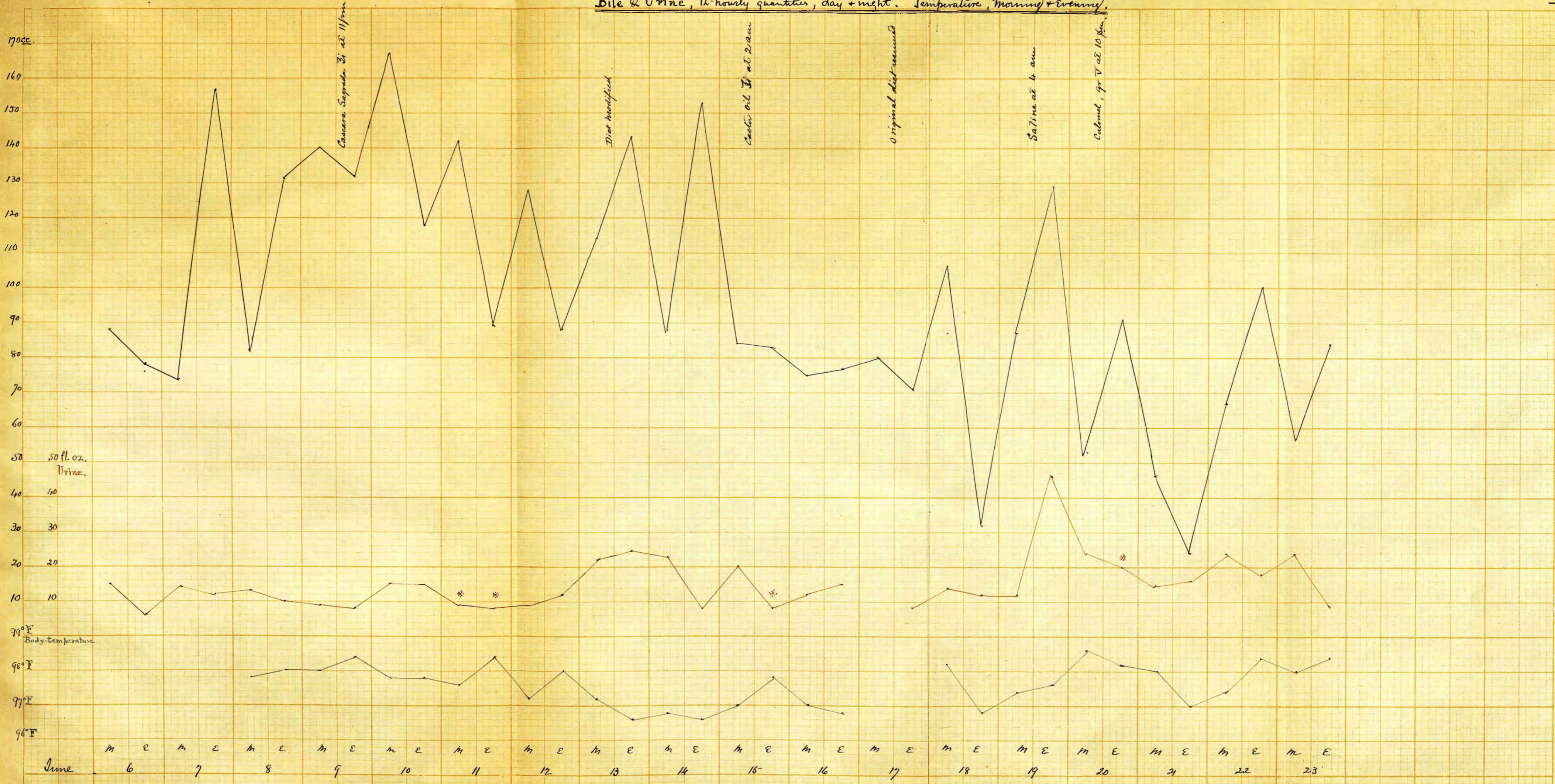
Original diet resumed.

Saline at 4 AM.

Calomel gr. V. at 10 P.M.

NOTE: M = 8am-8pm. E = 8pm-8am

Bile & Urine, 12-hourly quantities, day + night. Temperature, morning + evening.



Regards Bile & Urine M = 8 am - 8 pm, E = 8 pm - 8 am. * Some Urine lost.



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