

Thesis for the degree of Doctor of Medicine.

CLINICAL LABORATORY TESTS

in relation to

DISEASES of the SKIN.

GLASGOW, March, 1927.

Mary Sloan Smith.

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I N T R O D U C T I O N .

The investigations for this thesis suggested themselves from several papers on blood chemical analysis and urine analysis in relation to diseases of the skin by men in authoritative positions. Owing to the well recognised obscurity of the origin of diseases of the skin, and the consequent difficulty in treatment, it was thought advisable to carry out further investigations along these lines.

The following are briefly the assertions made by the different writers:-

- | | |
|--|--|
| (1) I.L.McGlasson, M.D.,
San Antonio, Texas,
November, 1923. | That in dermatoses there is very frequently a high fasting content of the blood sugar, and this is of significance, since by restricting the carbohydrates in the diet very striking improvement clinically is to be obtained. |
| (2) J.F.Schamberg, M.D.,
Director of the
Research Institute
of Cutaneous Medicine,
Philadelphia, and
H.Brown, B.Sc., Chemist
of the same Institute,
December, 1923. | That in some dermatoses there is very frequently a high uric acid content of the blood, a purin-free diet resulting in cure. |
| (3) F.C.Doble, M.R.C.S.,
Hon.Casualty Out-
patient Surgeon, St.
Paul's Hospital for
Skin and Genito-urinary
Diseases, London,
February, 1925. | That in some dermatoses there is a high degree of acidity in the urine, and cure is effected by bringing the urinary pH, with the aid of alkalis, within the range of normal, relapse tending to occur on overstepping the limit to the alkaline side. |

- (4) H.A.Ellis, B.A., M.B.,
Ch.B., Assistant
Physician to Queen
Margaret Street
Hospital for
Consumption,
May, 1925.
- That in some dermatoses the pH of the diseased skin is more acid than the normal surrounding skin, and in others more alkaline, and this may be of significance from the point of view of treatment, it being undesirable, for example, to apply an alkaline dressing to a lesion already too alkaline.
- (5) J.A.Ryle, M.D., M.R.C.P.,
Assistant Physician to
Guy's Hospital, and
H.W.Barber, M.D.,
Physician-in-Charge,
Skin Department, Guy's
Hospital, 1920; also
Dr. W. Herbert Brown,
Physician to the Skin
Department, Victoria
Infirmary, Glasgow,
May, 1925.
- That gastric analyses are of importance in dermatology, a subacidity, for instance, being frequent in rosacea, and treatment with large doses of HCl resulting at times in very striking improvement.
- (6) F.D.Ackman, M.D.,
Resident Physician,
Royal Victoria
Hospital, Montreal,
November, 1925.
- That a urinary examination alone may perhaps be substituted for a gastric analysis in a case of necessity, the urinary acidity varying inversely with the gastric acidity; a marked alkaline tide, for example, developing in a hyperchlorhydria, and no tide in a achlorhydria.

These investigations were begun in 1923 and have been carried out over a period of three years.

In addition, clinical laboratory tests have been employed in the investigation of special cases, and about thirty sugar tolerance curves have been included in the first section to find if by this means information of additional value might be obtained.

General medical cases have been included throughout as controls, the blood uric acid findings in kidney cases, for example, being compared with those in the dermatoses.

I am indebted to Dr. W. Herbert Brown for suggesting the line of these investigations and for supervising the work; to

Dr. Douglas W. Russell, for selecting the medical cases for investigation; and to Dr. Allison D. McLachlan, for additional skin cases; to Dr. John Anderson, I am indebted for the full facilities of the clinical laboratory. I wish here to express my thanks to all of them for the kindly interest they have taken in the work and for the help they have given.

I have to thank also the Directors of the Muirhead Trust for the two years' tenure of a scholarship in the Clinical Laboratory of the Victoria Infirmary, and Dr. J. Norman Cruickshank for very kindly demonstrating to me the Folin and Wu system of blood analysis; to Dr. Ian Murray also, I am indebted for a case of Parkinsonism following encephalitis lethargica.

For the three photographs I am indebted to Dr. Brown, and for the two plates, to Mr. H. W. Boot.

CLINICAL LABORATORY METHODS EMPLOYED.

- | | |
|--|---|
| (1) Blood Sugar determinations. | MacLean's ¹ . method. |
| (2) Blood Uric Acid and Blood Creatinin estimations | Folin & Wu ² . system of analysis. |
| (3) Blood Urea estimations and occasional Urea Concentration tests | MacLean's ³ method. |
| (4) Determination of the Urinary pH, &c. | At first by the Barnett and Chapman method as described by Stitt ⁴ ., and later, when simultaneous determinations of the pH of the skin were begun, by the capillator method (British Drug Houses ⁵ .). |
| (5) Determinations of the ratio between the free and combined acid in the urine. | By titration with NaOH, using phenolphthalein as an indicator, and neutralized formalin to liberate the combined acid. |
| (6) Fractional Gastric Analyses, with Chloride Curves | By Volhard's method. |
| and occasionally:- | |
| (7) Tests for Haematoporphyrin in the Urine | Spectroscopic, treating with glacial acetic acid and extracting with amylic alcohol. |
| (8) Tests for Haematoporphyrin in the Faeces | Spectroscopic ⁷ the method described by A.M.H.Gray ⁶ . was followed, the entire stool being treated with alcohol and ether, filtered, and the filtrate extracted with acetic ether: after washing the acetic-ether extract ten times with water, the ether extract was shaken out with 25% HCl. |
| (9) Clinical examinations of the Blood, including Platelet Counts | Platelets were counted against the red cells in a well stained film. The films from which the two plates are taken were stained with Jenner and Geimsa. |

- (10) Fragility Tests.
- (11) Van den Bergh Tests.
- (12) Haemoclastic Crisis.
- (13) Serum Calcium By Clark's method as described
by Myers⁷.
- (14) Coagulation Time ... Wright's⁸ method.

R E F E R E N C E S .

1. MacLean "Modern Methods in the Diagnosis and Treatment of Glycosuria and Diabetes".
 2. Folin "Laboratory Manual of Biological Chemistry", 1923: Appleton & Co., London.
 3. MacLean "Modern Methods in the Diagnosis and Treatment of Renal Disease", 1921: Constable & Co., Ltd., London.
 4. Stitt "Practical Bacteriology, Blood Work, Parasitology", 1923: Lewis & Co., Ltd., London.
 5. Cocking "PH Values, What they are and how to determine them": British Drug Houses.
 6. Gray "Quart. Journ. Med.", 1926, 75, 381.
 7. Myers "Practical Chemical Analysis of Blood", 1924: Kimpton, Lond.
 8. Wright "Technique of the Teat and Capillary Glass Tube", 1912: Constable & Co., Ltd., London.
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The SUGAR CONTENT of the BLOOD.

We first became interested in this subject of the blood sugar in its relation to diseases of the skin in 1923 on reading an article by McGlasson¹, entitled "Hyperglycaemia as an Etiologic Factor in Certain Dermatoses". This author had encountered with great frequency a hyperglycaemia in dermatoses patients, and had obtained very striking improvement in such cases by restricting the carbohydrates in the diet. We, therefore, thought it would be of interest to undertake an independent series of observations.

Since the end of 1923 we have examined a number of cases almost as large as that of McGlasson, and these have consisted of various forms of dermatoses - for the most part chronic. In the classifying of the cases some difficulty has been encountered, owing mainly to the want of unanimity of opinion regarding the forms of dermatitis to be included under the term "eczema". Sequeira² defines "eczema" as a "non-microbic inflammation of the skin occurring in certain susceptible subjects from external irritation or some internal cause of a toxic or nervous nature": he then writes, that redness, vesication, exudation, and the formation of crusts and scales are phenomena, common also in irritant dermatitis without special predisposition, and that the latter for convenience are classed usually as forms of "dermatitis". This distinction between "dermatitis" and "eczema" has been used throughout our series.

Again, the clinical differentiation of one type of case from another is often very different, e.g. a chronic eczema with severe pruritus may closely simulate a prurigo with secondary eczematization. We therefore have grouped the cases according to some of their main

clinical features to see if by such grouping any special blood findings would be found. Chronic eczemas with severe pruritus have been grouped apart from the main mass of eczema cases to be entered on the same page with prurigos, localised lichenoid eczemas similarly have been entered on the same page with lichen simplex chronicus.

The normal fasting blood sugar content ranges from 0.06 - 0.11%, though some people include also figures up to 0.12%. McGlasson considered 0.11% the upper limit of normal. After 50 gms. of glucose the blood sugar rises, reaching, in about thirty, or less frequently, sixty minutes, to a maximum of from 0.15 - 0.18%. The blood sugar then falls and within $1\frac{1}{2}$ - 2 hours regains its former level, or perhaps even reaches below it. Age has the effect of heightening and prolonging the curve, delaying its return to normal beyond the two hours. The threshold point is said to lie between 0.16 - 0.18%, glycosuria occurring with figures above this, unless, as is frequently the case, the threshold point be raised. In renal glycosuria the threshold being lowered, glycosuria occurs with figures below 0.16 - 0.18%. McGlasson determined the fasting blood sugar in his cases, we, for convenience, obtained the blood two to three hours after breakfast. In McGlasson's tables figures ranging from 0.15 - 0.2% are frequent: in our series such figures are extremely rare, occurring, if diabetics be excluded, in only one case.

The following Table gives a summary of the findings for the various groups and shows the main types of cases examined:-

S U M M A R Y

Condition.	Blood Sugar Average	No. of Cases	Highest Blood Sugar.	Percentage over 0.11%.	Percentage over 0.12%.
Lichen Simplex					
Chronicus ...	0.158%	3	0.22 %	100	100
Localized Lichenoid Eczema ...	0.123	5	0.137	100	40
Acne Vulgaris ..	0.116	3	0.120	66	nil
Prurigo	0.109	9	0.140	33	22
Chronic Eczema with severe pruritus	0.108	3	0.118	66	nil
Pruritus	0.105	14	0.146	50	35
Urticaria	0.104	4	0.125	50	25
Sycosis	0.103	8	0.125	37	12
Seborrhoeic Dermatitis	0.103	15	0.132	42	6
Chronic Eczema..	0.100	42	0.147	39	19
Miscellaneous ..	0.097	16	0.128	37	6
Rosacea	0.094	7	0.118	28	nil
CONTROLS	0.094	12	0.112	8	nil
Summer Eruptions	0.084	4	0.090	nil	nil

In the summary the points of interest are:-

The tendency in the dermatoses for blood sugar values to be higher than in the controls.

The approximation to one another of some of the groups having some main clinical features in common, viz. lichen simplex chronicus and localized lichenoid eczemas, prurigos and chronic eczemas with severe pruritus. This would suggest some constancy in the blood findings associated with special clinical features, e.g. pruritus with lichenification.

While in the majority of McGlasson's Tables 77 - 90% give readings of over 0.12%, and 90% or more readings above 0.11%, in our series the numbers are strikingly less. High values are constant in the lichen simplex chronicus group, but the group consists of only three cases.

The blood sugar average for the summer eruptions is relatively low.

Our results with dieting also have been as negative as our other findings. In the following Tables the findings for the different groups are given in more detail:-

LICHEN SIMPLEX CHRONICUS.

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
1.	9/2/24	41.	Lichen Simplex Chronicus.	1 year	0.220%	Put on diet.
	5/3/24				0.156	
	4/6/24				0.124	Much improved.
	15/11/24				0.088	Now better.
2.	19/10/24		do.		0.130	
3.	14/6/24		do.	2 years	0.125	
Average .. 0.158%			Number over 0.11% .. 3 = 100%			
			Number over 0.12% .. 3 = 100%			

ECZEMA - LOCALIZED LICHENOID FORM.

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
1.	8/7/25	54	Lichenoid Eczema (localized).	4 years	0.390%	Diabetic
2.		58	do.	2 years	0.137	On diet.
	17/9/24				0.118	Almost well.
3.	28/6/24		do.		0.120	
4.	7/2/25		do.		0.118	
5.	9/6/24		do.		0.118	
Average (excluding Diabetic) 0.123%			Number over 0.11% .. 5 = 100%			
			Number over 0.12% .. 2 = 40%			

In the first case of lichen simplex chronicus a gradual fall in the blood sugar is seen to accompany the gradual clinical improvement with dieting, reaching normal on recovery.

In both Tables there is a marked tendency for values to be on the high side, all of the first group and two of the second being definitely abnormal; 100% of the values in both exceed 0.11%.

Restriction of carbohydrates in the diet appeared to benefit some of these patients.

ACNE VULGARIS

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
1.		25	Acne Vulgaris		0.120%	
2.	16/6/24	20	do.	2½ years	0.118	
3.		17	do.		0.111	
Average .. 0.116%						
Number over 0.11% .. 2 = 66%.						
Number over 0.12% .. nil						

Here again there is a decided tendency for values to be on the high side, although not strictly abnormal. The group, however, consists of only three cases.

CHRONIC PRURIGO

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
1.	12/10/25	61	Chronic Prurigo	8 months	0.140%	Put on diet
	14/10/25				0.133	
	19/10/25				0.113	I.S.Q.
2.	23/1/24		do.		0.137	Put on diet
	8/3/24				0.114	
	9/8/24				0.106	I.S.Q.
3.	12/4/26	61	do.		0.116	
4.		48	do.	14 years.	0.109	
5.	27/9/24	56	do.	9 months	0.106	
6.		30	do.	10 years	0.100	
7.	6/10/26	36	do.		0.100	Tolerance Curve
8.	13/12/24	15	do.		0.090	
9.	23/11/26		do.	10 months	0.089	Tolerance Curve
Average .. 0.109%						
Number over 0.11% .. 3 = 33 %.						
Number over 0.12% .. 2 = 22 %.						

CHRONIC ECZEMA with Severe Pruritus.

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
1.	5/3/24	47	Chronic Eczema with severe pruritus.	several years.	0.118%	
2.	7/10/25		do.		0.115	
3.	24/6/26	53	do.	4 years	0.092	
Average .. 0.108%						
Number over 0.11% .. 2 = 66 %.						
Number over 0.12% .. nil						

U R T I C A R I A

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
1.	15/10/24	13	Urticaria	Some months	0.125%	
2.	15/10/24	12	"	1 year	0.112	
3.	16/8/26	40	"	2 years	0.100	3 Curves
4.	31/5/26	2	"		0.080	

Average .. 0.104%
 Number over 0.11% .. 2 = 50%
 Number over 0.12% .. 1 = 25%

This group is very small but contains one definitely abnormal figure and one on the border-line.

S Y C O S I S

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
1.	6/12/24	22	Sycosis	1½ years	0.125%	
2.	17/9/24	26	"	9 months	0.118	
3.	13/9/24	43	"	6 months	0.112	
4.	17/9/24	20	"	2 years	0.100	
5.	9/6/24	32	"		0.100	
6.	23/4/24	27	"	7 years	0.094	
7.	24/8/25	35	"		0.088	
8.	6/12/24	28	"	2 years	0.086	

Average .. 0.103%
 Number over 0.11% .. 3 = 37%
 Number over 0.12% .. 1 = 12%

The blood sugar in case 1 is definitely abnormal and two (2 and 3) are on the border-line.

SEBORRHOEIC DERMATITIS

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
1.	6/12/24	47	Boils also present.	1 month	0.132%	
2.	25/4/25	4	Acute.		0.118	
3.	29/9/26	5		1 year	0.113	
4.	18/1/24	21		6 weeks	0.112	
5.	28/1/25	21		3 years	0.112	
6.	28/6/25	5			0.111	
7.	24/8/26	30		1 year	0.109	Curve
8.	7/7/26	54		2 months	0.105	Curve
9.	7/6/24	5			0.100	
10.	21/9/26	45	Acute - boils also.	2 weeks.	0.100	Curve
11.	13/9/24	38		1 month	0.100	
12.	4/6/24	9			0.090	
13.	2/7/24	3			0.090	
14.	20/5/25	76		1 year	0.068	

Average .. 0.103%. Number over 0.11% .. 6 = 42%
 Number over 0.12% .. 1 = 6%

In this group, only the first case is definitely abnormal, and here boils complicate the case. There is a tendency on the whole, however, for values to be towards the higher percentage.

CHRONIC ECZEMA

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
1.	27/2/26		Chronic Eczema		0.211%	Diabetic, great improvement with insulin.
2.		42	Severe generalized eczema.	2 years	0.147	High blood uric acid also - improved on restricted protein diet.
3.	14/6/24 20/9/24	32	Chronic Eczema	10 years	0.146 0.100	Put on diet. Great improvement.
4.	23/9/25		" "	6 years	0.143	
5.	16/4/26	53	Acute Eczema.		0.131	

(contd.)

CHRONIC ECZEMA (contd.).

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
6.		25	Chronic Eczema	25 years	0.130 %	
7.			" "		0.130	
8.			" "		0.129	
9.			" "		0.127	
10.	2/4/24		" "		0.118	
11.		8	" "	10 months	0.118	
12.	17/9/24	16	" "	16 years	0.118	
13.	26/1/25	18	" "	6 years	0.115	
14.	20/9/24	38	" "		0.113	
15.	1/2/24	56	" "	1 year	0.112	
16.	22/11/24	4	" "		0.112	
17.	22/10/24	47	" "	18 years	0.110	
18.	22/10/24	47	" "	2 years	0.106	
19.	15/10/24	44	" "	5 years	0.106	
20.					0.106	
21.		60	" "	15 years	0.100	
22.	30/7/24		" "		0.100	
23.	1/11/24	24	Vesicular	6 years	0.100	
24.	1/9/25	22	Acute	2 weeks	0.095	
25.	2/2/25		Recurring Eczema- Dysidrosis.		0.090	
26.	4/5/25	13	Chronic Eczema.	4 years	0.090	
27.	27/5/26	53	" "		0.090	
28.		29	" "	28 years	0.086	
29.	22/11/24	2	" "		0.083	
30.	10/11/24	59	" "	8 months	0.082	
31.	15/2/25		" "		0.081	
32.		13	" "		0.081	
33.	11/6/24	19	Vesicular	8 months	0.080	
34.	18/5/24	37	Generalized lichenoid eczema.	10 years.	0.080	
35.	25/10/26	56	Chronic Eczema	20 years	0.078	
36.		22	" "	10 years	0.078	
37.	22/9/24	9	" "	7 years	0.071	
38.	22/3/24		" "		0.070	
39.		6	" "		0.063	
40.	18/1/27	53	" "	9 years	0.062	
41.	26/11/24	22	" "	9 years	0.062	
42.	29/10/24	33	" "	18 months	0.058	

Average (excluding
diabetic) 0.100%

Number over 0.11% .. 16 = 39%
Number over 0.12% .. 8 = 19%

Here, nine show definitely raised values: the group, however, is large and contains also some very low values. The findings in the eczema group, therefore, do not endorse those of McGlasson, 19% only, instead of 77 - 90%, giving values of over 0.12%, and only 39% instead of over 90% values exceeding 0.11%.

M I S C E L L A N E O U S .

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
1.	14/9/26		Multiple Boils	4 weeks	0.128%	Curve.
2.	2/5/25	53	? Acne Varioliformis.		0.120	
3.	6/6/25		Hyperkeratosis of palms.		0.105 0.120	
4.	28/4/26	61	Psoriasis.		0.118	
5.	30/6/24	42	Erythrodermia.	5 months	0.113	
6.	29/10/24	53	Stocking Dermatitis.	1 year.	0.112	
7.	22/3/24		Arsenical Dermatitis.		0.110	
8.	28/4/24	62	Varicose Eczema.	2 years.	0.110	
9.	11/6/24	58	Septic Varicose Ulcer.		0.106	
10.	10/7/25		Mycosis Fungoides		0.087	
11.	23/6/24	54	Irritative condition of finger tips.	2½ years	0.081	
12.	4/10/24	19	Erythema Iris.	1 week.	0.080	
13.	25/11/26	40	Recurrent Boils.	5 weeks	0.077	Curve
14.	17/9/24		Varicose Dermatitis, with ulcer.	1 year.	0.075	
15.	16/11/26		Pemphigus Foliaceus.		0.073	3 Curves.
16.	13/4/24		Psoriasis.		0.056	6 months pregnant. Curve.

Average .. 0.097% Number over 0.11% .. 6 = 37%
Number over 0.12% .. 1 = 6%

This group contains only one definitely raised value, belonging to the case of multiple boils. About half the number, however, give border-line readings. The value in Case 16 is very low.

R O S A C E A

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
1.	20/9/24	37	Rosacea	7 years	0.118%	
2.	7/7/26	40	"	3 years	0.112	
3.	13/9/24	38	"	1 year	0.100	
4.	29/10/24	33	"	6 years	0.093	
5.	29/10/24	33	"	3 years	0.086	
6.	2/7/26	40	"		0.081	
7.	24/4/26	34	"	2 years	0.068	

Average .. 0.094% Number over 0.11% .. 2 = 28%
 Number over 0.12% .. nil

In this group none of the readings is definitely high, although two are on the border-line.

S U M M E R E R U P T I O N S .

No.	Date	Age	Condition	Duration	Blood Sugar	Remarks.
1.	25/8/26	19	Hydroa Aestivale		0.090%	2 Curves. Curve.
2.	13/8/26	9	"		0.086	
3.	28/6/24	11	Dermatitis. Herpetiformis with summer prurigo.		0.081	
4.	13/9/24	35	Summer Dermatitis.	20 years.	0.080	

Average .. 0.084% Number over 0.11% ... nil.

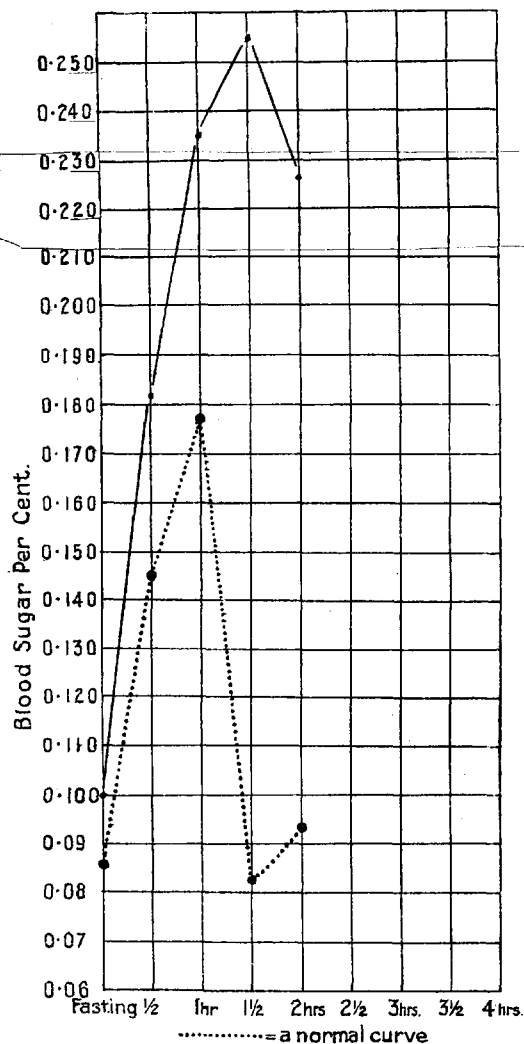
In this group all the values are within normal limits.

Our results though failing to confirm those of McGlasson are yet in agreement with those of other workers, - Pels, for example, and Schamberg, who found very little variation from the normal, though it was remarked by the former that the tendency was for values to be towards the higher percentage. Our results are not unlike also those of Schwartz, Heimann, and Mahnken³, who, although they found a hyperclycaemia frequently in seborrhoea, acne and sycosis, as compared with other dermatoses, yet did not obtain the high figures of McGlasson, but figures on a level more with our own raised findings.

Owing to the relatively negative nature of our findings with the determination of a single blood sugar, it was thought worth while to include a few sugar tolerance curves, to see if by that means information of a more positive character might be obtained. Haldin-Davis and Wills⁴ in 1925 carried out sugar tolerance curves on twenty cases of eczema and found thirteen of the number, or 60%, to show some abnormality. Either the fasting blood sugar was too high, or there was too great a rise in the blood sugar following the ingestion of glucose. In some of the cases there was prolongation of the curve and in others not. Davis had found dietetic treatment in eczema cases to be very unsatisfactory, improvement resulting in only exceptional instances. Six cases of skin disease, not eczema, were also included in their series. The only two cases in which mention was made of the presence of lichenification, are of interest. The one, a case of eczema with obstinate patches of lichenification, had an abnormally high fasting blood sugar and a high, markedly prolonged curve. In the other, an old-standing case of lichen hypertrophicus with much pruritus, the blood sugar before glucose

was normal and returned to normal one-and-a-half hours after, but at the half-hour rose to the exceptional height of 0.34%. The findings in these two cases would seem to be quite in keeping with our own.

There are diseases in which frequently some alteration in the sugar tolerance curve is to be found. Examples therefore of some abnormal types of curves will be given before enquiring into the forms of curve obtained in dermatoses patients. As the diabetic type of curve is so well known, only one example will be given, a Mild Diabetic:-

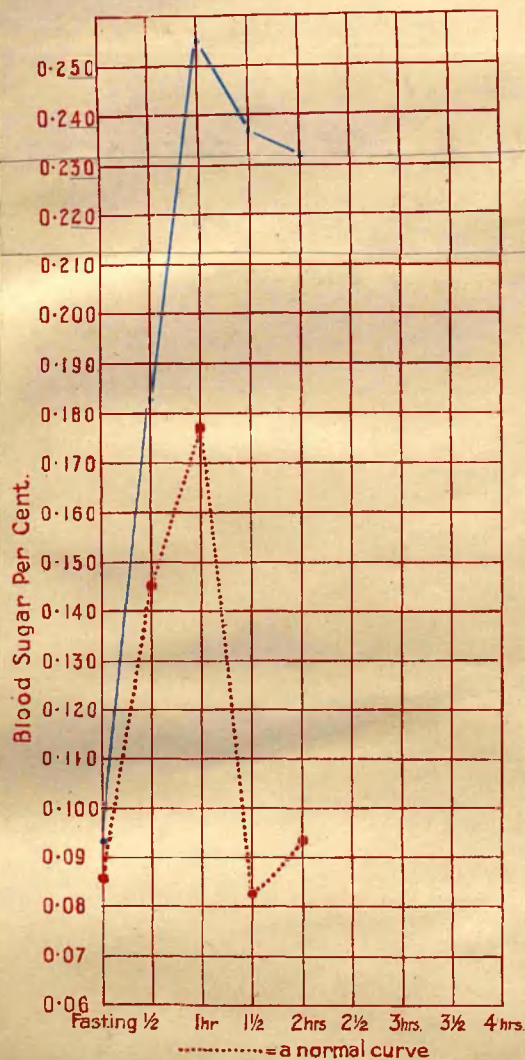


Notwithstanding the normal fasting level in this case, the blood sugar after glucose is seen to rise well above normal, continuing the rise until the end of $1\frac{1}{2}$ hours. At the 2 hours it falls slightly, but by this time normally, it should have regained its former fasting level.

The urine before glucose contained a trace of acetone, but no sugar: after glucose sugar was present but no acetone.

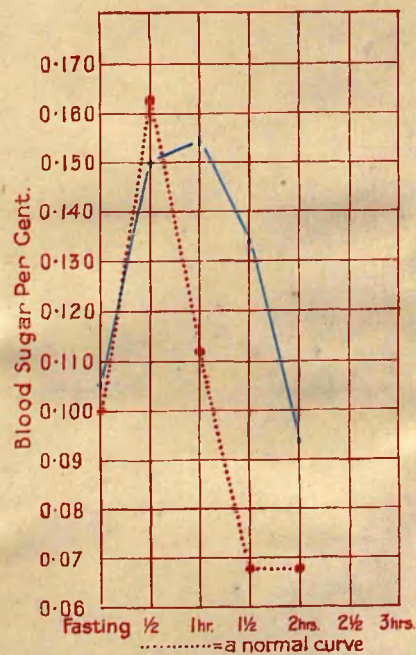
This heightening and prolonging of the curve, with glycosuria, is typical of diabetes.

In exophthalmic goitre the curve may be normal or resemble the diabetic in form. Examples of both types are given:-



This curve resembles closely the previous curve from mild diabetes, showing the same high rise and prolongation. There was no glycosuria.

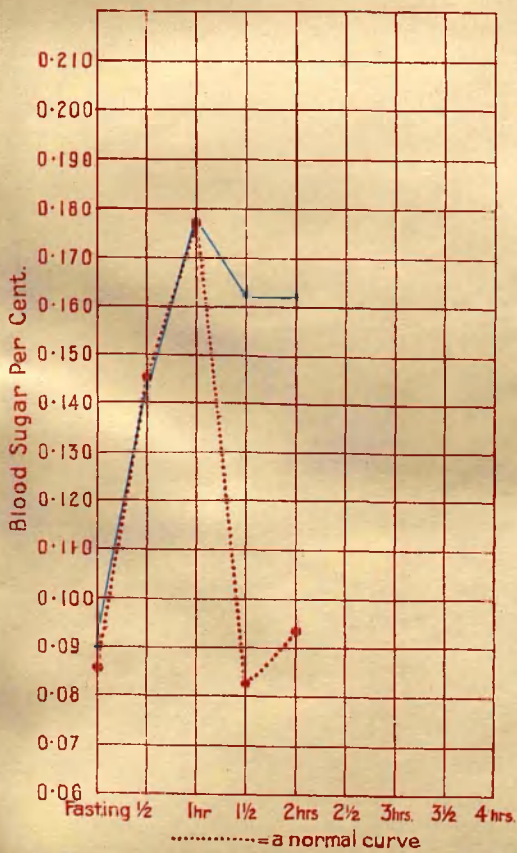
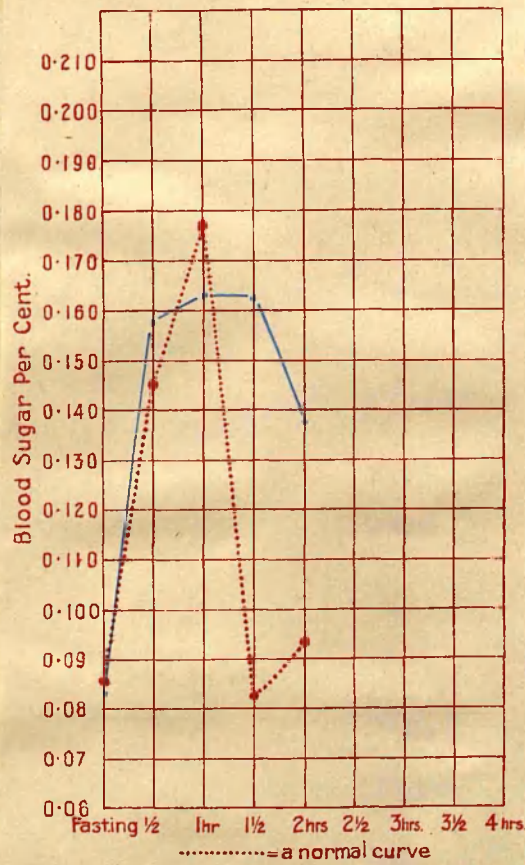
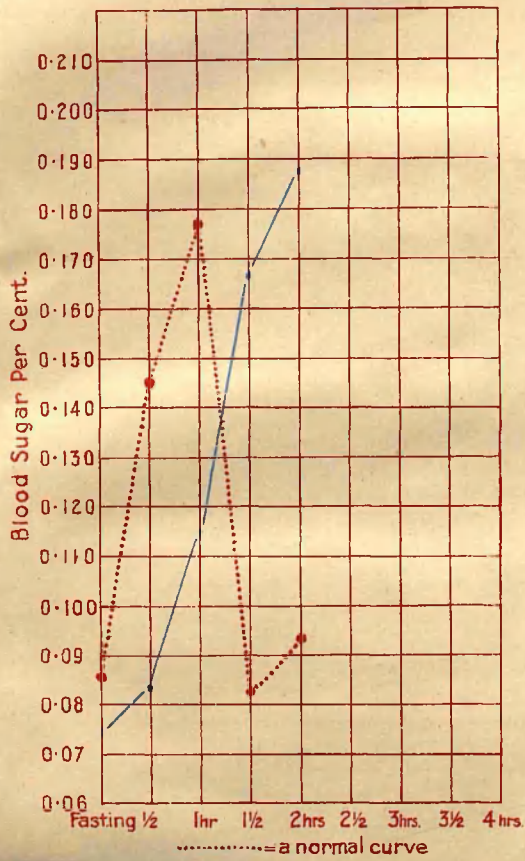
In exophthalmic goitre there is generally, as in this case, a normal fasting blood sugar.



Normal.

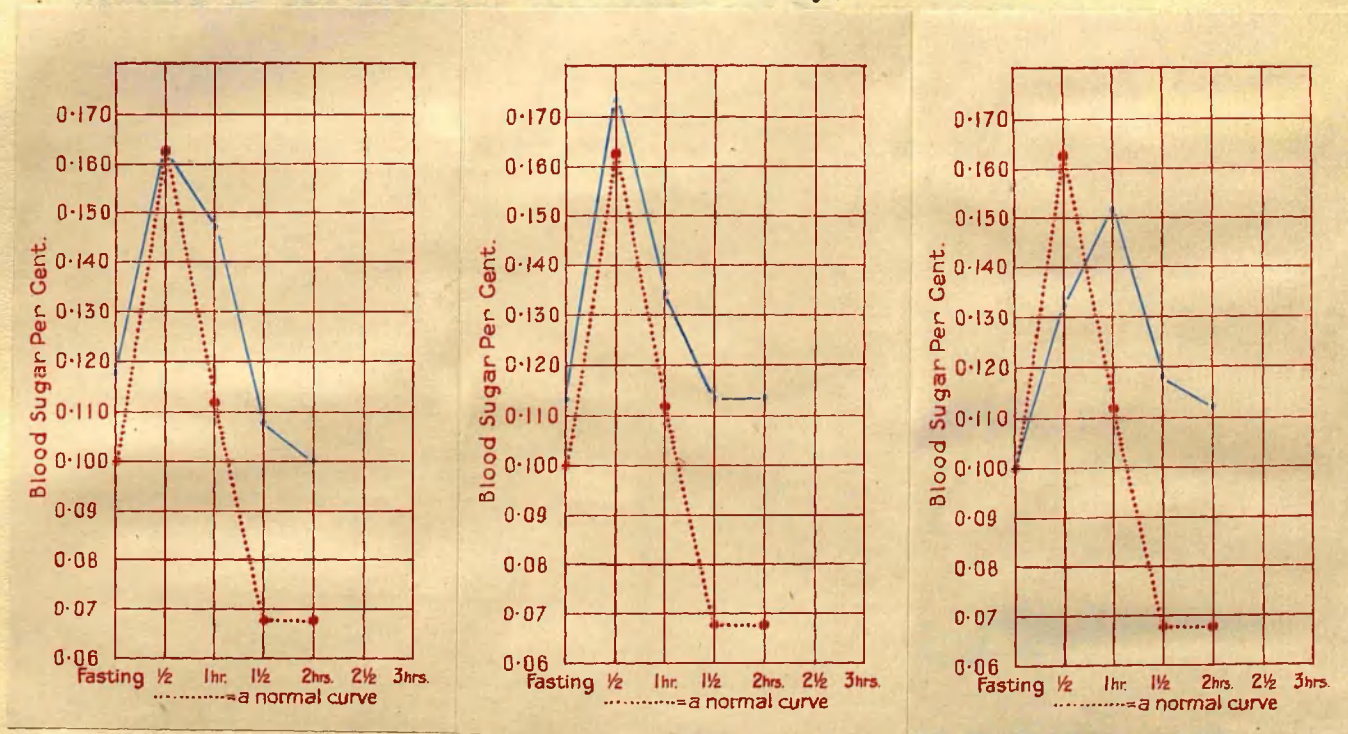
In Parkinsonism following encephalitis lethargica, also, a diabetic type of curve is frequently obtained. The following three examples were taken from severe cases of Parkinsonism, two being ward patients, and the third an out-patient during a relapse while still on hyoscine.

Severe Parkinsonism -

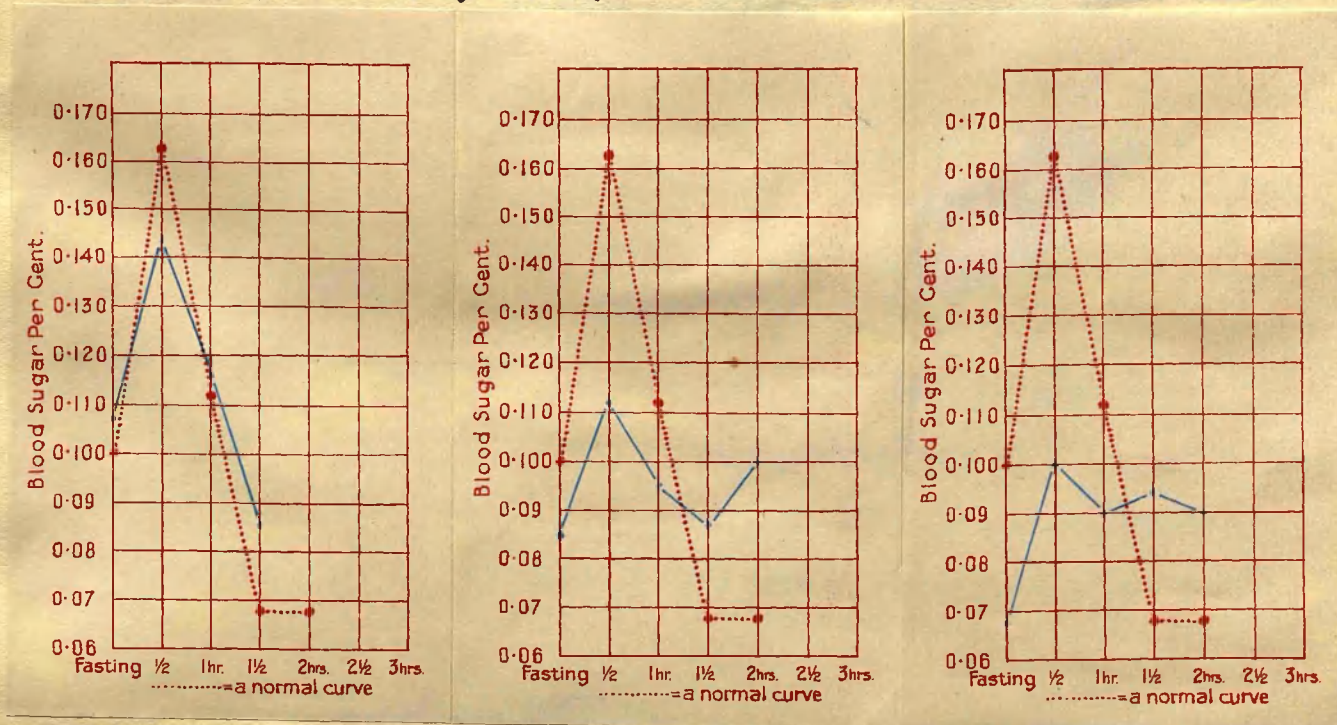


These three cases show at least the definite prolongation of the curve. In none of the three was glycosuria present.

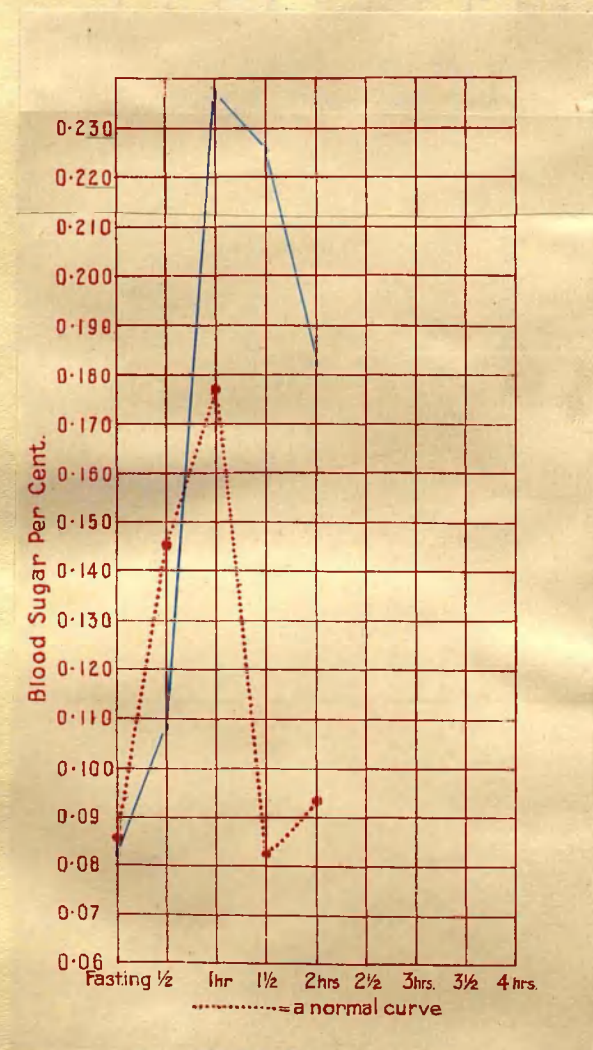
The following are examples of normal curves obtained from cases of Parkinsonism of medium severity:-



And below are given the curves obtained from three cases of Parkinsonism showing very definite improvement with hyoscine. These curves are very low. McCowan, Harris and Mann⁵ in 1926 demonstrated a lowering of the sugar tolerance curve in patients with Parkinsonism responding well to hyoscine.



This low type of curve just demonstrated is found also in certain of the diseases characterised by insufficiency of one or other of the endocrine glands, e.g. myxoedema, cretinism, Addison's disease, and pituitary disease. In pituitary disease, however, the opposite type of curve may be found, especially in the early stage. An example of this diabetic type of curve sometimes encountered in early pituitary disease is given below:-



This woman was 23 years of age and weighed 13 st. Two years previously she had risen in weight, in two months, from 7 st. 8 lbs. to 11½ st. She suffered from severe headaches and had vomiting without nausea on occasions.

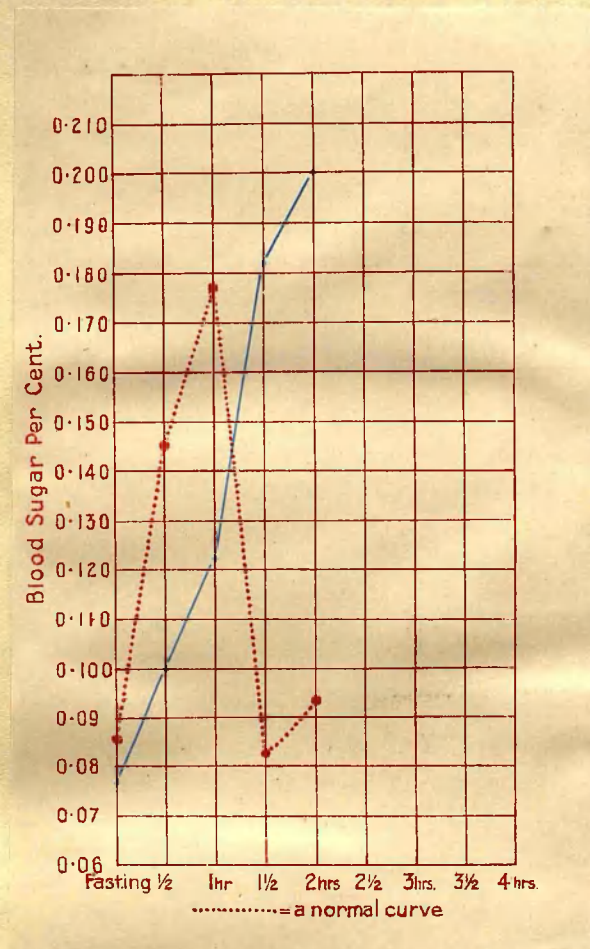
The urine before glucose contained no sugar, but the specimens at the one and two hours both contained sugar.

100 gms. of glucose were given in her case, but McLean says that this should produce no greater rise than 50 gms. Other authors do not agree with McLean, but at least there should have been no glycosuria.

In the only case of Addison's disease in this series, the curve did not resemble the very low curve generally considered typical of the disease. Yet the case clinically

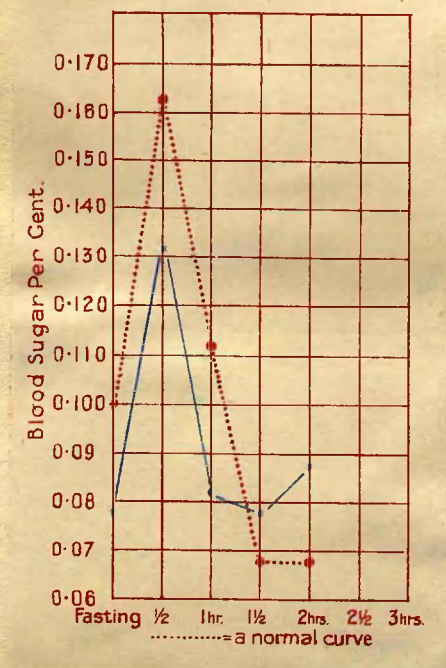
was absolutely typical, showing the pigmentation of skin and mucous membranes, marked asthenia, and gastro-intestinal disturbance. Post mortem, the suprarenals were found replaced by fibrous tissue, and

there was a fibrosis also of the other organs, including the pancreas. The curve from this case of Addison's disease is given in the accompanying chart:-



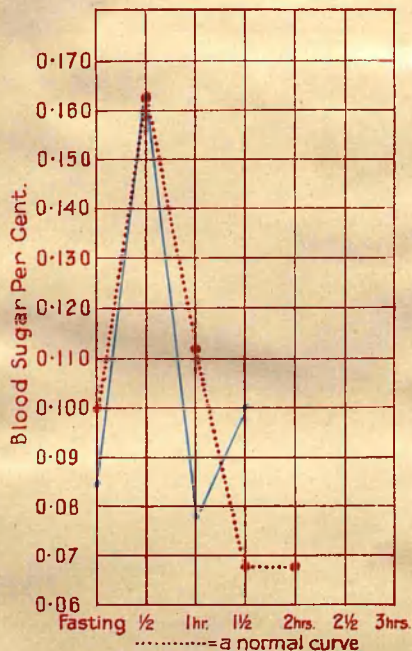
The rise is seen to be markedly delayed, and the blood sugar, instead of remaining low as is expected in this type of case, rises in the end to the normal maximum or above it, still rising at the two hours.

And now renal glycosuria only remains to be described. As a rule the curve in this condition is lower than the usual normal. The curve below is typical of renal glycosuria:-



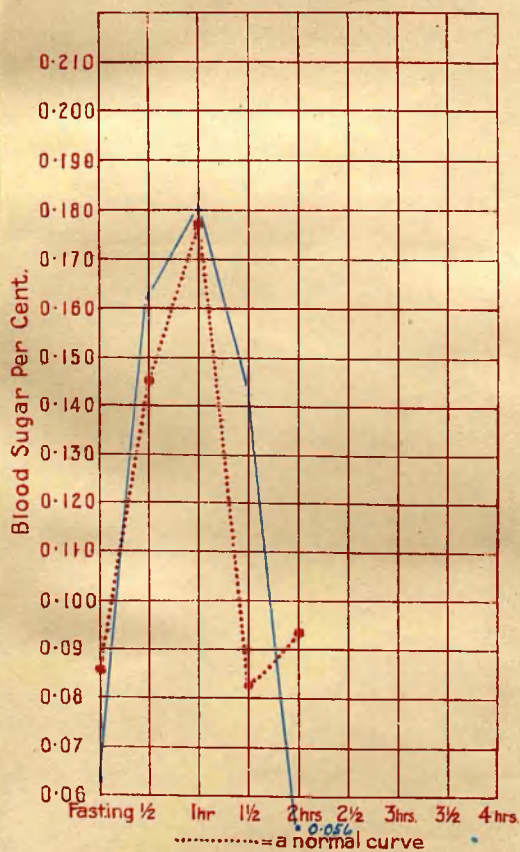
The urine before glucose contained no sugar but at one hour 1.6% of sugar was present in the urine: by the two hours the urine was again sugar free.

Of the 23 dermatoses patients examined only six gave normal sugar tolerance curves. These will be shown first:-



Case 1. - Sclerodermia

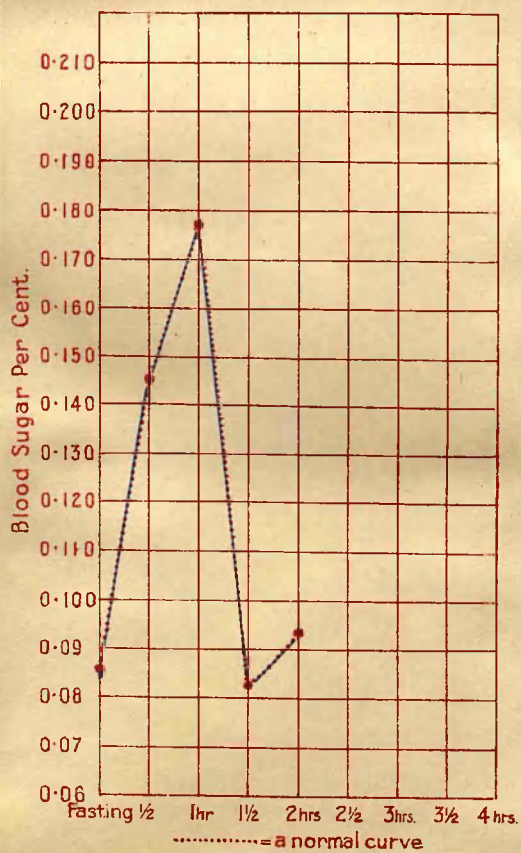
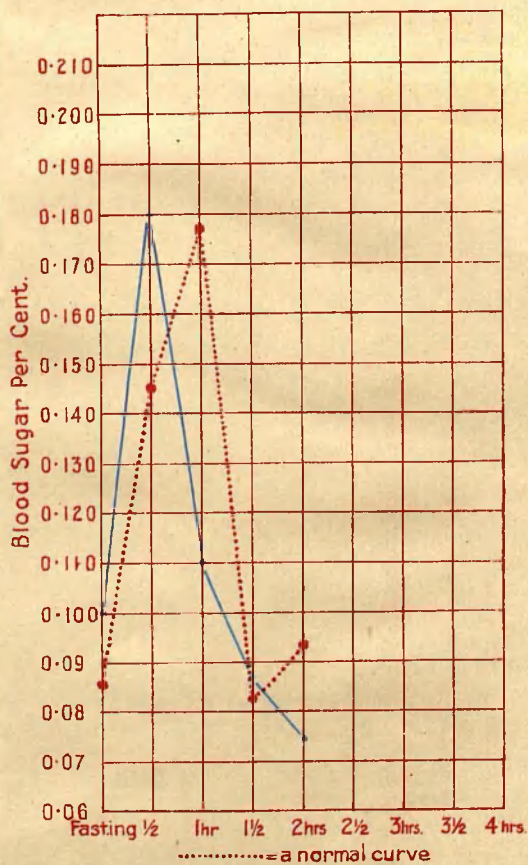
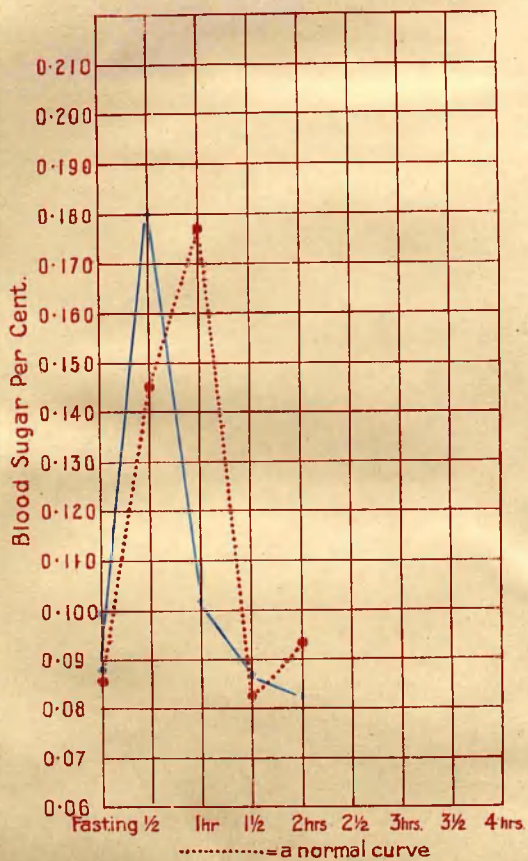
In sclerodermia a low curve rather is expected, indicating the use of thyroid in treatment.



Case 2. - Psoriasis complicating pregnancy.

The low level of the blood sugar before glucose and 2 1/2 hours after is to be noted here. This very low level of the fasting blood sugar is given as a cause of the morning sickness of pregnancy.

Cases 3 and 4. - Chronic Prurigo with eczematization.

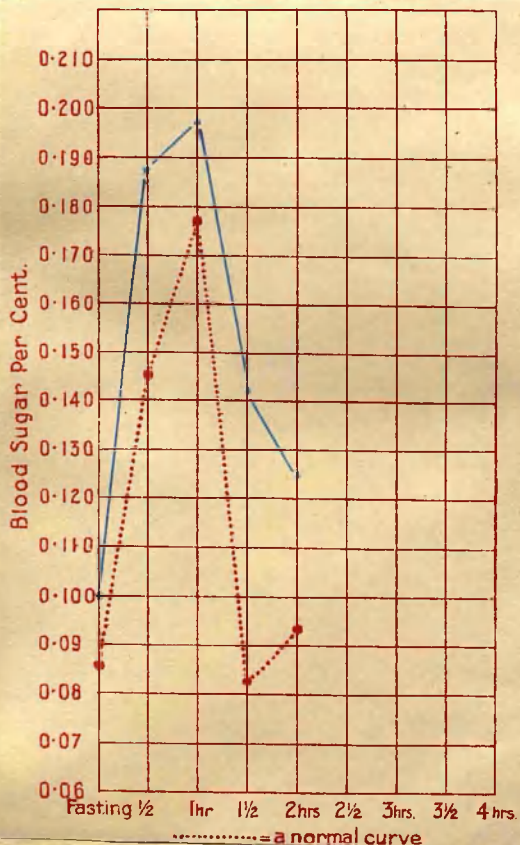
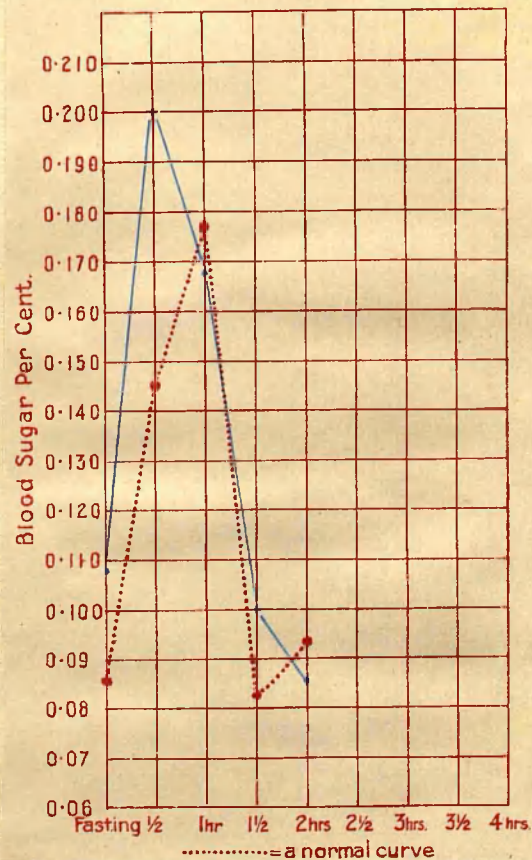
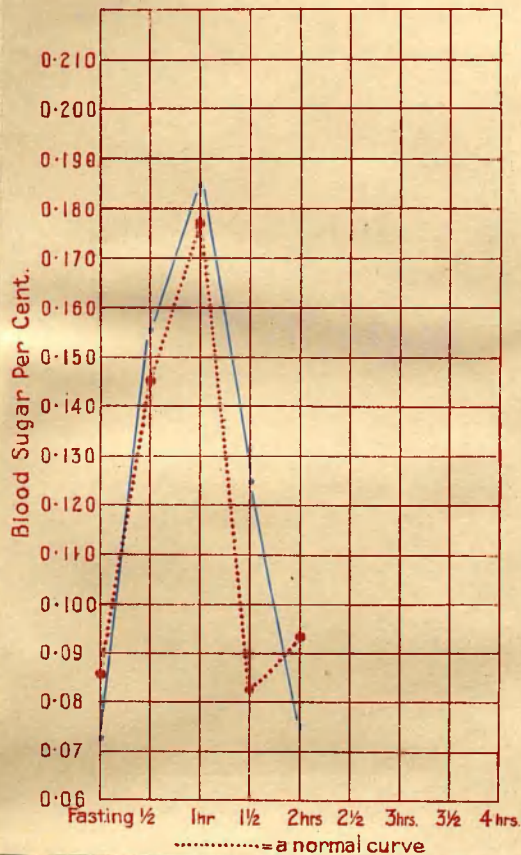


Case 5. - Chronic Eczema with severe pruritus.

These three cases in addition to their clinical resemblance, show a close resemblance in their sugar tolerance curves. They were the only cases of this type examined.

The sixth of the normal curves belongs to the next group of seborrhoeic dermatitis, consisting of three cases:-

Cases 6 and 7. - Seborrhoeic Dermatitis.



Case 8 - Seborrhoeic Dermatitis with boils.

Case 6, aet 54, shows a slight tendency to prolongation of the curve, probably accounted for by his age.

Some authors would consider the rise in case 7 still within normal limits, but a very slight glycosuria at the one hour was abnormal.

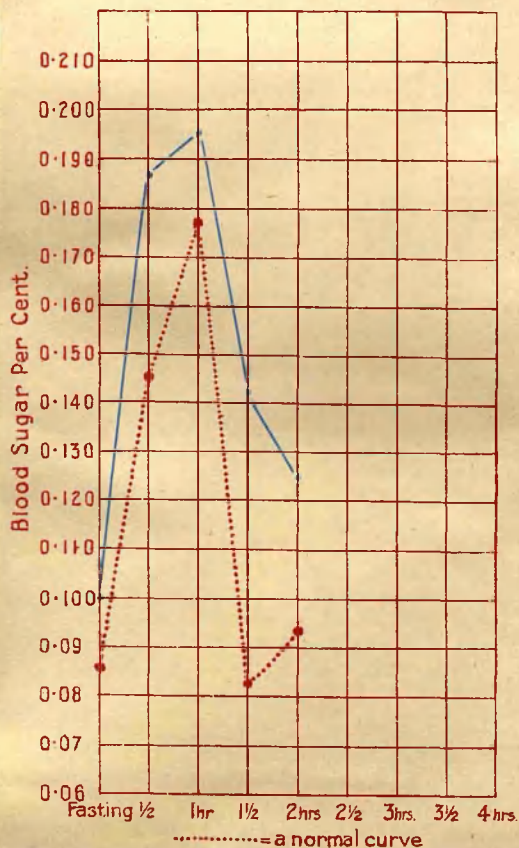
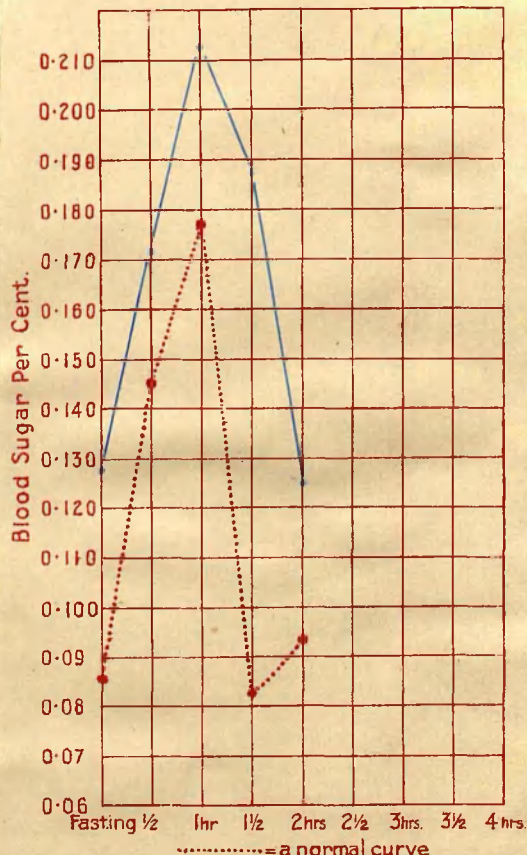
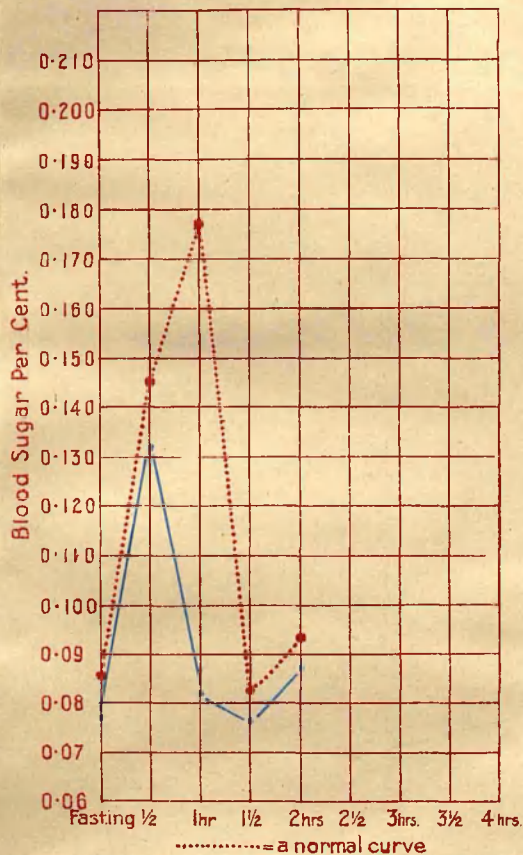
There is definite prolongation of the curve in case 8; the presence of boils, however, complicate this case.

All three curves show a tendency to be on the high side, or to be prolonged.

The next group consists of three cases, suffering from boils:

all three curves show abnormality:-

Cases 9 and 10. - Multiple Boils.



Case 8. - Boils complicating Seborrhoeic Dermatitis.

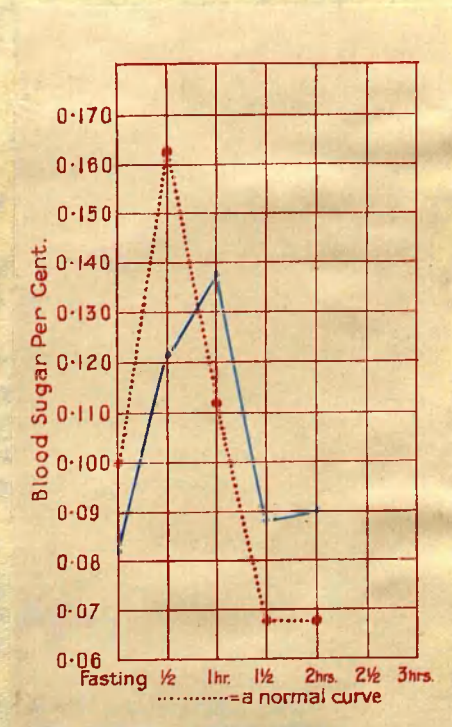
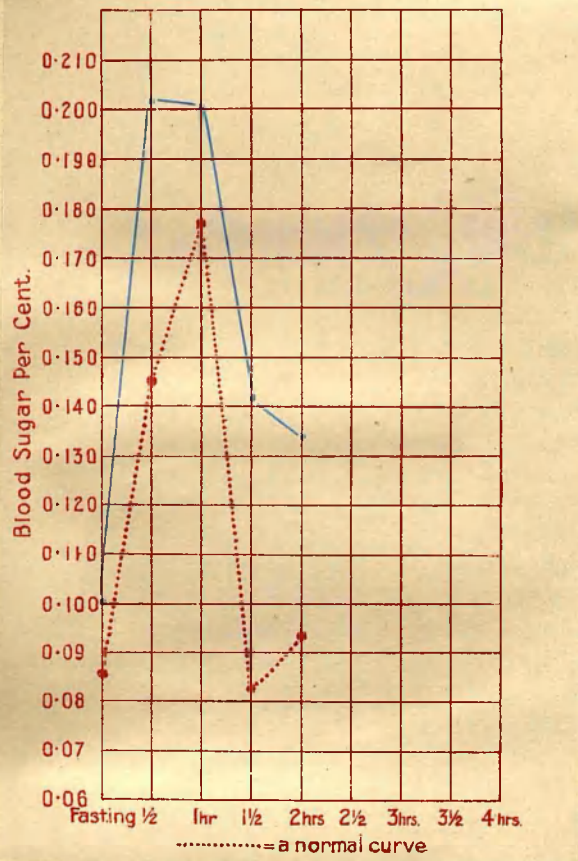
Case 9 is an example of renal glycosuria, sugar being present in the one hour sample of urine.

The curve in case 10 is typically diabetic in form, the fasting blood sugar also being raised and the curve definitely prolonged. There was no glycosuria but this patient may be a potential diabetic.

Case 8 has already been included in the previous group of seborrhoeic dermatitis. The curve resembles that of case 10 in the high rise and prolongation of the fall beyond the two hours.

One case only of urticaria was examined. Three curves obtained in her case are given below, to show the effect of dieting on the curve.

Case 11. - Acute Urticaria, intermittent over two years.

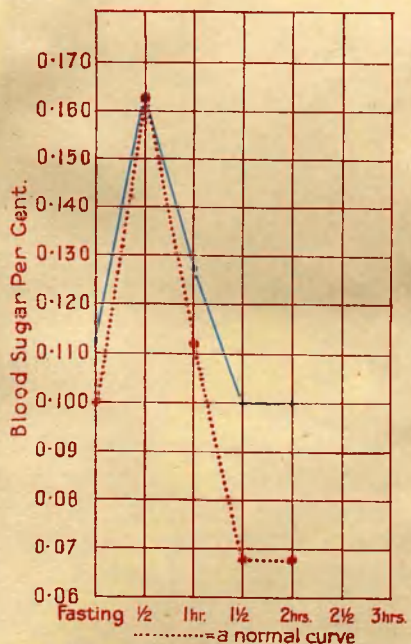


The first curve is seen to be abnormally high and prolonged. An achlorhydria was also present.

Treatment with large doses of HCl was begun, and rigid restriction of carbohydrates in the diet. Marked improvement followed, although the achlorhydria persisted.

The second curve, taken 2 months later, shows the marked lowering as the result of treatment.

The third curve was taken a month later again, while not so well, it is higher than the previous one, but quite normal. Diet had been as strict, but as the patient was menstruating, this may have been the cause of the relative rise in the blood sugar.



When seen the week following she was again greatly improved.

Only one case of pemphigus is included in the series, a pemphigus foliaceus of over two years duration:-

This case proved to be of interest from the striking resemblance between its sugar tolerance curve and that obtained from the case of Addison's disease. A repeat curve was done, and although lower, was found to have the same main characteristics as the previous one.

It was thought, therefore, that it might be of interest to try the effect of adrenalin in this case. Treatment with daily subcutaneous injections of 3 mins. was begun, and the patient began steadily to improve, the dose of adrenalin being gradually raised until at the end of a month she was having 10 mins. daily.

Three days later, however, she developed troublesome diarrhoea which persisted for about a week. The adrenalin was stopped and four days later a sugar tolerance curve was done. This curve, though still not normal, seemed definitely to approach more to the normal.

Her skin condition continued to improve until in less than a fortnight it required no dressing at all. She developed diarrhoea again, however, with this time, blood in the stools. The melaena persists up to date, more than a fortnight later, but the diarrhoea has stopped, and the patient wishes to go home, the skin condition being well.

It is a striking coincidence that the steady improvement in this patient's condition should date from the commencement of adrenalin in treatment.

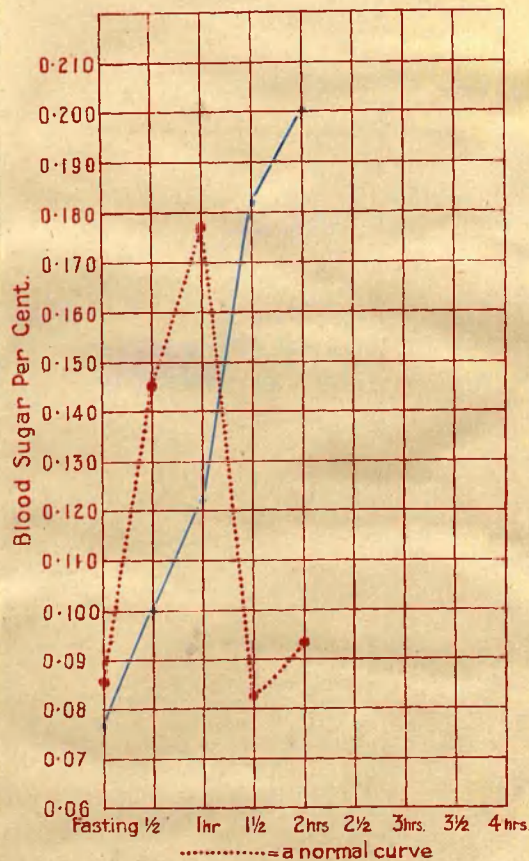
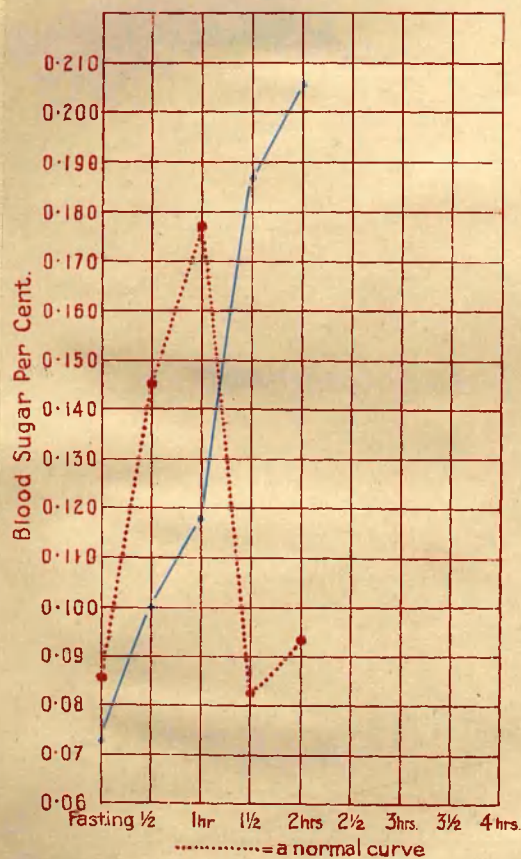
The curves belonging to this case are given in the following page, together with, for comparison, the curve from the case of Addison's disease.

Owing to the improvement which seemed to follow the administration of adrenalin in this case of pemphigus, the effect of adrenalin in another bullous type of disease, e.g. dermatitis herpetiformis, was tried:-

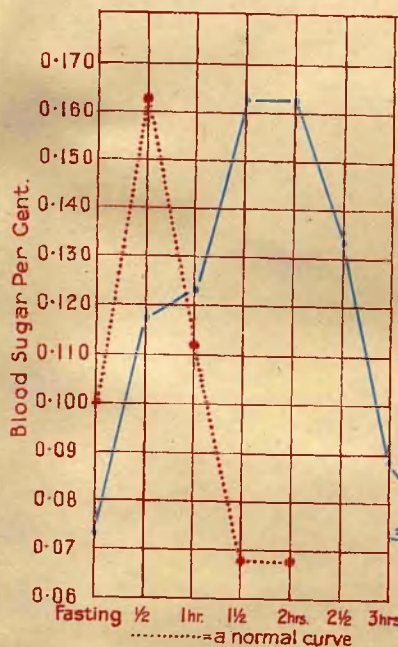
The child, aet 5, had had the disease for three years. Small doses of 2mins. were given to begin with thrice weekly, and in the first ten days there was not the slightest improvement. In the next few days, however, when put on to 4 mins. doses there seemed to be a definite improvement, no fresh vesicles appearing. She was then lost sight of, unfortunately, owing to a severe scalding accident.

Case 12 - Pemphigus Foliaceus

Addison's Disease.



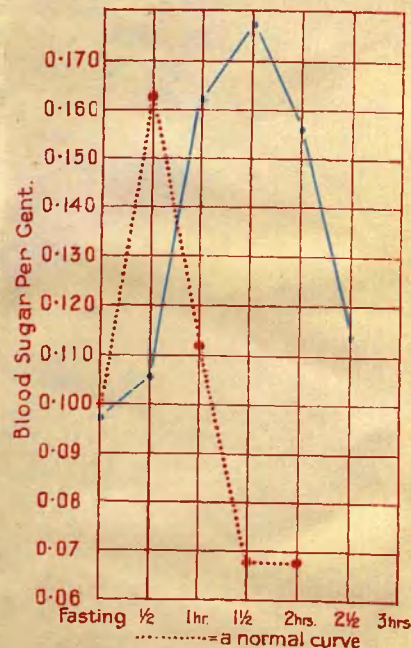
Repeat Curve.



The striking resemblance between the first two curves is seen, the delayed rise to normal or above, reaching its maximum at the two hour.

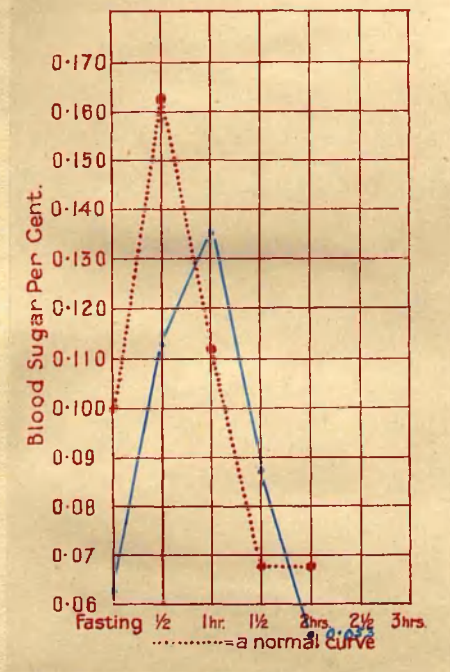
The same characteristics are seen in the repeat curve.

The fourth curve shows a quicker rise, and a fall not much delayed beyond the two hours.



The next group consists of two cases of eczema, both over 50 years of age:-

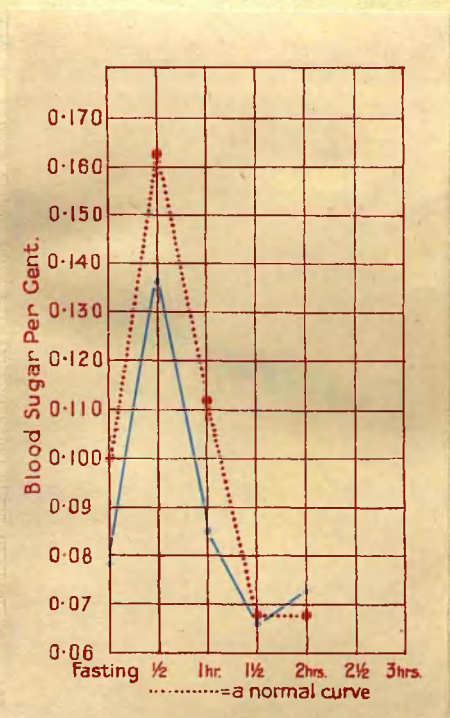
Case 13 - Chronic Eczema.



His condition was of nine years' duration. For a week previous to the taking of the curve he had been on thyroid gr.1, nightly.

In spite of his age and the thyroid, his curve is seen to be lower than the usual normal.

Case 14 - Chronic Eczema.

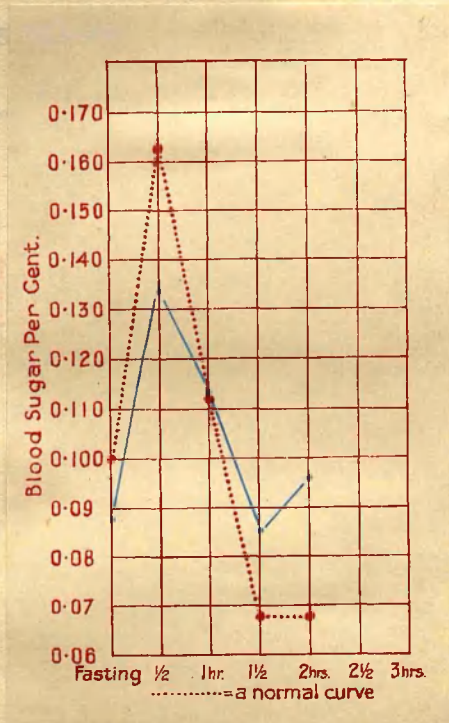


This curve also in spite of the patient's age, is seen to be on the low side of normal. As, in two other cases showing a low curve, it was thought that several factors pointed to a suprarenal insufficiency, this patient was put on adrenalin, but by the mouth.

As a substitute for what was ordered she was given 5 grs. of suprarenal gland in tablet form, thrice daily. A week later the original lesion appeared improved, but the fingers had become irritable. Three days later the hand became much worse, swollen, and septic. She was then lost for observation.

There is only one case in this group:-

Case 15 - Mycosis Fungoides.



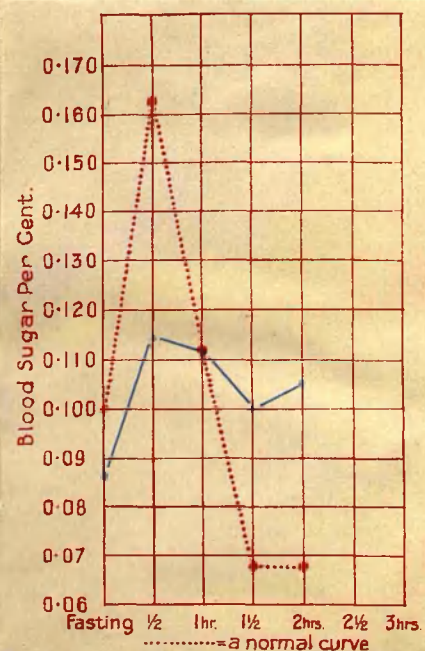
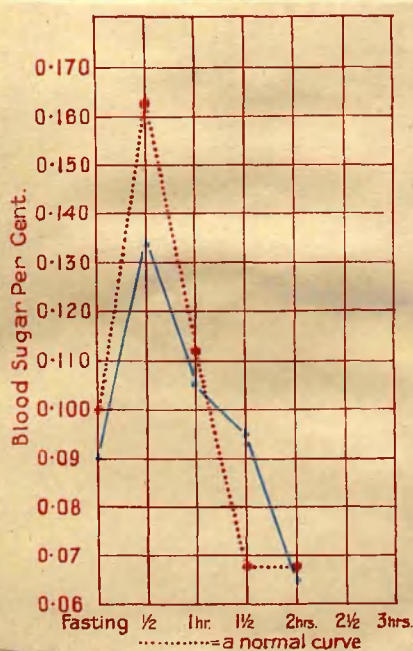
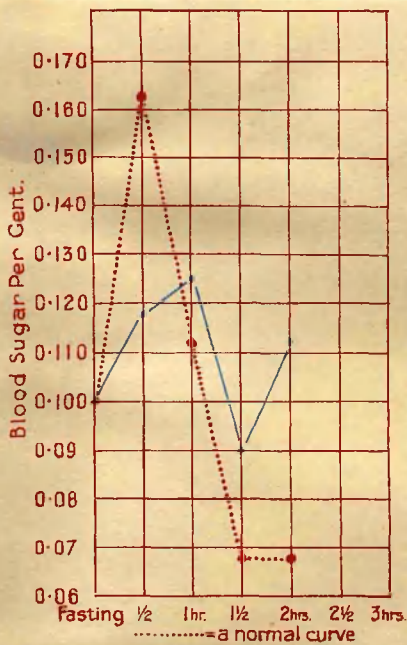
The curve here is lower than the usual normal.

The next group consists of two cases, in one of whom a repeat curve was done:-

Case 16 - Hydroa Aestivale.

Repeat Curve

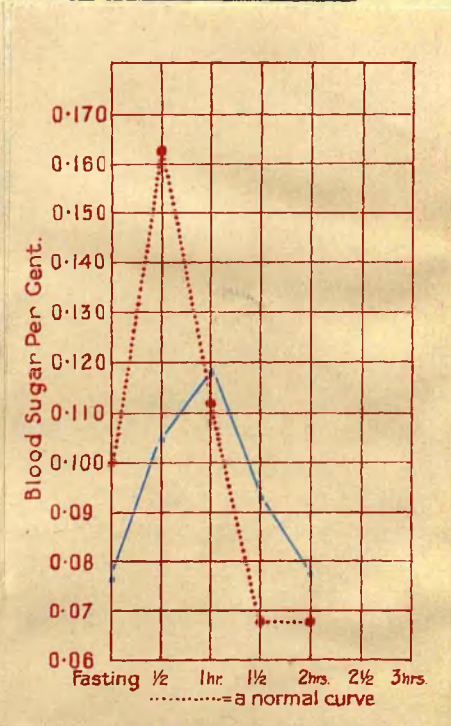
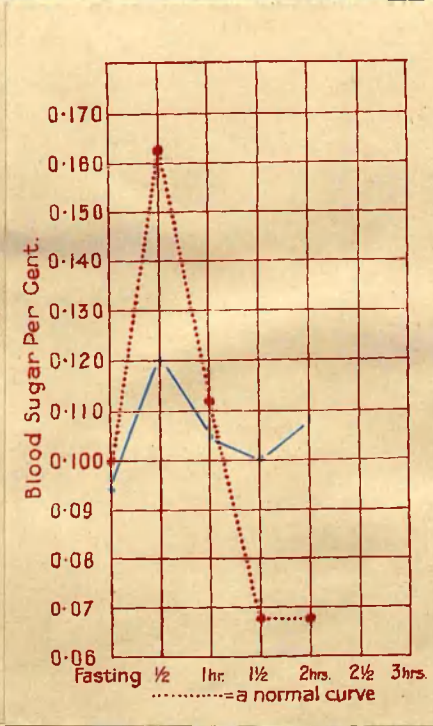
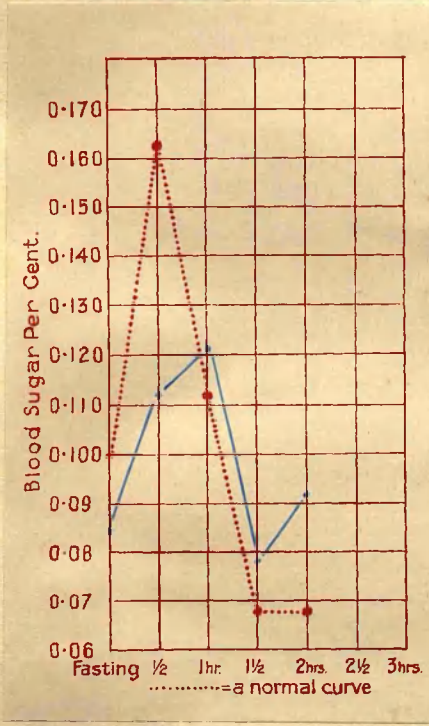
Case 17 - Hydroa Aestivale.



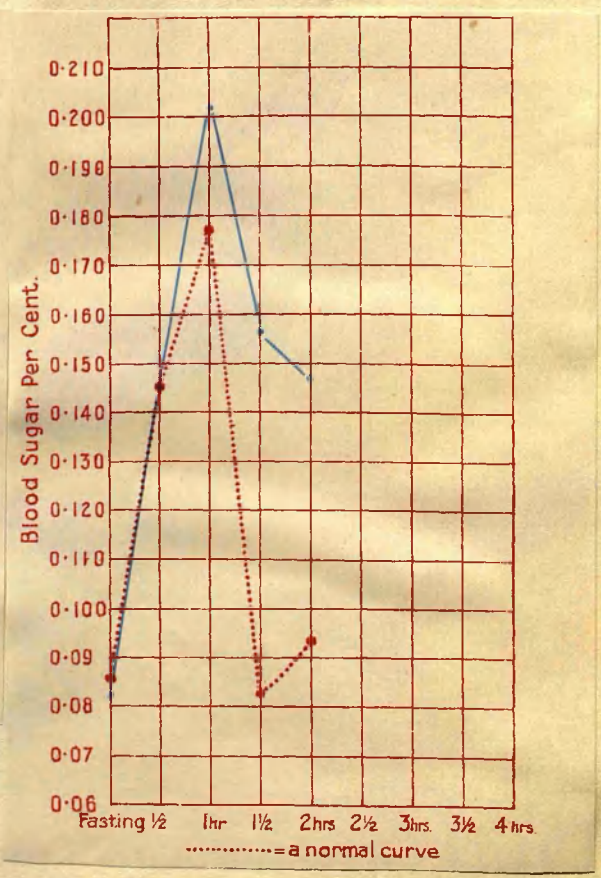
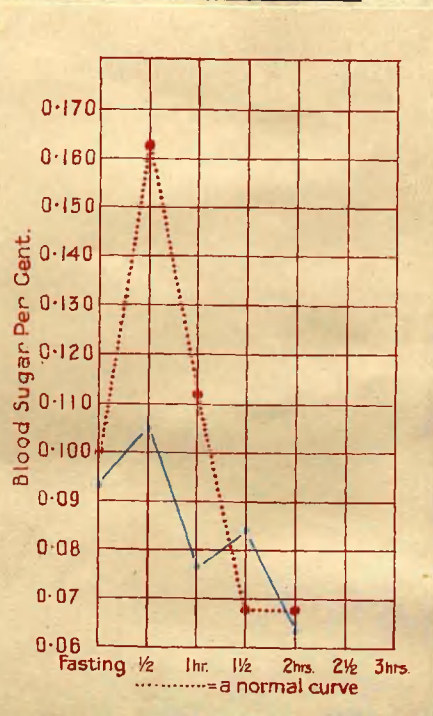
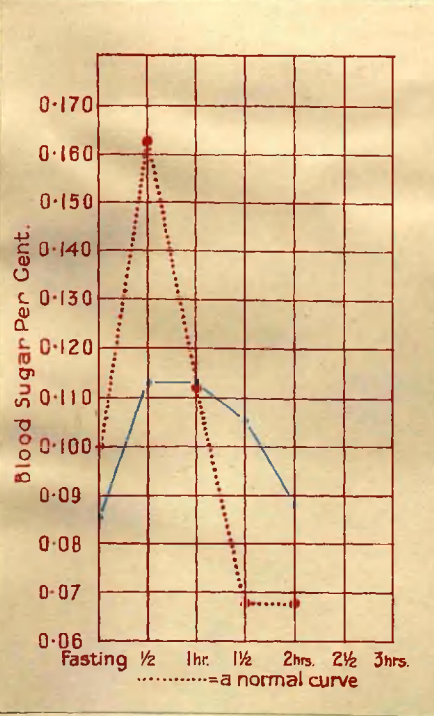
The three curves are all low. These two cases are described at length in a later section.

The only cases remaining to be described belong to the group of pruritus ani and pruritus vulvae. This group consists of six cases whose original curves are presented below:-

Case 18 - Pruritus Ani. Cases 19 and 20 - Pruritus Vulvae.



Cases 21, 22 and 23 - Pruritus Vulvae.



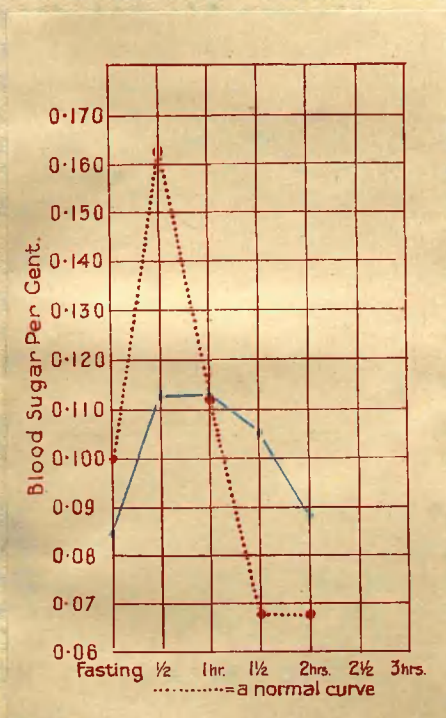
All the curves are very low except the sixth, which is abnormally high and prolonged.

The findings in this group are very striking, five out of the six yielding curves closely similar. As the curves were very low treatment with adrenalin was tried in most cases:-

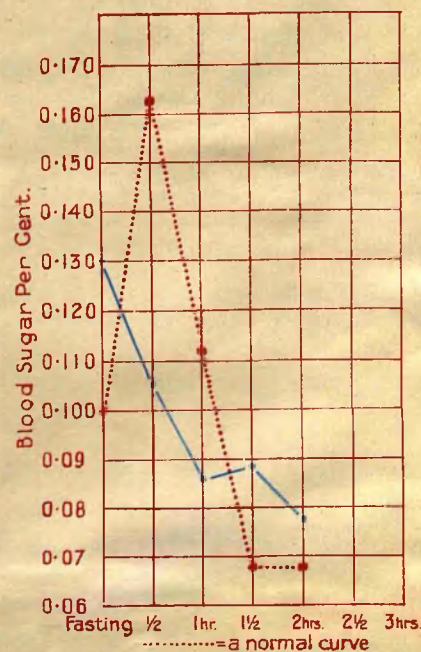
The first two cases of the group were private patients, and the duration of the complaint in each was 6 years. Only one examination was made in their case. Both were put on adrenalin, but without result.

The third case of the group was discharged from hospital before interest in this group of cases had been aroused. The low curve in her case is all the more significant as she was over 70 years of age.

The fourth case had had the condition for $3\frac{1}{2}$ years. She was put on adrenalin in gradually increasing doses from 3 mins. daily. At the end of a week there was absolutely no improvement, also, unlike the others on adrenalin, she was having no reaction in the form of trembling after the injection. The curve obtained after a week's treatment is compared below with the original.



There is seen to be little difference in the two curves. The high reading in the second, before glucose, is accounted for by the fact that the patient had breakfasted an hour before.



The patient was then given 8 mins. of adrenalin daily, but showed no improvement until six days later after a dose of 9 mins.: then she had a day and night of comparative freedom from itch, the adrenalin also was causing trembling after the injection. Another good day followed this one, the dose being increased to 10 mins. The itch then returned, however, for two days, to be followed by a day of freedom, then a relapse. The adrenalin accordingly was stopped as it was thought that any good effect likely to arise from the injections should in this time, viz. three weeks, have declared itself more definitely.

In the fifth case the duration of the complaint was nine months. After her first injection of adrenalin she experienced great relief. The injections were, therefore, given thrice weekly, the patient living a long distance away. Relief always followed on the nights of the injections, but on intervening nights the itch was troublesome, and the patient herself suggested coming every day. The dose was gradually raised, and at the end of a week she was having 6 mins. daily.

At about the end of ten days treatment, however, the adrenalin began to be less effective, the itch being troublesome some nights. Ten days later 7 mins. doses were tried, but with no lessening in the itch. The adrenalin, therefore, was stopped. On the day of the last dose almost intolerable itch began four hours after the injection and continued all the next day.

A sugar tolerance curve was done the next day during the severe itch and was found to be entirely changed in character. The curve after glucose showed a rise well above normal, whereas the previous one taken before treatment showed practically no rise.

For a week following the taking of this curve the patient remained free from itch without injections. The itch then returned, however, with its old severity. An estimation done on the third day of this relapse showed a return to the very low type of curve. Adrenalin was again tried in small daily doses, ranging from 2 - 5 mins., definite relief being experienced the first night. On succeeding nights, however, the results were variable and there was difficulty in determining whether the return of the itch was due to too much adrenalin or to too little.

A fourth curve was done one morning following a night of itch and was found to be normal. It was concluded therefore that the dose of 5 mins. the previous day had been too large, but that the effects of excessive dosage had just worn off.

Adrenalin was stopped again and the itch returned. She is now, however, having X-ray treatment and is doing well.

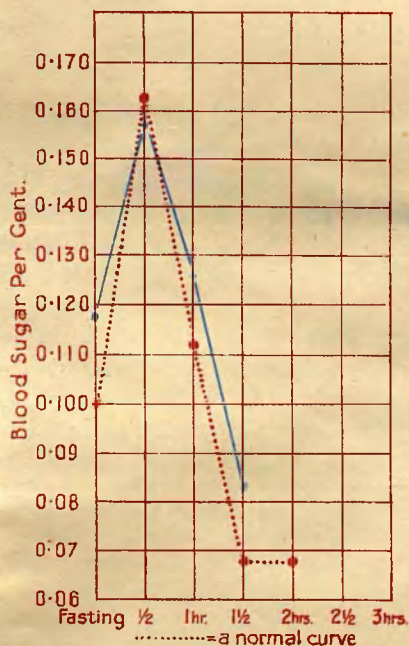
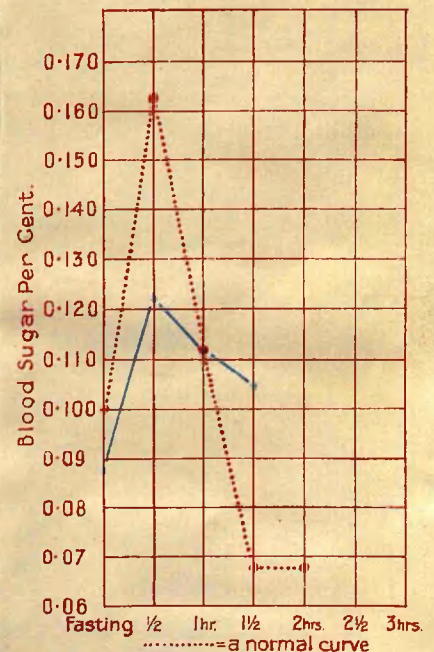
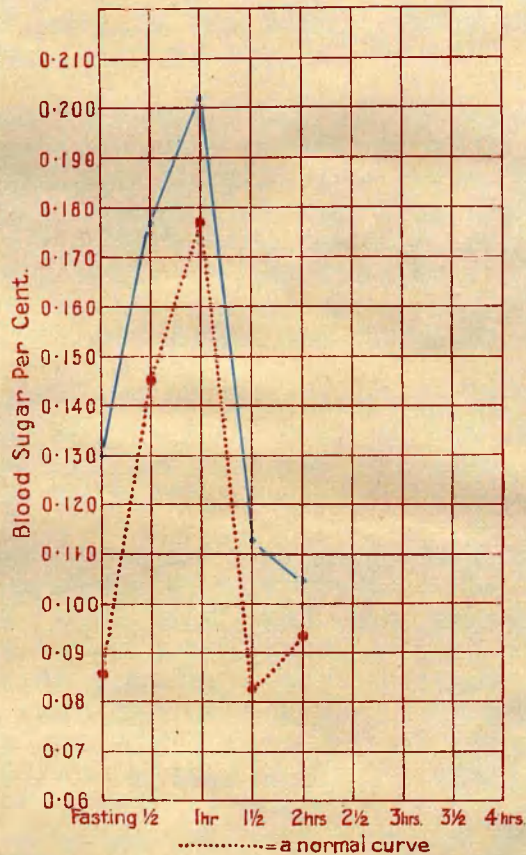
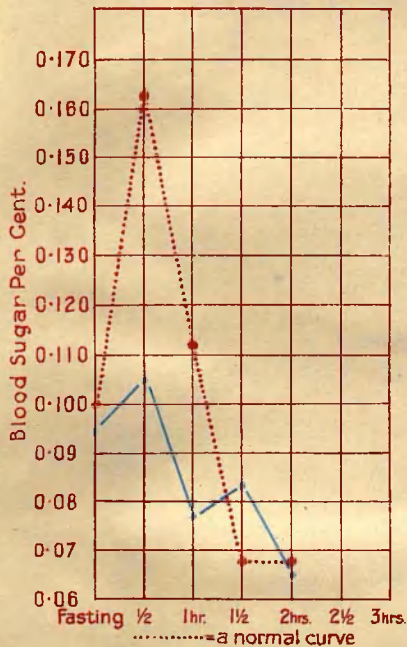
The low type of curve, together with the success at first attending the administration of adrenalin in this case, would suggest suprarenal insufficiency as a possible factor in the etiology of her condition, or some more complex endocrine disturbance. The ultimate failure may have been due entirely to the difficulty encountered in regulating the dosage to her requirements.

If adrenalin be absorbed from the alimentary tract, then by following Sajous' method and giving the dry extract along with, perhaps, thyroid, the dose might be more easily regulated. Sajous frequently, in hypoadrenia, gave 1 gr. of both with 1 gr. of Blaud's pill, .t.i.d., but stressed the importance of giving a dosage according to the requirements of the patient, one neither too large nor too small. As more than one endocrine gland is probably involved in this condition, the combination with thyroid might hasten and increase any good effect arising from the administration of suprarenal.

It is of interest that in this case the disease was of shorter duration than in those already described.

The following are the curves from the fifth case just described, showing the effect of treatment with adrenalin:-

Case 22 - Pruritus Vulvae.



The first curve is the original low one obtained before treatment.

The second shows the excessive rise in the curve as the result of over-dosage of adrenalin.

The third shows the return to the original low type of curve on stopping the adrenalin.

The fourth is a normal curve obtained just as the effects of excessive dosage again were passing off.

The sixth case had had pruritus vulvae for six months. As the sugar tolerance curve was high and prolonged and dieting had not helped her condition, it was thought that some degree of hyperthyroidism might be present. On this assumption she was given 5 units of insulin twice daily. Immediately she began to improve, until, on the fifth day, she had complete freedom from itch. From that day, however, the insulin ceased to have the same effect, and red blotches appeared at the sites of the injections. This lasted for a week, then the dose was cut down to 5 units once daily and a different brand of insulin was used. There was then slight improvement, but in a day or two the insulin was stopped.

Next day a curve was done and found to be just on the low side of normal. As the previous case seemed at this time to be improving with adrenalin, this patient also was given injections daily, increasing gradually from 3 mins. up to 6 mins. There were occasional nights of severe itch however, and she was never so well as she had been while on the insulin. The adrenalin was stopped, therefore, at the end of three weeks and a sugar tolerance curve done on the following day was found to be normal.

When seen a month later after the stopping of all medicines internally, she was not so well even as she had been while on the adrenalin. A sugar tolerance curve was done, and was found, unexpectedly, to be very low.

To explain this finding it is suggested that this patient resembles exactly the other members of her group. As it happened, her own doctor, before the first test, had been treating her with mammary gland extract. It is just possible, if, as is frequently the case, the tablets contained some pituitary extract, that this might have caused the slight rise and prolongation of the curve originally encountered. With the administration of insulin this abnormality would be rectified, and relief would be obtained when the blood sugar returned to normal. A normal blood sugar would indicate the attainment of a proper balance between the various members of the endocrine system. On continuing the insulin, the balance would be again upset, with a lowering of the sugar tolerance curve and a return of the itch. It was probably the cutting down of the insulin rather than the use of a new brand which caused the slight improvement before stopping the insulin finally.

It was a surprise in this case, after three weeks' treatment with adrenalin, to obtain a normal curve, as the previous patient, on practically the same doses, and more obviously in need of adrenalin, had shown such a rise in the curve following its use. It might have been feared in this patient that the adrenalin would aggravate what appeared to be a tendency to hyperglycaemia. With the stopping of all medicines, there was a return to her true type of curve, seen for the first time, and an increase in the itch. A very slight glycosuria was present at the one hour in this curve, pointing to a condition of renal glycosuria. In none of the others of the group was a glycosuria found to afford an explanation of the low nature of the curve.

It is possible that a suprarenal insufficiency, as indicated by a low sugar tolerance curve, might arise as a secondary result of the exhaustion following insomnia in this condition, but if so, why should adrenalin alone, in the fifth case of this group, have caused such marked relief at first?

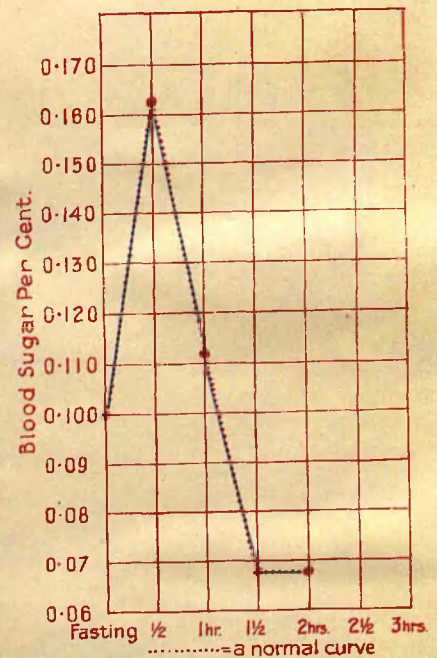
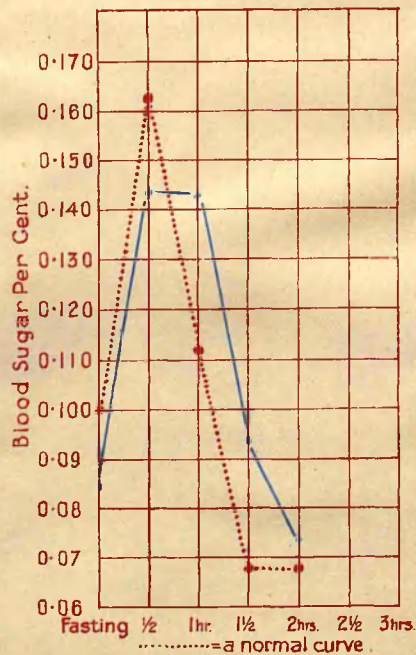
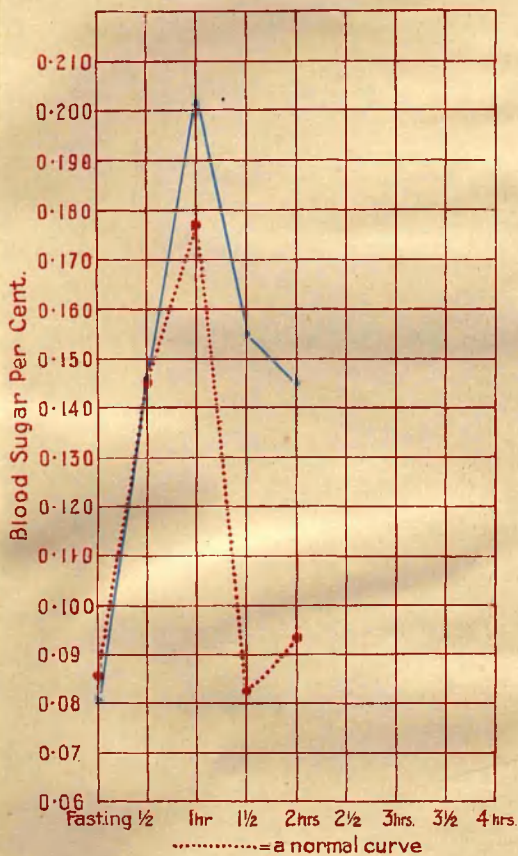
Though mention has been made only of the role the suprarenals may play in this condition, it is quite possible, considering the complex nature of the endocrine system and the inter-relationship existing between its various members, that other members of the system are **involved**.

The four curves belonging to this case are given on the following page.

The study of these few cases has shown the sugar tolerance curve to be of much more value than the determination of a single blood sugar. This would seem to be due chiefly to the possibly important part played by the endocrine system in the etiology of some dermatological conditions.

Last year some French writers⁷ published an article giving the results they had obtained with the use of insulin in certain chronic dermatoses accompanied by hyperglycaemia but not glycosuria. With some cases they were very successful, but with others not. Insulin had a rapid action in a case of pruritus vulvae and in two cases of perforating ulcer of the foot, and benefited also a case of psoriasis and a case of pemphigus. It produced no effect, however, in two other cases of psoriasis, two cases of Duhring's disease, and two cases of erythema.

There would seem to be a wide scope for research in this direction, in the relation of the sugar tolerance curve to endocrine disturbance in dermatoses.

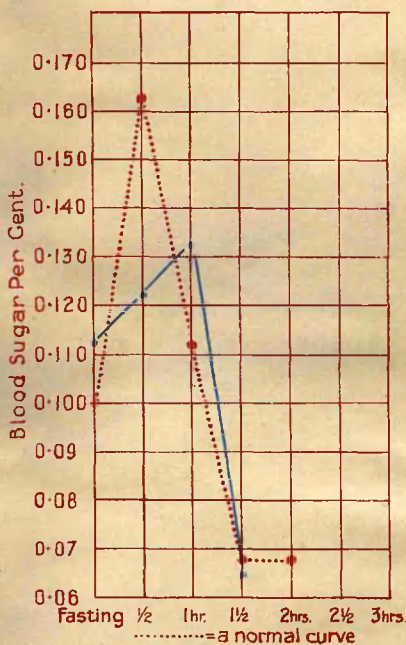
Case 23 - Pruritus Vulvae.

The first chart shows the abnormal height and prolongation of the curve. She had been having mammary gland extract up to the night before.

The second curve taken on stopping the insulin, is seen to be on the low side of normal.

The third curve at the end of adrenalin treatment is normal.

The fourth curve is the curve of renal glycosuria, very slight glycosuria being present at the one hour. This curve is lower than normal, resembling the other members of this group of cases. The curve was taken about a month after the stopping of all medicines internally.



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The URIC ACID CONTENT of the BLOOD.

Estimations of the uric acid content of the blood in eczema and other dermatoses were undertaken in 1923 by Schamberg and Brown.¹ In eczema and pruritus raised values were frequent, but in other dermatoses, infrequent. Cases yielding a high blood uric acid were found to respond very satisfactorily to dietetic treatment, previously obstinate cases often clearing up on on purin-free diet.

The usual range for the blood uric acid in healthy individuals is from 2 - 3 mgs. per 100 cc., and as the extremes of normal, Myers² gives figures of from 1 - 3.8 mgs., variations being said to depend in part probably on dietary factors. Schamberg and Brown chose 3.7 mgs. as their commencing pathological figure, and of 161 eczema cases, found 44% to give values of 3.7 mgs. or over, and more than 30% values of 4 mgs. or over.

Our series consists of forty-four cases in all, of whom nineteen were eczema cases. Of the whole number, one only could be said to give a definitely raised value, viz. 5.1 mgs., and five were on the border-line. This abnormally high reading belonged to the eczema group, but the border-line readings to other groups.

The following Table gives a summary of the findings for the various groups and shows the main types of cases examined:-

S U M M A R Y

Condition	Average Blood Uric Acid.	No. of Cases	Highest Reading	Lowest Reading	Percentage with values of 3.7 mg. or over.
Prurigo	3.37 mg.	3	3.75 mg.	3.00 mg.	33 %
Seborrhoeic) Dermatitis)	3.18 mg.	7	3.75 mg.	less than 2.20 mg.	28
Pruritus	3.11 mg.	5	3.75 mg.	2.60 mg.	20
Miscellaneous	2.96 mg.	10	3.70 mg.	2.70 mg.	10
Eczema	2.94 mg.	19	5.10 mg.	2.10 mg.	5

The eczema group far from heading the list is seen to have the lowest average of all the groups, and that, notwithstanding its one high value of 5.1 mg. No definite conclusions can be drawn regarding the other groups, their numbers being much too small.

The eczema case from whom the high value of 5.1 mg. was obtained seemed certainly to respond satisfactorily to restriction of proteins in the diet; he was at the same time, of course, at rest in bed and having local treatment: with dieting his blood uric acid, as shown in the eczema table, came down to normal and he was discharged well. About **three months** later, however, during a relapse, his blood uric acid was found to be still normal. The high blood uric acid, therefore, could not have been the only factor of importance in the etiology of his condition.

The findings for the different groups are given in more detail in the following tables:-

CHRONIC PRURIGO and PRURIGINOUS ECZEMAS

No.	Date	Age	Condition	Duration	Blood Uric Acid in mg. per 100 cc's.	Remarks.
1.		30	Chronic Prurigo	10 years	3.75 mg.	
2.	27/9/24	56	" "	9 months	3.36 mg.	
3.	23/11/26		" "	10 months	3.00 mg.	

Average ... 3.37 mg. Number with values of 3.7 mg. or over 1 = 33%.

The first case of this group exceeds 3.7 mg. and values on the whole tend to be on the high side of the usual normal. The group, however, consists of only three cases.

SEBORRHOEIC DERMATITIS.

No.	Date	Age	Condition	Duration	Blood Uric Acid in mg. per 100 cc's.	Remarks.
1.	24/6/24	76	Seborrheic Dermatitis.	1 year	3.75 mg.	
2.	6/12/24	47	Acute.	1 month	3.75 mg.	
3.	7/7/26	54		2 months	3.60 mg.	
4.	24/8/26	30		1 year	3.40 mg.	
5.		19		8 months	3.10 mg.	
6.	21/9/26		Acute - with boils.	2 weeks	2.50 mg.	
7.	25/4/25	4	Acute.		less than 2.20 mg.	

Average ... 3.18 mg. Number with values of 3.7 mg. or over 2 = 28%.

There is a decided tendency in this group for values to be on the high side of normal: the low reading obtained in case 7 is only what might be expected considering the age of the child. This tendency, coupled as it is with a similar tendency in the case of the blood sugar, seen especially in the sugar tolerance curves, would suggest for consideration in treatment an all round restriction in the diet.

P R U R I T U S.

No.	Date	Age	Condition	Duration	Blood Uric Acid in mg. per 100 cc's.	Remarks.
1.	16/2/25	59	Pruritus Vulvae with lichenoid eczema.	2 years	3.75 mg.	
2.	14/10/26	32	Pruritus Vulvae.	6 months	3.30 mg.	
3.	1/7/26	39	" "	3½ years.	3.20 mg.	
4.	26/1/25	62	Pruritus - scalp and shoulders, with slight lichenification.	1 year.	2.70 mg.	
5.	30/10/26	40	Pruritus Vulvae with ? lichen simplex of neck.	7 months	2.60 mg.	

Average ... 3.11 mg. Number with values of 3.7 mg. or over 1 = 20%.

The average blood uric acid for the group here exceeds the usual normal, and the first case gives a value of over 3.7 mg.

MISCELLANEOUS CASES.

No.	Date	Age	Condition	Duration	Blood Uric Acid in mg. per 100 cc's.	Remarks.
1.	19/10/25		Lichen Simplex.		3.70 mg.	
2.	2/6/25	53	? Acne, Varioliformis.		3.10 mg.	
3.	17/9/24		Varicose Dermatitis with ulcer.	1 year.	3.00 mg.	
4.	24/8/25	35	Sycosis	7 years	3.00 mg.	
5.	16/8/26	40	Urticaria		3.00 mg.	
6.	7/7/26	40	Rosacea.	3 years	2.90 mg.	
7.	14/9/26		Multiple Boils.	4 weeks.	2.80 mg.	
8.	20/8/26	19	Hydroa Aestivale.		2.70 mg.	
9.	16/8/26	9	" "		2.70 mg.	
10.	30/6/24	42	Erythrodermia.	5 months.	2.70 mg.	

Average ... 2.96 mg. Number with values of 3.7 mg. or over 1 = 10%.

One case here gives a value of 3.7 mg., but readings on the whole lie within the usual range of normal.

CHRONIC ECZEMA.

No.	Date	Age	Condition	Duration	Blood Uric Acid in mg. per 100 cc's.	Remarks.
1.	27/9/24	42	Severe Generalized Eczema.	2 years	5.10 mg.	
	10/11/24				3.80 mg.	While on protein restricted diet.
	23/3/25				3.15 mg.	Very great improvement.
					2.60 mg.	During a relapse.
2.	2/2/25		Recurring Eczema - hands (Dysidrosis).		3.60 mg.	
3.	25/10/26	56	Chronic Eczema.	20 years	3.30 mg.	
4.	1/6/25		" "		3.30 mg.	
5.	26/1/25	18	" "	6 years.	3.10 mg.	
6.	13/10/25		Chronic Eczema with severe pruritus.		3.00 mg.	
7.	18/5/25	37	Generalised lichenoid eczema.	10 months.	3.00 mg.	
8.	4/5/25	13	Chronic Eczema.	4 years.	3.00 mg.	
9.	7/2/25	56	Lichenoid Eczema.	5 months	3.00 mg.	
10.	28/1/25	56	Chronic Eczema.	1 year.	2.80 mg.	
11.	9/6/25	29	" "	28 years.	2.76 mg.	
12.	10/11/24	59	" "	8 months	2.70 mg.	Two readings.
13.		22	" "	10 years.	2.70 mg.	
14.	14/6/24	32	" "	10 years.	2.70 mg.	
15.	28/1/25	24	Vesicular Eczema.	6 years	2.70 mg.	
16.	27/5/26	53	Chronic Eczema.		2.50 mg.	
17.	24/6/26	53	Chronic Eczema with severe pruritus.	4 years	2.40 mg.	
18.	23/9/25		Scaly Eczema.	6 years.	2.20 mg.	
19.	1/9/25	22	Acute Eczema.	2 weeks.	2.10 mg.	

Average ... 2.94 mg. Number with values of 3.7 mg. or over 1 = 5%.

In case 1 there is seen to be a gradual fall in the blood uric acid on restricting the proteins in the diet, great improvement in the patient's condition taking place as the uric acid approaches normal. During the relapse the blood uric acid is seen to remain normal.

No other case of the group exceeds 3.7 mg.

Our results then fail to confirm those of Schamberg and Brown: for this reason it has been thought advisable to include as controls some general medical cases. In many of these a rise in the blood uric acid might be anticipated.

Kidney cases form the bulk of the controls, and in many of these simultaneous estimations of the blood urea and creatinin have been made. The cerebrospinal urea also has been estimated in three instances.

The normal range for the blood urea is from 15 - 40 mg. and for the blood creatinin 1 - 2 mg. Opinion differs as to the normal range for cerebrospinal urea. Beaumont and Dodd³ give as the general opinion Leopold and Bernard's figures of from 15-28.9 mg., while stating that they personally find the figure to be higher than this and approaching more the values for the blood.

The first of the following two tables consists of cases of terminal nephritis. Values for the blood urea, uric acid, and creatinin, therefore, and cerebrospinal urea, ought to be at their height. This is not invariable, however, as cases of uraemia occur in which an examination of the blood or cerebrospinal fluid may be of no help whatever in diagnosis, as in case 7 of this table.

Almost all the cases of this table were proved, post-mortem, to be suffering from chronic interstitial nephritis, and it is in chronic interstitial nephritis that the greatest retention of the blood uric acid takes place.

TERMINAL NEPHRITIS.

Case.	Age	Clinical Diagnosis.	Date.	Blood Analysis mg. per 100 c.c's.			Cerebro- spinal Urea mg. per 100 c.c's.	Remarks.
				Urea	Uric Acid	Creat- :inin.		
1.	29	Uraemia	6/10/26	217	8.0	3.7	-	Died 16/10/26.
			11/10/26	296	8.0	6.0	-	- P.M. (see
			14/10/26	440	10.0	7.5	-	note).
2.	38	Purpura with chronic nephritis.	18/10/26	421	8.8	7.5	-	Died 26/10/26 (see note)
3.	36	Uraemia.	9/6/25	360	10.0	-	-	Died 10/6/25 - P.M. (see note).
4.	55	Anuria	15/6/25	268	7.9	-	-	Decapsulation 16/6/25: Died 17/6/25 -P.M. (see note).
			16/6/25	298	8.8	-	-	
5.	31	Acute Nephritis.	14/7/25	-	-	-	160.0	Died 20/7/25 - P.M.(see note)
			15/7/25	179	4.9	3.0	-	
			20/7/25	280	9.0	4.6	-	
6.	45	Uraemia	10/6/26	100	4.5	1.8	-	Died a month later (see note).
7.	58	? Specific or Uraemia.	13/8/25	-	-	-	29.6	Died 14/8/25 - P.M.(see note)
			14/8/25	44	-	-	-	
8.	15	Uraemia	21/9/25	-	-	-	310.0	Died 22/9/25

In the terminal stages of a chronic interstitial nephritis the blood urea may rise to 600 mg. or over, the blood uric acid to 10 mg. or over, **Myers** having obtained the enormous figure of 27 mg. in one case. With a blood creatinin of 5 mg. or over, death as a rule is imminent and the prognosis is very unfavourable with a creatinin of over 4 mg. The blood creatinin has been known to rise to over 30 mg. and the cerebrospinal urea to about 500 mg.

N O T E S.

Case 1. Admission 2/10/26 as a case of mitral stenosis and nephritis with a history of dimness of vision for three days. Anaemia was very marked, the red cell count being 1,600,000. The urine contained blood and abundant albumin, also epithelial, granular, and blood casts. The systolic blood pressure was 180 m.m. Hg. and the diastolic 148; retinal haemorrhages were present. Her condition, as shown in the table, steadily deteriorated, dyspnoea being marked. She died 16/10/26.

P.M. examination revealed a condition of the body like that found in pernicious anaemia with thrush - breast, heart and fatty degeneration of the various organs. There was evidence of old endocarditis at the mitral valve, with marginal thickening of the valves, and the aorta showed advanced atheromatous sclerotic patches. Both kidneys also were the seat of chronic interstitial nephritis, cortex and medulla being difficult to differentiate.

Case 2. Admitted 6/10/26 on account of purpura of five months' duration and epistaxis of a fortnight's duration. She had suffered from vomiting also for a month. There was great prostration. The blood showed a profound anaemia, also a thrombopenia and delayed coagulation time. There was slight oedema and the urine contained abundant albumin and granular casts. Kidney symptoms, however, were not obtrusive, the systolic blood pressure being 120 m.m. Hg. and the diastolic 44. Owing to the continuance of the epistaxis and purpura she was given a transfusion of 500 c.c.'s. of blood, but after a temporary improvement died four days later, 25/10/26. There was no P.M.

Case 3. The urine contained two Esbach of albumin, and granular casts, but no blood. Convulsions were present before death.

P.M. examination revealed a chronic interstitial nephritis with granular contracted kidneys, one being reduced to one-third of its normal size. The brain and lungs were oedematous and the heart hypertrophied.

Case 4. Had anuria for four days, but without signs of uraemia. $1\frac{1}{2}$ ozs. of urine were obtained on the fourth day by catheter and contained .5 Esbach of albumin. His systolic blood pressure that day was 172 m.m. Hg. and the diastolic 100. Decapsulation of both kidneys was performed on the fifth day, but the man died twenty-four hours later.

P.M. examination revealed an enlarged prostate and an acute exacerbation of a chronic nephritis, the kidneys being slightly granular. There was some hypertrophy of the heart and slight oedema of brain and lungs.

Case 5. Had retinal haemorrhages, and the urine contained albumin and blood. The systolic blood pressure was 222 m.m. Hg. and the diastolic 170, and he had convulsions before death.

P.M. examination showed the kidneys to be the seat of marked interstitial change, with a superadded acute inflammation. The heart was greatly hypertrophied, and the aorta and coronary arteries atheromatous.

Case 6. This patient went home a month later without consent, the urine containing abundant albumin and blood; the blood pressure had risen from 160 and 95 m.m. Hg. to 204 and 198. She died a few days later. Probably had her blood been examined before discharge the values would have been found to be considerably higher than those given in the table.

Case 7. This patient was unconscious on admission, and died with a terminal oedema of the lungs. There was the history of an occasional convulsion over some period of time and of occasional lapses of memory. The urine contained a trace of albumin.

P.M. examination revealed a general arteriosclerosis with arteriosclerotic kidneys, also oedema of lungs and brain. Examination of the blood and cerebrospinal urea in this case failed to throw much light on the condition, the blood urea being very little above normal, and the cerebrospinal urea normal, or, if Leopold and Bernard's figures be taken, just above normal.

Case 8. This child was said for six months previously to have been attending as an out-patient at another hospital, with chronic nephritis. She was, therefore, probably suffering from an acute exacerbation of a chronic nephritis. There was marked oedema on admission.

In early chronic interstitial nephritis the blood uric acid is said to be the first of the nitrogenous constituents to be retained: later, all three show retention. In acute nephritis also there may be nitrogenous retention, but to a less degree, and in parenchymatous nephritis there is little or no nitrogenous retention. Cases of nephritis are encountered in which a moderate increase in the blood urea may occur with little or no increase in the blood uric acid.

The second table gives a more miscellaneous collection

of cases:-

MISCELLANEOUS, NEPHRITIS and Others.

Case	Age	Clinical Diagnosis.	Date	Blood Analysis mg. per 100 c.c's.			Cerebro- spinal Urea mg. per 100 c.c's.	Remarks.
				Urea	Uric Acid	Creat- :inin.		
1.	32	Acute Nephritis.	6/8/25 10/9/25	89 35	3.8 3.4	1.5 1.4	- -	Now convalescent.
2.	36	"	7/7/24	84	6.75	-	-	Had nephritis in childhood, also ? exacerbation of a chronic nephritis.
3.	54	Chronic Nephritis.	5/12/24	81	4.4	-	-	
4.	49	Myeloid Leukaemia.	21/4/25	79	7.8	-	-	Albuminuria also. Urea Concentration Test - 1.6% urea in urine.
5.	30	Chronic Nephritis.	2/11/26	66	3.3	1.1	-	
6.	45	Chronic Lead Poisoning.	18/10/26	65	3.3	1.5	-	No albumin in urine.
7.	68	Cirrhosis	12/10/26 1/11/26	53 33	5.7 2.2	1.2 1.1.	-	Ascites very much less with ammonium chloride.
8.	33	Pyelitis	18/9/25	33	3.8	1.4	-	
9.	27	Acute Nephritis.	6/10/26	21	3.3	1.2	-	Very oedematous.
10.	50	Rhinorrhoea	10/12/24	25	2.7	-	-	
11.	28	"	2/2/25	23	3.0	-	-	
12.	27	Haemolytic Jaundice.	5/1/25	20	2.7	-	-	

SUMMARY and CONCLUSION.

Schamberg and Brown in investigating the uric acid content of the blood in dermatoses found a high blood uric acid frequently in eczema and pruritus, but infrequently in other dermatoses.

In the majority of cases showing a high blood uric acid, a purin-free diet was effective in clearing up the condition.

As the commencing pathological figure for the blood uric acid they accepted 3.7 mg. per 100 c.c's., and of 161 eczema cases found 44% to give values of 3.7 mg. or over, and more than 30%, or about one in three, values of 4 mg. or over.

Our results fail to confirm those of Schamberg and Brown.

Forty-four dermatoses patients were examined, of whom nineteen were suffering from eczema of various forms. Of the whole number, one only gave a definitely high value, viz. 5.1 mg. This case belonged to the eczema group, and was the only value of the group exceeding 3.6 mg. Of the eczema cases, therefore, 5% gave values of 4 mg. or over, as contrasted with Schamberg and Brown's 30%, and 5% values of 3.7 mg. or over as contrasted with their 44%.

The eczema case from which the value of 5.1 mg. was obtained improved certainly on a restricted protein diet while at rest in bed and having local treatment, the blood uric acid reaching normal on recovery. During a relapse, however, three months later, the blood uric acid was found to be still normal. Confirmation in his case, therefore, that the high blood uric acid was the factor of importance in causing his condition, was not obtained.

Our findings for the controls, which are for the most part kidney cases, agree more or less closely with those of various writers. We are inclined, therefore, to place more reliance on our results in relation to the dermatoses.

In speaking of renal disease as a cause of eczema Whitfield⁴ writes:-

"This is according to many writers, a prolific source of eczema, but I am in agreement with those who find that gross changes, such as albuminuria, diminished urea excretion, or excess of uric acid are not particularly common in eczematous patients";

and Sequeira writes -

"Gout, I take it acts not by excess of uric acid but by intoxication from the alimentary canal".

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The HYDROGEN ION CONCENTRATION of URINE and SKIN.

Early in 1925 an article appeared in the "Lancet" dealing with the pH of the urine in diseases of the skin. The author, F. C. Doble¹, had found certain diseases of the skin to be characterised by a high degree of acidity in the urine, and had, in treating such cases with alkalis, obtained very striking results. In the course of treatment the pH of the urine had to be watched, improvement almost invariably being obtained once the urinary pH had been brought within the range of normal; on going beyond that range, however, to the alkaline side, there was a tendency to relapse, or even to become worse.

To obtain some idea of the normal range for the urinary pH a large number of healthy men had been examined, the range being found to lie between 6.4 - 6.8. In some dermatoses on the other hand; .e.g. seborrhoea, seborrhoeic dermatitis, acne, and cheiropompholyx, values had been found to lie, without exception, between 4.8 - 5.8. In infantile eczema, as contrasted with seborrhoeic conditions, normal values had been obtained.

Doble noted that it was not in the titratable acid that indication of the high acidic value of the urine was to be found, but in the hydrogen ion concentration. As possible causes for this, he suggested:-

- "(1) The excretion of an abnormal acid of high dissociation constant.
- (2) The deficient excretion of one or more of the normal urinary buffers so that normal urinary acids cause a marked increase in the hydrogen ion concentration.

"(3) The abnormal excretion of some element which causes increased dissociation of one or other of the urinary constituents which are combinations of a weak base and strong acid, and vice versa".

Doble used the first specimen passed in the morning and the last at night for his determinations, and later 12 hour samples. We, for our determinations, used only the first specimen passed in the morning. In the following Table a summary of our findings is given:-

S U M M A R Y

Condition	No. of cases	Average pH.	No. under 5.8	No. over 5.8	Lowest value.	Highest value.
Lichen Planus	2	6.1	2	nil	6.3	6.0
Urticaria ...	7	6.0	4	1	6.5	5.3
CONTROLS ...	25	5.9	7	13	6.6	5.3
Rosacea	5	5.7	2	3	6.6	5.1
Prurigos	7	5.6	2	5	6.1	5.4
ECZEMA	40	5.6	15	23	7.0	4.6
ACNE	4	5.6	nil	4	5.7	5.5
SEBORRHOEIC DERMATITIS ...	34	5.5	6	26	6.8	4.8
Sycosis	3	5.5	nil	3	5.5	5.5
Dermatitis Herpetiformis.	3	5.1	1	1	6.0	4.8
CHEIROPOMPHOLYX	6	5.4	1	5	6.4	4.7
Lupus Erythematosus	5	5.4	1	4	6.6	5.0
Pityriasis ...)	2	5.4	nil	2	5.6	5.3
Rubra Pilaris)						
Miscellaneous..	21	5.4	5	12	6.0	4.8
Pruritus Vulvae	6	5.2	nil	5	5.8	4.7
Lichen Simplex.	2	5.0	nil	2	5.2	4.9

From the summary it will be seen that in the first group values to the alkaline side of 5.8 are relatively frequent; in the second group, on the other hand, they are relatively infrequent. Among the dermatoses of the second group are included those mentioned by Doble, viz. acne, seborrhoeic dermatitis, and cheiropompholyx.

It will be seen also that values for the controls are decidedly higher than those obtained by Doble, 13 out of the 25 giving values above 5.8, and although not shown in the Table, 20 out of the 25 gave values above 6.4, the upper limit of normal as ascertained by Doble. The range in our controls excepting the one high reading of 5.3 was from 5.5 - 6.6.

From the summary also it will be seen that pH values in dermatoses tend to be on the high side of normal. The lichen planus group, as it consists of only two cases, need not be considered.

In urticaria the readings were all relatively low, except in one case, a child with a toxic dermatitis urticarial in type, in whom the lesions had become septic. The presence of the sepsis here might account for the high reading.

Without treatment in some of the cases the readings varied from day to day, and many of the low readings entered in the summary were obtained on only one occasion. For this reason, in calculating the averages the first two readings for each case have been used.

The numbers in practically all the groups are much too small for statistical purposes, but the groups are entered separately to give some impression of the values encountered and of the types of cases examined.

In acne, seborrhoeic dermatitis, and cheiropompholyx, alkali treatment seemed undoubtedly to have a beneficial effect, being more marked perhaps in the latter groups than in acne vulgaris, where, as Doble pointed out, energetic local measures had also to be carried out. In other dermatoses, e.g. eczema, alkali treatment was occasionally helpful, but not so frequently as in those already mentioned. Our results on the whole have not been so striking as Doble's.

One of our first cases, and the most striking of all, is charted opposite the next page. It belonged to the eczema group:-

June July August September

2.4 27th 11th 12th 18th 29th 26th

Remarks

9 S.O.
very sinking
temperature
Still improving
"
"
very well.

pH Values

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0

urine

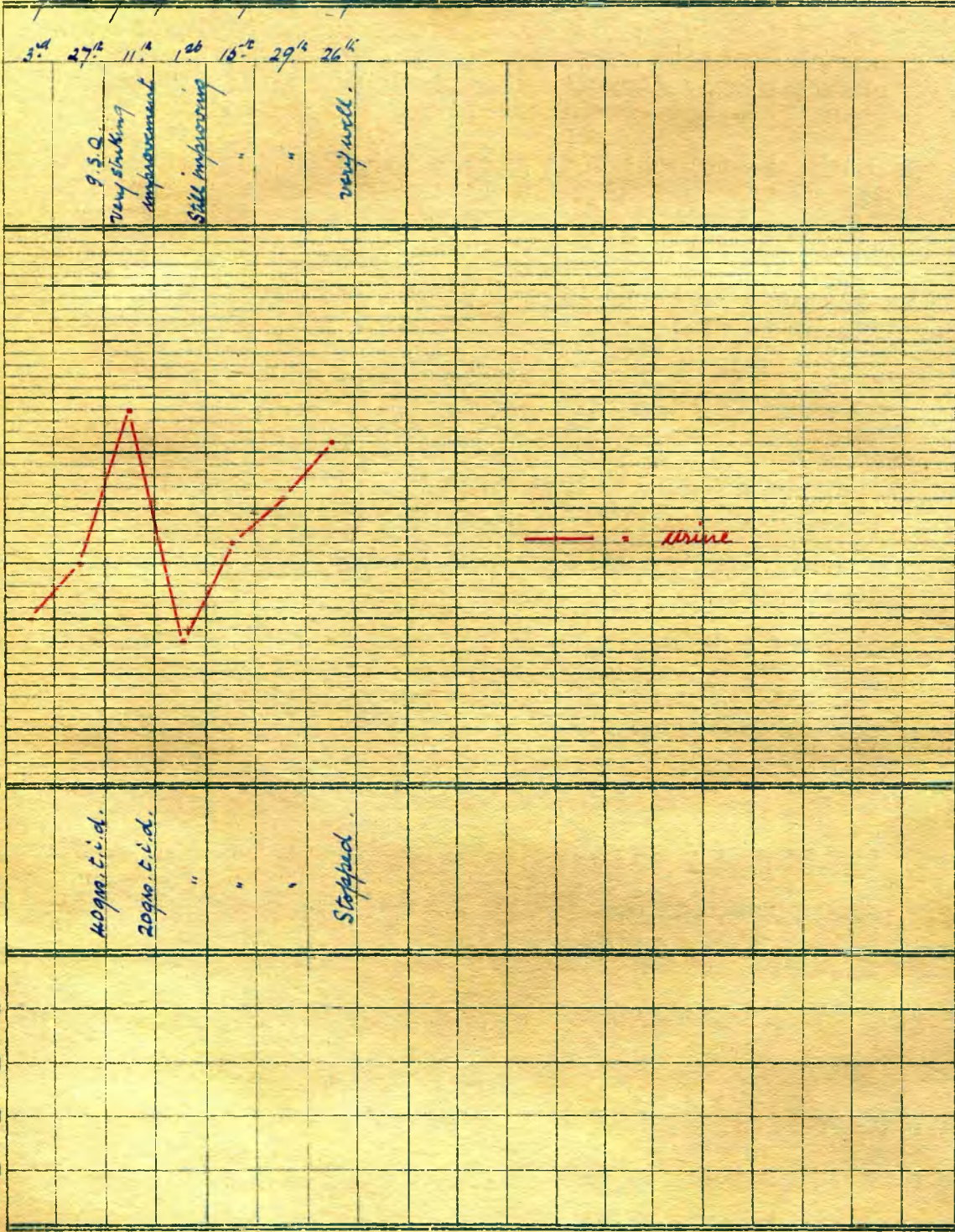
Alkalies

40grs. t.i.d.
20grs. t.i.d.
"
"
"
Stopped.

Urine

Free to Combined Acid

4.0
3.0
2.0
1.0
0



The child was 7 years of age and had suffered from chronic eczema of the genitals and groins for five years.

He was put on alkalis, and returned in about three weeks no better. He had been on holiday for a fortnight and had gone without the mixture; there was now weeping of all the eczematous surfaces.

In the next fortnight, however, with 40 gr. of alkali thrice daily, there was very striking improvement in his condition; the skin became quite dry, and he had not been so well for many years.

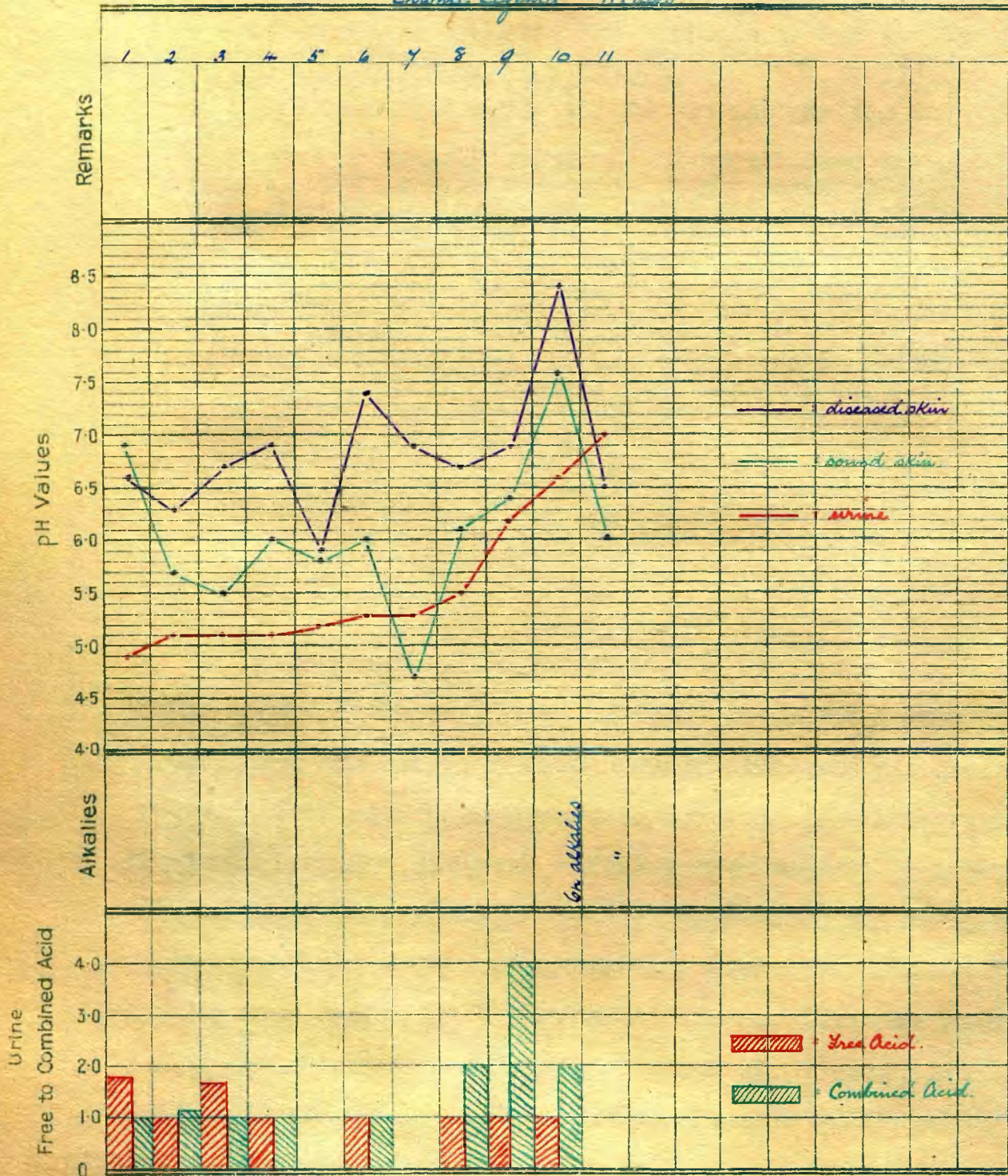
In the next three weeks the knees, previously also involved, became well, and the genitals and groins, although some thickening of the skin persisted. He continued to improve and in two months was so well that the medicine was stopped.

From the chart it will be seen that the improvement took place when the urine was definitely alkaline, and that relapse, as might have been expected from such a urine, did not occur. The improvement was maintained also, when on cutting down the dose of alkali, the pH rose, on the other hand, too far to the acid side.

Alkali treatment would seem, in this case, to have been the cause of the very striking improvement.

A few cases more will be described in detail once mention has been made of the relation of the hydrogen ion concentration of the skin to dermatoses. This formed the subject of a paper by H.A. Ellis² in 1925. He had found that the pH of the skin seemed to vary in different dermatoses, being, for example, more acid than the normal surrounding skin in eczema and acne, and more alkaline in conditions such as impetigo and intertrigo. He suggested that this variation might be of importance from the point of view of treatment, as it would be unwise, for example, to give alkalis either internally or locally in a case where, from an examination of the skin, the error seemed to lie in excessive alkali production, and vice versa. As the limits for variation in the pH of the skin, figures of from 4 - 8.5 are given, and as the more usual range Ellis gives from 5 - 7.

Chronic Eczema - 11 cases



He states that normally the skin as a whole has a uniform reaction but that in selected places it may vary from .4 - .6.

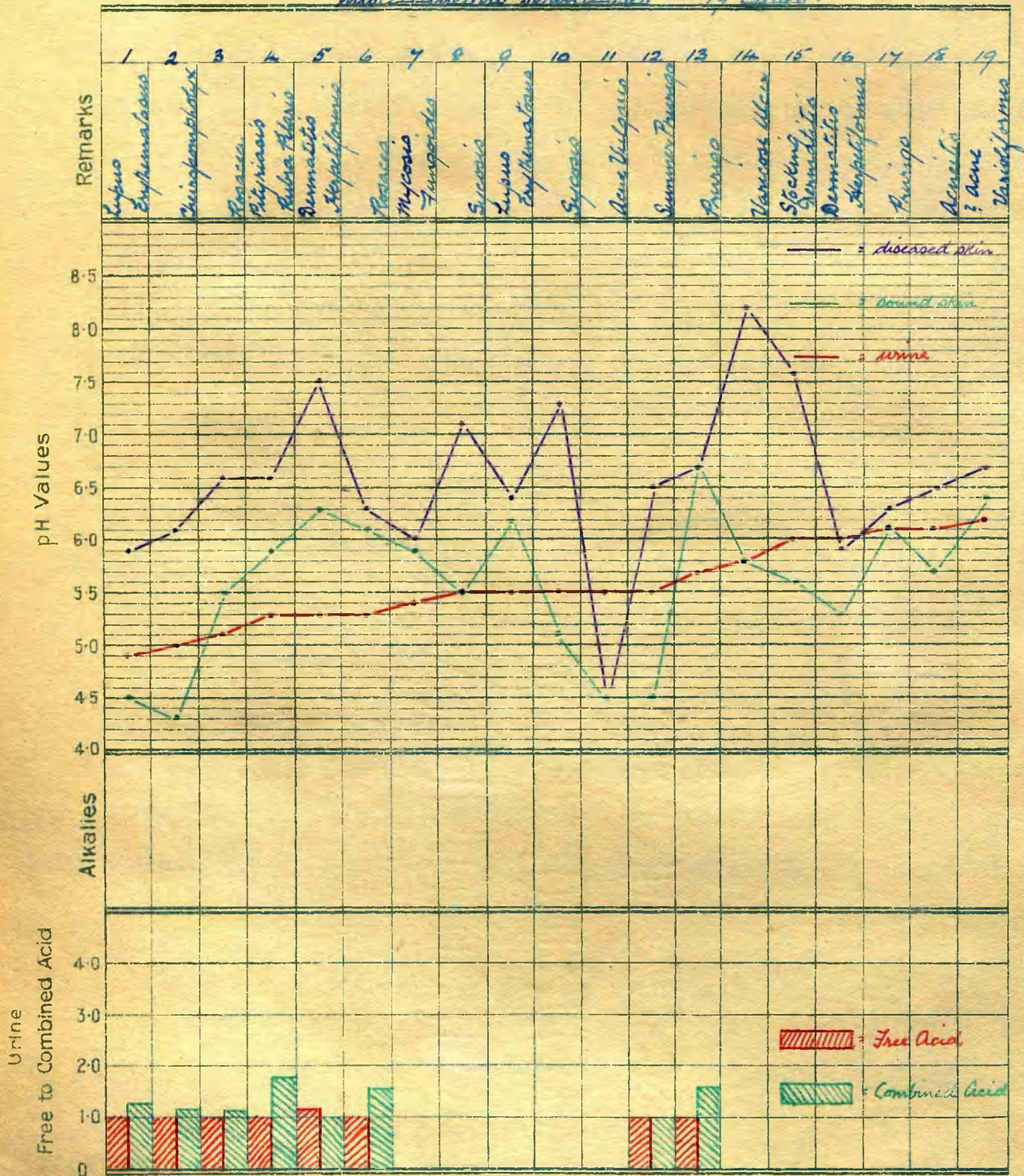
In the same article he deals with the ratio of the free, to the combined, acid in the urine, the free being excreted mainly in the form of phosphoric acid, and the combined in the form of ammonium salts. Normally there should be 1 of free to 1.5 - 2 of combined (1:1.5 - 1:2). In individuals with an acid diathesis the ratio moves to the left, becoming, for example, 1:1, and in an alkaline diathesis moves to the right - to 1:3 for example, or more. Ellis suggests that in dermatology this ratio should be of importance as a guide in treatment. The ratio of an acid diathesis may readily be converted into a normal one by the administration of alkalis, but an alkaline one, not so readily, as pointed out by the author in a different paper. In the alkaline diathesis, acids of course would be used.

On the opposite page is charted a summary of our findings in the eczema group. They are charted thus to show principally the relationship between the pH of the diseased skin and that of the sound skin. The urinary pH for that day is also charted, with, in some cases, the ratio between the free and combined acid in the same specimen or urine.

It will be seen, that but for the first case, the pH of the diseased skin is in all the cases lower than that of the sound skin. This is not in agreement with Ellis' findings. He had found the diseased skin in eczema to be more acid than the sound.

In the chart opposite the next page a summary is given of the findings in all the dermatoses, except eczema and seborrhoeic dermatitis.

Miscellaneous Dermatoses - 19 cases.



In this chart, in spite of the variety of the dermatoses included, the pH of the diseased skin is again seen to be almost constantly lower than that of the sound skin.

Only one case of acne vulgaris was examined. In acne the pH of the diseased skin is said to be more acid than that of the sound skin. In this case the relationship varied, it had on several occasions the same pH; on one occasion, however, the pH was higher than that of the surrounding skin, and on another, lower.

This case seemed definitely to improve as the result of alkali treatment, up to a point, then remained stationary, requiring, as pointed out by Doble, energetic local treatment in addition.

In connection with this acne case it is to be noted that in one of the sycosis cases, although the diseased skin in general had a lower pH than the sound skin, yet when the pH of the skin over an unbroken pustule was done, it was found to have the same pH as the sound skin.

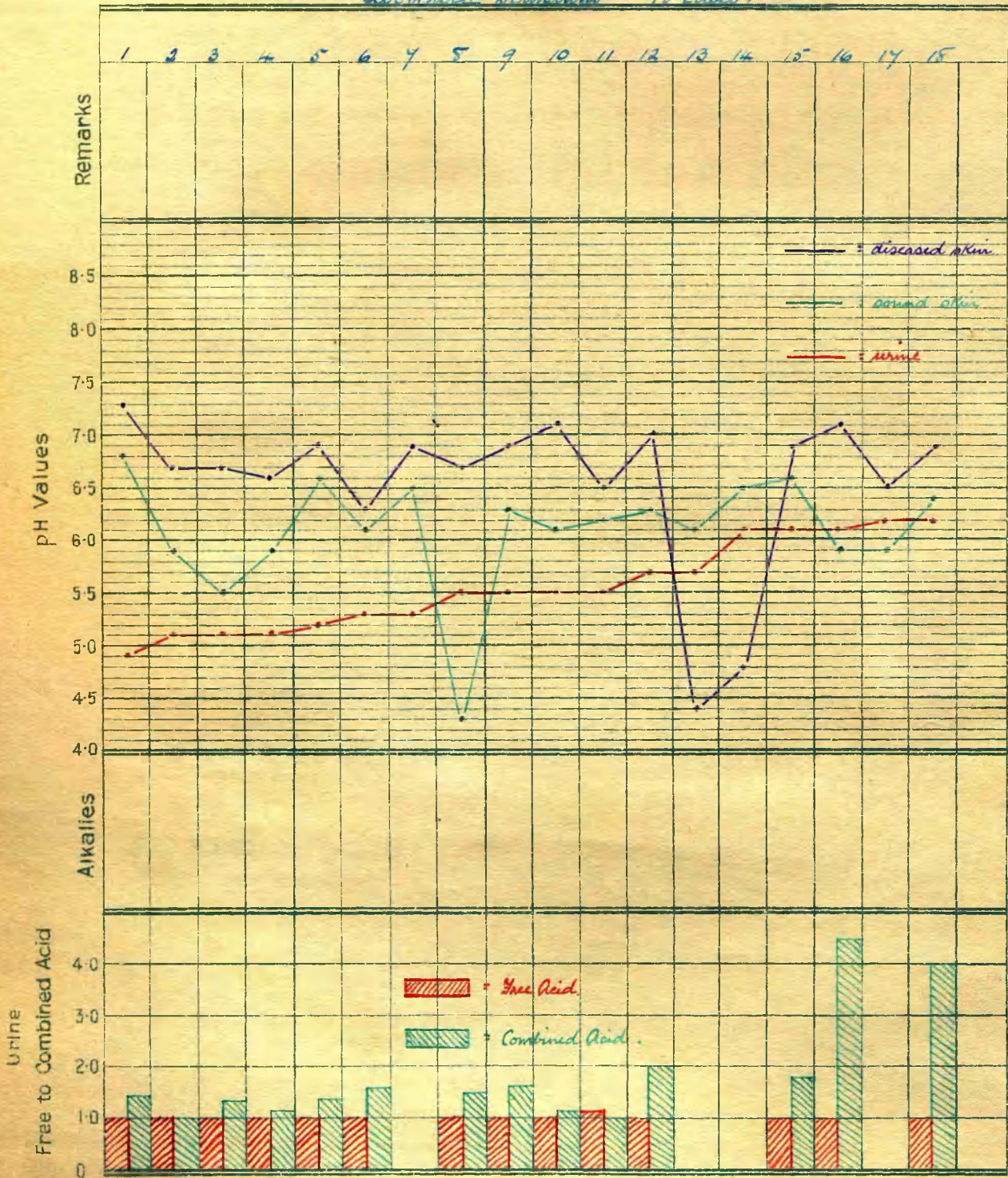
Similarly, in dermatitis herpetiformis, the pH of the skin over a broken bulla might be 7.5, and that over an unbroken vesicle practically the same as the sound skin, e.g. 4.4 with a normal skin of 4.3, no greater variation than might occur normally over different areas of skin.

At this point attention should be given to a finding in one of the seborrhoeic cases, a severe generalised seborrhoeic dermatitis in a child. The pH of the various diseased areas varied, as in all the dermatoses examined, the variation seeming to depend on the amount of exudation present.

In this child, the pH of the worst lesion, viz. over the cheek, was 6.9. A lesion at the back of the hand had a pH of 6.7. The pH over normal areas of the skin varied from 6.3 - 6.5. On the palms of the hands the lesions had a different appearance from elsewhere, being quite dry. Owing to their position they were more deepseated and, on account of the thicker skin of the palm had not yet begun to exude on the surface. The pH of the dried skin over these palmer lesions was the same on both sides, and more acid than that of the sound skin, being as high as 5.6.

The findings in this case suggest that characteristic changes in the pH of the diseased skin probably do not belong to particular forms of dermatoses, except in so far as regards the

Seborrhoeic Dermatitis - 18 cases.



presence and degree, or absence, of exudation in their lesions.

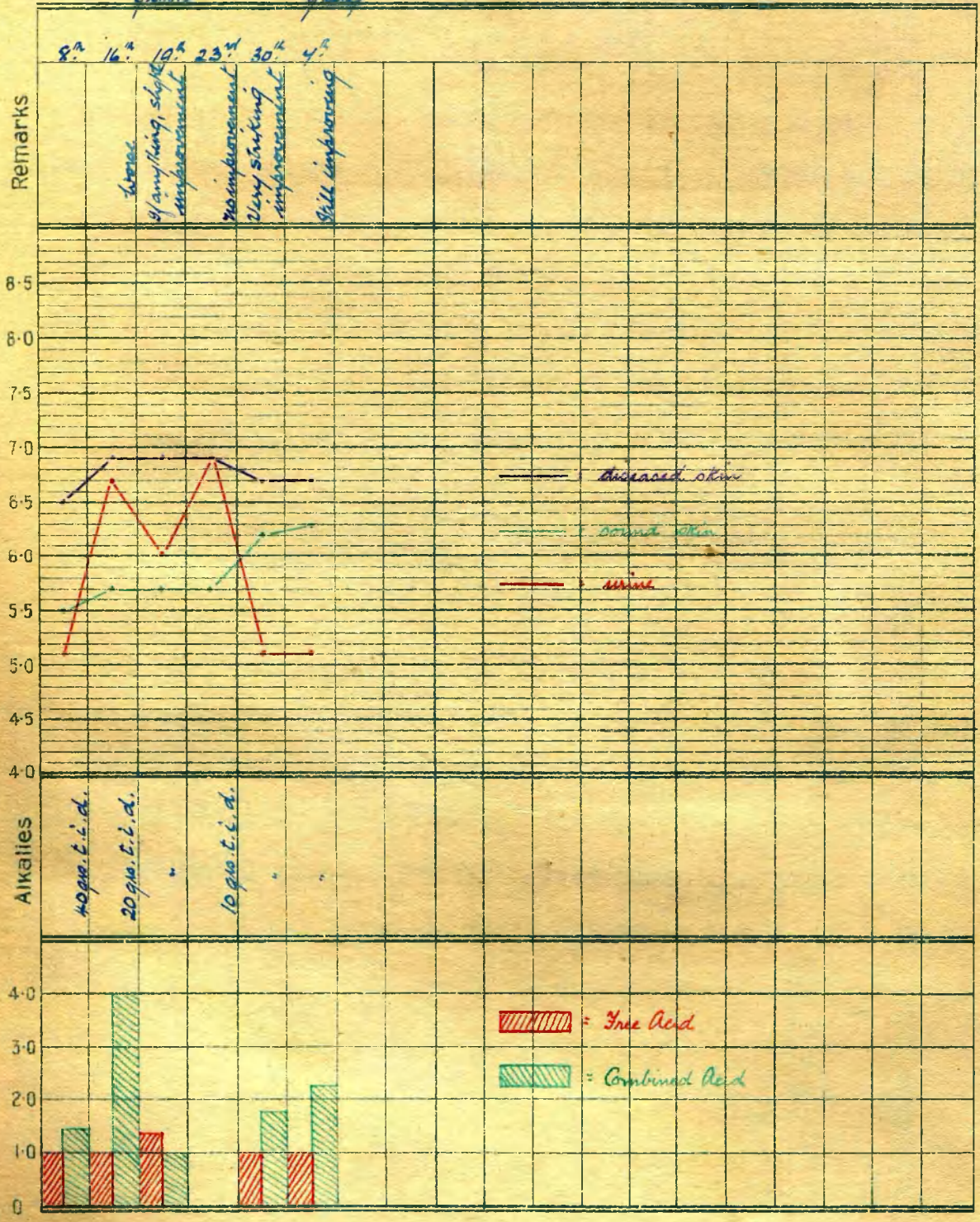
The chart opposite gives a summary of the findings in the group of seborrhoeic dermatitis. As in the others the pH of the diseased skin is almost constantly lower than that of the sound skin. Cases 13 and 14 are exceptions.

As regards the ratio between the free and combined acid in the urine, a determination of this ratio was included in many of the cases to serve as a check on the urinary pH. It was expected that with a normal urinary pH, the ratio also would be normal, and that with an abnormally high pH, the ratio also would show displacement in the acid direction.

From an examination of the chart opposite, however, this is proved not to be the case. In this chart, as in all the others, the ratio is seen to bear no constant relationship to the pH, yet for the determination of both, the same specimen of urine is always used. Cases 2, 3 and 4 illustrate this point, having the same pH, but different ratios, and cases 8, 9, 10 and 11.

This want of constancy in the relationship of the ratio to the urinary pH would seem to be of significance in the following two cases. These two belong to the group of seborrhoeic dermatitis and are, in addition, included in the few outstanding successes resulting from alkali treatment.

June July



pH Values

Remarks

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0

Alkalis

Urine
Free to Combined Acid

— diseased skin
— sound skin
— urine

▨ = Free Acid
▨ = Combined Acid

Seborrhoeic Dermatitis.

Case 1.

This case charted on the opposite page was a man of 45 years, suffering from severe seborrhoeic dermatitis of the scalp, ears, neck and face, pustulation being present over cheeks and chin. He had had the condition for 7 months.

With 40, and later 20, grs. of alkali t.i.d., instead of improving, he became decidedly worse as recorded on the chart, and it was not until as small a dose as 10 gr. was given that the very striking improvement took place; then, in a week he became better than he had been for three months. The pustules practically disappeared from the face, and the whole skin appeared drier and less inflamed looking, the scalp also being improved though still crusted: the right ear remained greatly swollen with weeping and crusting, but the left was improved. By another week he was even better, the skin over the face appearing almost normal, but red: the left ear was practically healed and the scalp shared in the general improvement: the right ear also was slightly improved.

A month later he returned during a slight relapse, having omitted the alkalis for a fortnight. Some pustules had reappeared over the cheeks in the following week. It was noticed, however, that by now both ears were practically normal.

An explanation is sought naturally, for the intolerance to alkalis at first displayed. This would seem to be supplied in the ratio between the free and combined acid. Before treatment in this case the ratio is seen to be very close to the normal, being 1:1.4 instead of the normal 1:1.5 - 1:2. With alkalis there is a much greater disturbance in the ratio, to the alkaline side, and the very striking improvement is obtained only when the normal ratio is at last established - in this case 1:1.8.

The points to be noted in the chart are:-

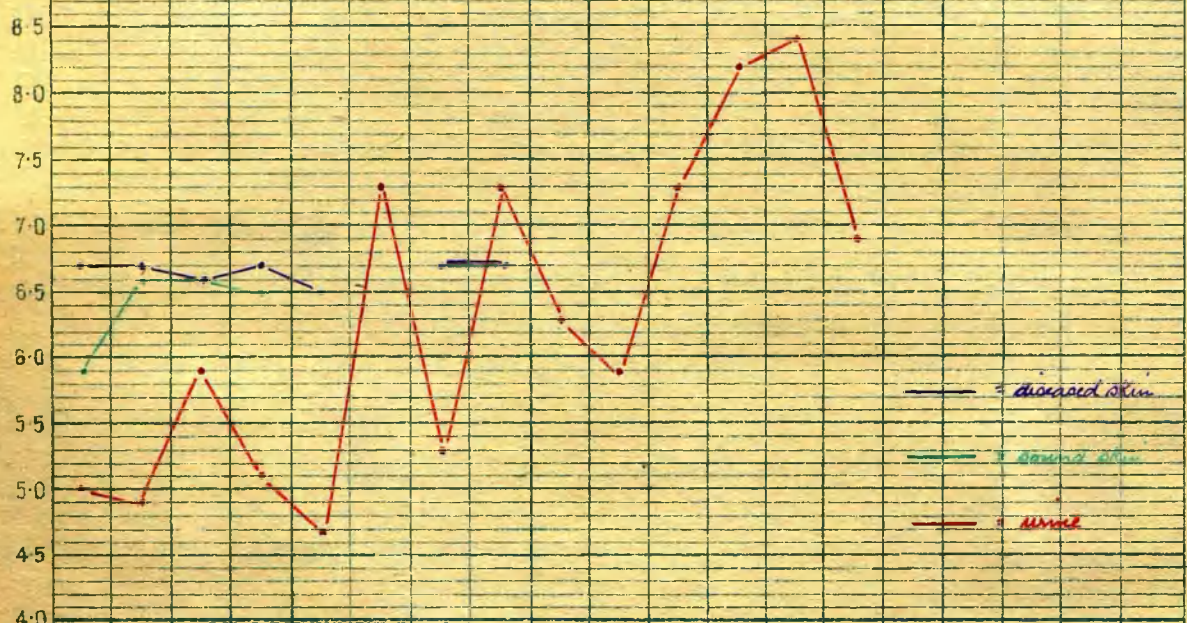
- (1) The consistently lower pH of the diseased skin as compared with the sound skin.
- (2) The approximation of these two curves to each other as improvement takes place.
- (3) The aggravation of the patient's condition as the urine pH, though still within normal limits, tends to the alkaline side; and the disproportion in the ratio of the free to combined acid at these times.
- (4) The improvement in the patient's condition on acquiring a normal ratio in the urine.
- (5) The tendency with treatment to a lowering in the pH of the sound skin.

October

November

18 th	20 th	23 rd	25 th	27 th	30 th	3 rd	6 th	8 th	10 th	13 th	17 th	22 nd	24 th
Definite improvement	Great improvement	Improvement	Still improving	Great improvement	Not so well	Not so well	Much improved	Great improvement	Still improving	Not quite so well	Very well	Still improving	

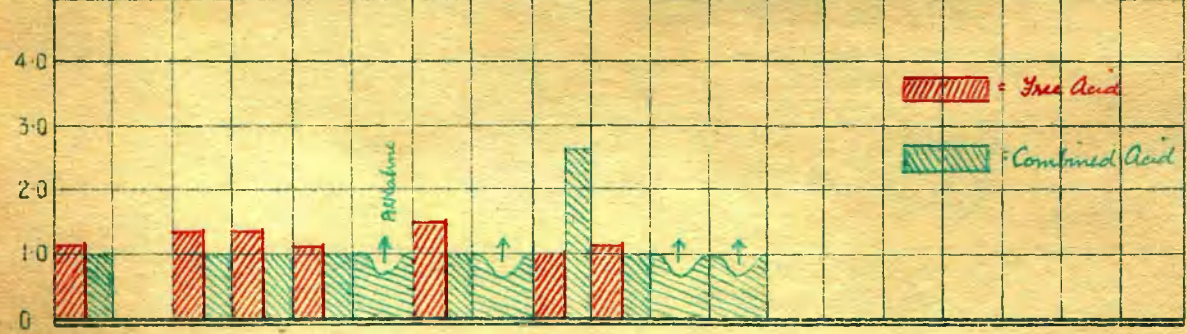
pH Values



— = diseased skin
 — = sound skin
 — = urine

40 grs. t. c. d.	60 grs. t. c. d.	60 grs. q. i. d.	"	90 grs. t. c. d.	45 grs. t. c. d.	90 grs. q. i. d.	"	"	"	60 grs. t. c. d.	30 grs. c. c. d.	"	"
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URINE
Free to Combined Acid



▨ = Free Acid
 ▨ = Combined Acid

Case 2.

This case charted on the opposite page was a man of 29 years, suffering from a severe attack of acute seborrhoeic dermatitis, the face, arms and trunk being involved. The duration of the attack had been a fortnight.

The interest in this case arises from the marked tolerance evinced towards alkalis, the dose being raised from 40 gr. thrice daily to as high as 90 gr. four times daily, and the very striking improvement following their administration, although little change was at first apparent in the urine.

After two days' treatment here, the skin, which previously had been red, raw, and angry looking, became dry and scaly, and much quieter in appearance. This improvement continued on increasing doses of alkali, signs of intolerance being noted on only two occasions, when the urine had just become alkaline. Towards the end the patient was still improving, and very well, with a urine pH of 8.4; the dose was then cut down however.

The ratio of the free to combined acid in this case also seems to offer an explanation of the behaviour towards alkalis. Although the urinary pH in this case was exactly the same before treatment as in the previous case, there is a distinct difference in this ratio in the two cases: in the former it was 1:1.4, practically normal; in the latter it was 1:1.1, decidedly to the acid side. This displacement of the ratio to the acid side became actually more marked at first with alkalis notwithstanding the improvement clinically, and would seem to account for the relapse on first cutting down the dose of alkali, the ratio then becoming 1.5:1, the most acid yet.

There is nothing of particular note otherwise in this case. Note in the chart that:-

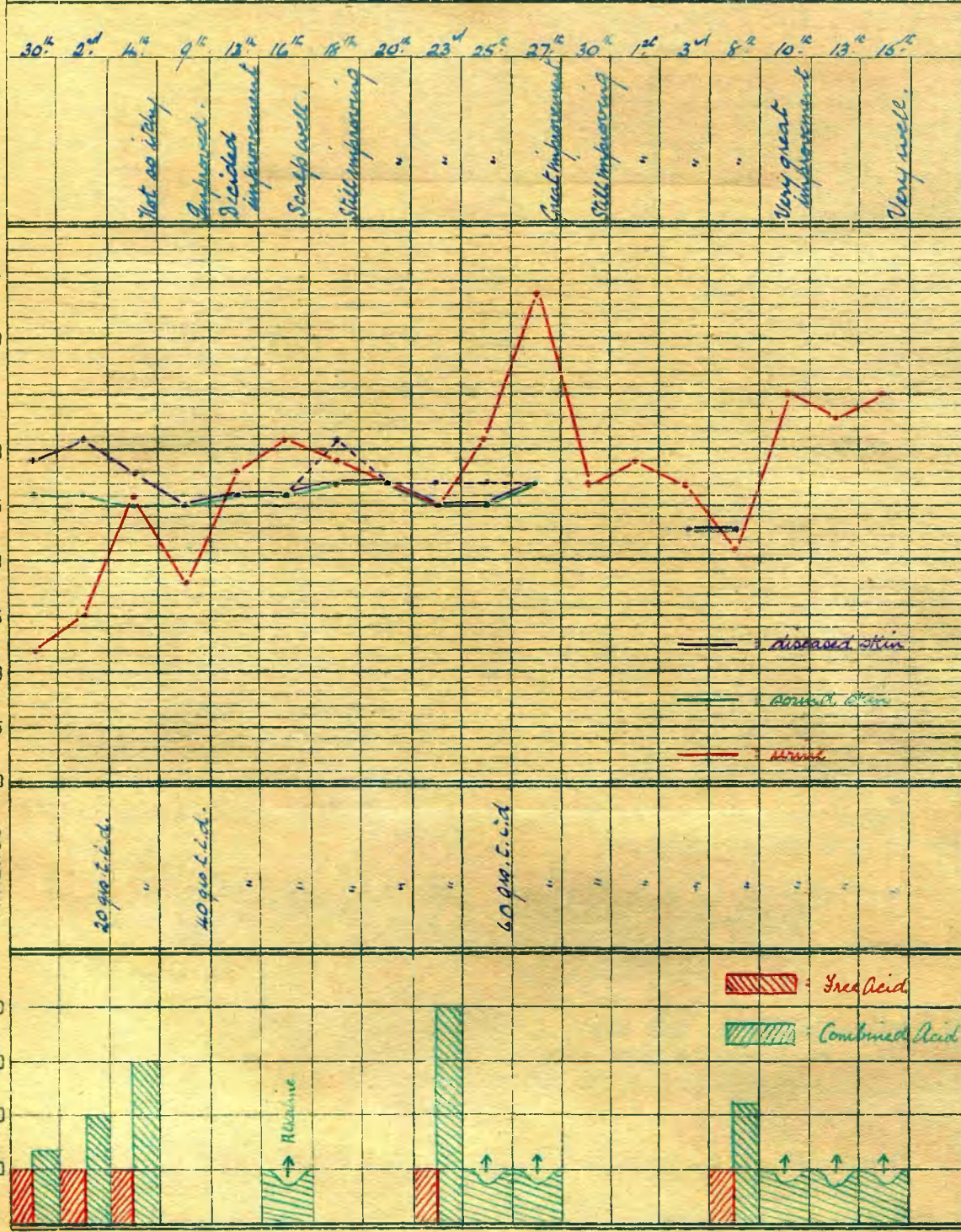
- (1) The pH of the diseased skin is constantly below the level of the sound skin, or, particularly in phases of improvement, on a level with it.
- (2) There is the same tendency seen in some of the other charts to a lowering of the sound skin pH with alkali treatment.

A record of some other cases will now be given, noting the points of interest as they arise.

September

October

November



Case 3.

The photograph and the chart opposite are those of a boy of 5½ years with seborrhoeic dermatitis of the scalp of one year's duration. Practically the whole vertex, as shown in the photograph, was raw and devoid of hair. Redness and scaliness were present also over the eyebrows and round the mouth, and ears and body were involved to a less extent.



With an initial dose of 20 gr. of alkali the child began at once to improve, noticing first a lessening in the itch. By ten days a skin had formed over the scalp, **only** the nape of the neck **remaining** red and angry; it also in time became drier and paler. The scaliness of eyebrows and mouth, however, was more resistant, and the blepharitis persisted. Spots over the body cleared up and only an occasional redness in the axillae remained. By 8 - 10 weeks hair had grown in quite thickly over the vertex.

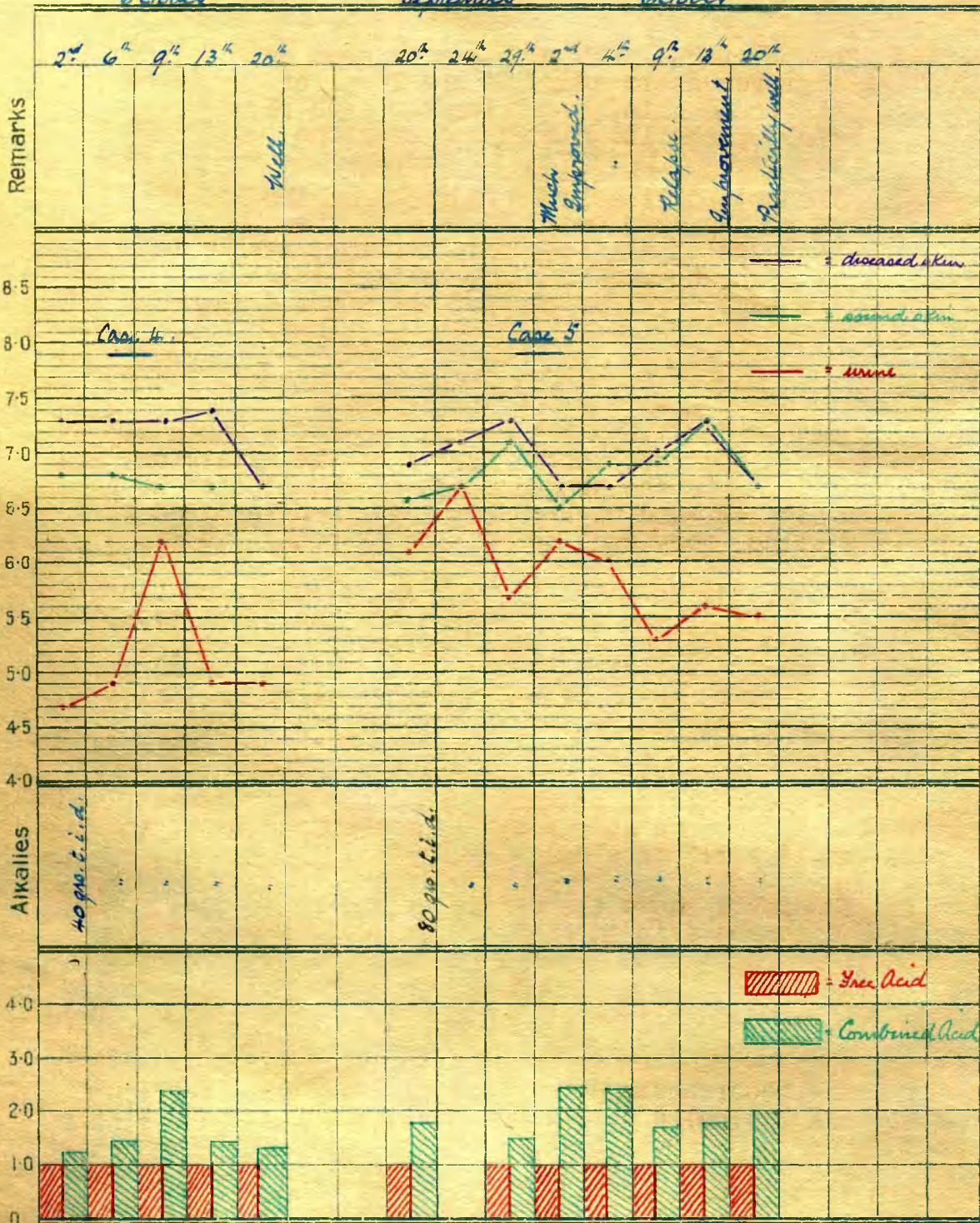
This child displayed a marked tolerance to alkalis, improving on 60 grs. thrice daily, and having at one point a urinary pH of 8.4. During most of the time, the urine was to the alkaline side of normal.

Before treatment the urinary pH was high, but the ratio was not so much upset as in some of the cases, being **normal**, actually the day he was put on alkalis. With treatment the urine either became frankly alkaline, or the combined acid was present in more than its normal ratio.

October

September

October



On stopping the mixture at the end of two months the urinary acidity returned to 5.5, and the ratio of free to combined acid to 1:1.1. The child, however, remained very well. In the chart:-

- (1) The pH of the diseased skin is seen on improvement to approach the level of the sound skin, acquiring the same pH, once epithelium had formed over the vertex.

The dotted line later represents the pH of the skin over the nape of the neck, which was longer in healing; its pH also, however, on improvement reaches the same level as that of the sound skin.

Case 4.

The first of the two cases charted opposite was a man of 54 years who had had seborrhoeic eczema of the wrists and arms for five months. On the second month of the disease he had been put on alkalis, and eight weeks later had returned with an alkaline urine, very much worse, the pH being 7.8.

He was admitted to hospital four weeks later, on the fifth month of the disease, and with rest in bed and local treatment began to improve: at the end of a fortnight, however, as he had begun to hang fire, alkalis were administered in 40 gr. doses thrice daily; then, within three weeks of beginning alkali treatment, he was well enough to be discharged.

There is no indication from the urine in this case that alkalis were the means of bringing about the improvement, there being little difference in the urine before treatment, and on recovery, while still on alkalis.

- (1) The chart shows the return of the pH of the diseased skin to that of the sound skin.

Case 5.

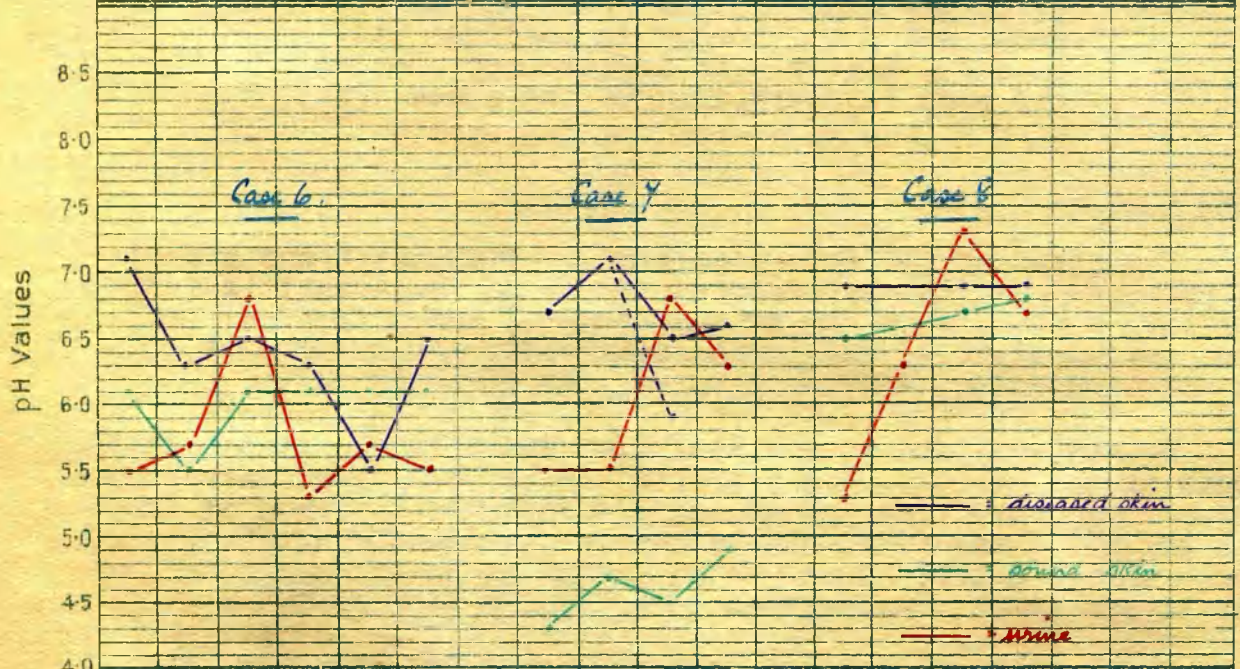
The second of the cases charted opposite was a man aet. 43 with an acute seborrhoeic dermatitis of the face, limbs and trunk, of a fortnight's duration, multiple boils being also present.

With rest in bed and alkali treatment, 80 grs. t.i.d., he improved steadily but, for one relapse as recorded in the chart, when the face became fired again. He improved however.

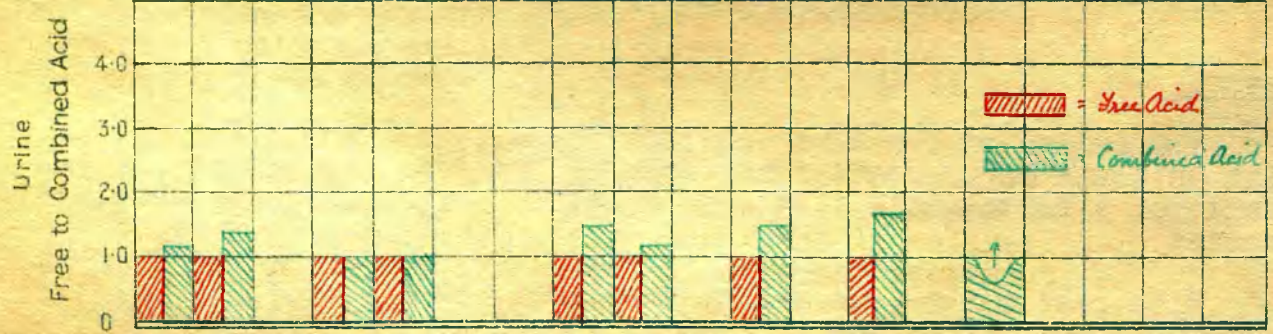
- (1) The pH of the diseased skin is seen to approach the level of that of the sound skin on improvement, at one point becoming even higher than it.

May June July May June June July

31 st	4 th	14 th	21 st	1 st	12 th	22 nd	24 th	29 th	2 nd	5 th	12 th	19 th	3 rd
	Improving							Improving		Much improved	Relapses	Very striking improvement	



15 grains i. d.	20 grains i. d.	nil	40 grains i. d.
-----------------	-----------------	-----	-----------------



- (2) During the relapse little difference is seen in the pH levels of the diseased and sound skin, and this may be accounted for by the absence of weeping, the face looking red and angry, but not moist. Both are seen to come together again when the patient was so well as to be almost ready to go home.

During the relapse the urinary pH is certainly at its highest level, but the ratio between the free and combined acid is normal.

- (3) On improvement finally, while still on alkalis, the urinary pH in this case is higher than on commencing treatment.

Case 6.

The first of the three cases charted opposite was a child of 1½ years who had suffered from seborrhoeic dermatitis from the age of two months. The scalp, ears, neck, face and limbs were involved.

With alkali treatment, 15-20 grs. t.i.d., he improved, the scalp becoming cleaner and drier, and the face and limbs clearing. Up to the present, however, i.e. a year later, he has never been completely well, suffering from frequent relapses, now of the scalp, now of the face. Only a portion of the chart is given to show really the rising of the pH of the diseased skin to above the level of the sound on improvement. The lowering of the pH next day is due merely to an active lesion having been chosen this time, the lesion of the previous day being by now scaly and dry and practically healed.

Case 7.

The second chart is from a woman of 29 years suffering from an acute attack of seborrhoeic dermatitis of a fortnight's duration the scalp, neck and arms being involved. She was not put on alkalis, but improved without, the neck and arms clearing quickly, but the head more slowly, probably owing to lack of co-operation on the part of the woman.

- (1) The urinary pH is seen to fall towards normal, and the diseased skin pH to rise in the direction of the sound. The dotted line represents the rise in the pH of the lesion of the day before, now practically healed. Unless otherwise stated, the pH of the most active lesion is at all times entered in the charts.

Case 8.

The third case had suffered from seborrhoeic dermatitis of the face for over three years. He had been on alkalis before and had

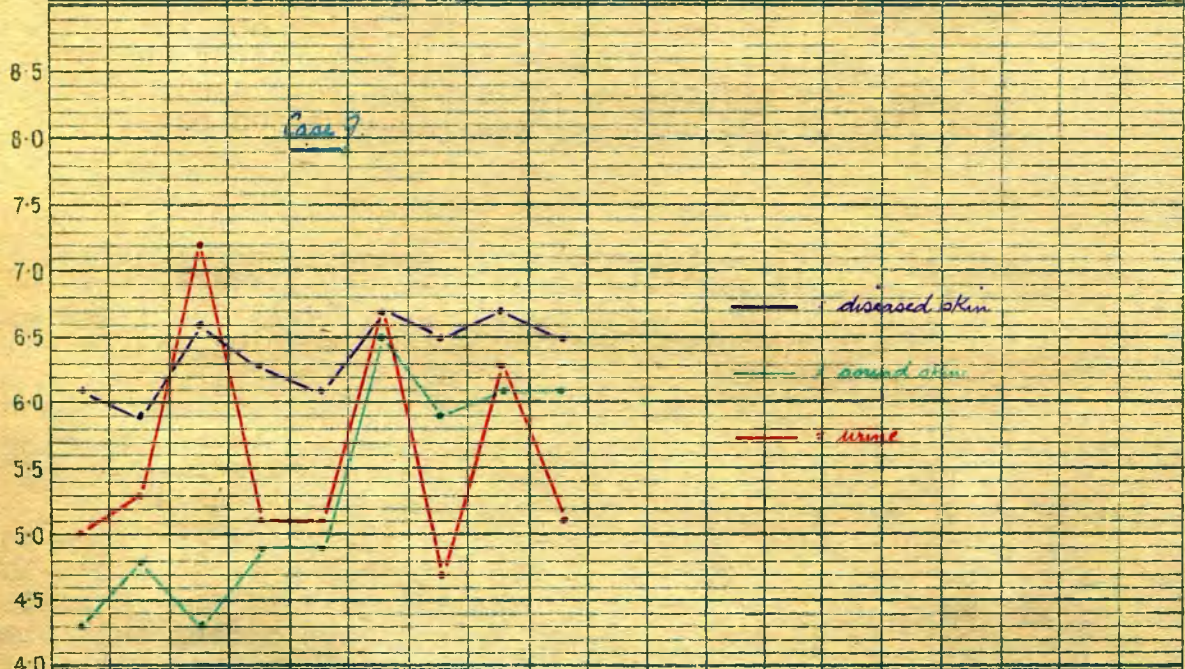
May June July

26th 31st 5th 9th 16th 19th 23rd 30th 5th

Remarks

great improvement
P.S.D.
P.S.D.
almost well
still improving
very well

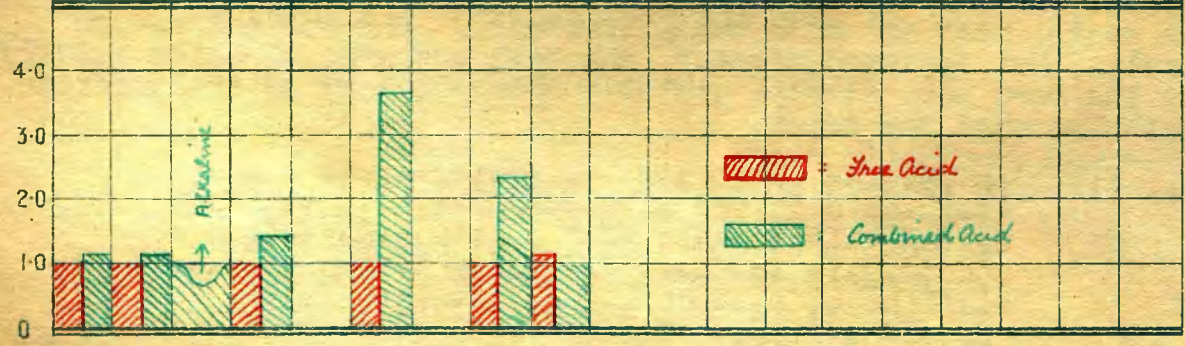
pH Values



Alkalies

40grs. t.i.d.
20grs. t.i.d.
40grs. t.i.d.
"
"
"
Stopped

Urine Free to Combined Acid



improved. Now, some time later he returned during a relapse, and improvement this time was very much more striking.

With 40 grs. of alkali, this time his face immediately improved, relapsing however on the urine's becoming alkaline. A month later he was better than he had ever been in the three years, the urine now having a pH of 6.3. Only a patch at the scalp remained red and moist. Three weeks later, when he returned during a slight relapse, having gone off the mixture, this patch was found to be healed for the first time.

- (1) The lesion pH is seen to remain constantly low; this is owing to the fact, that as the face healed, the lesion at the scalp was chosen, being now the most active lesion; as already mentioned, after the rest of the face had healed, this patch persisted until the time of the next relapse, not charted here.

Case 9.

The patient charted opposite was a girl of 19 years, with an acute dysidrosis of the hands of a fortnight's duration. The dysidrotic bullae had ruptured, leaving a raw, weeping, surface underneath.

After five days with 40 grs. of alkali t.i.d. there was a decided improvement in the hands: the flat bullae were gone, and the entire hand which before had been raw and moist was now considerably drier. From then on the hands rapidly improved, the palms becoming normal in appearance, and the backs of the hands; the fingers, however, were longer in healing, remaining dry and scaly. In another fortnight she was practically well, but for some dryness of the skin. In the chart it is seen:-

- (1) That the first great improvement occurred when the urine was definitely alkaline, the pH being 7.3. The improvement in fact becomes more obvious all through as the urine tends in the alkaline direction. This is seen again in the ratio between the free and combined acid.
- (2) Before treatment the urinary pH was definitely high, and the ratio also was upset in the acid direction being 1:1.1. instead of at least 1:1.5. With treatment and improvement the free and combined acid gradually assumed their normal relationship. The ratio then becomes upset again in the opposite direction to the alkaline side, becoming for example 1:3.7 instead of 1:2: improvement, however, is very marked at these times.
- (3) On stopping treatment the urinary pH and the ratio return to their original level, there being no ill effects clinically.

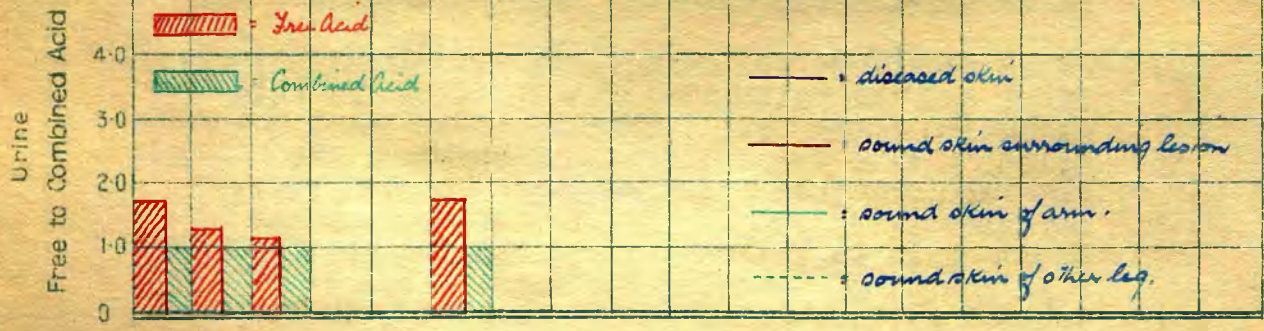
May June July Dec Jan Feb March May Sept.

27th 2nd 12th 26th 30th 1st 4th 23rd 26th 4th 11th 13th 18th 10th 3rd 19th 15th

Remarks
 9.5 A.
 Great improvement
 Relapse in arse
 Relapse in face
 Very Well



Alkalies
 30910.6 i.d.



- (4) The pH of the diseased skin is seen always to be lower than that of the sound skin, but shows with improvement a tendency to approximate more to the level of the sound skin. In this case again, the alkalis would seem to have a lowering effect on the pH of the sound skin, as shown in the second half of the chart.

Case 10.

The first of the opposite charts is from a woman of 53 years, with a chronic eczema of the face, neck and wrists. It is included to show the lowering in the pH of the diseased skin in eczema.

This patient improved on 30 grs. of alkali t.i.d., and was lost sight of for a time. On her return three months later she was as well as she had been for years.

The face and neck first became improved, as recorded, when the urinary pH was 6.7. On that day, however, pustules had begun to appear over the wrists. By the next day, although the face was still better than it had been, the wrists were definitely worse, and the urine was again very acid. On the last day charted the wrists were almost well again, but this time the face had relapsed, the urine being almost at the lower limit of normal.

- (1) From the high urinary pH and the very marked displacement of the ratio to the acid side in this case, alkali treatment would seem to have been indicated.
- (2) The dotted lines represent the lesions charted on the previous day, now healing.

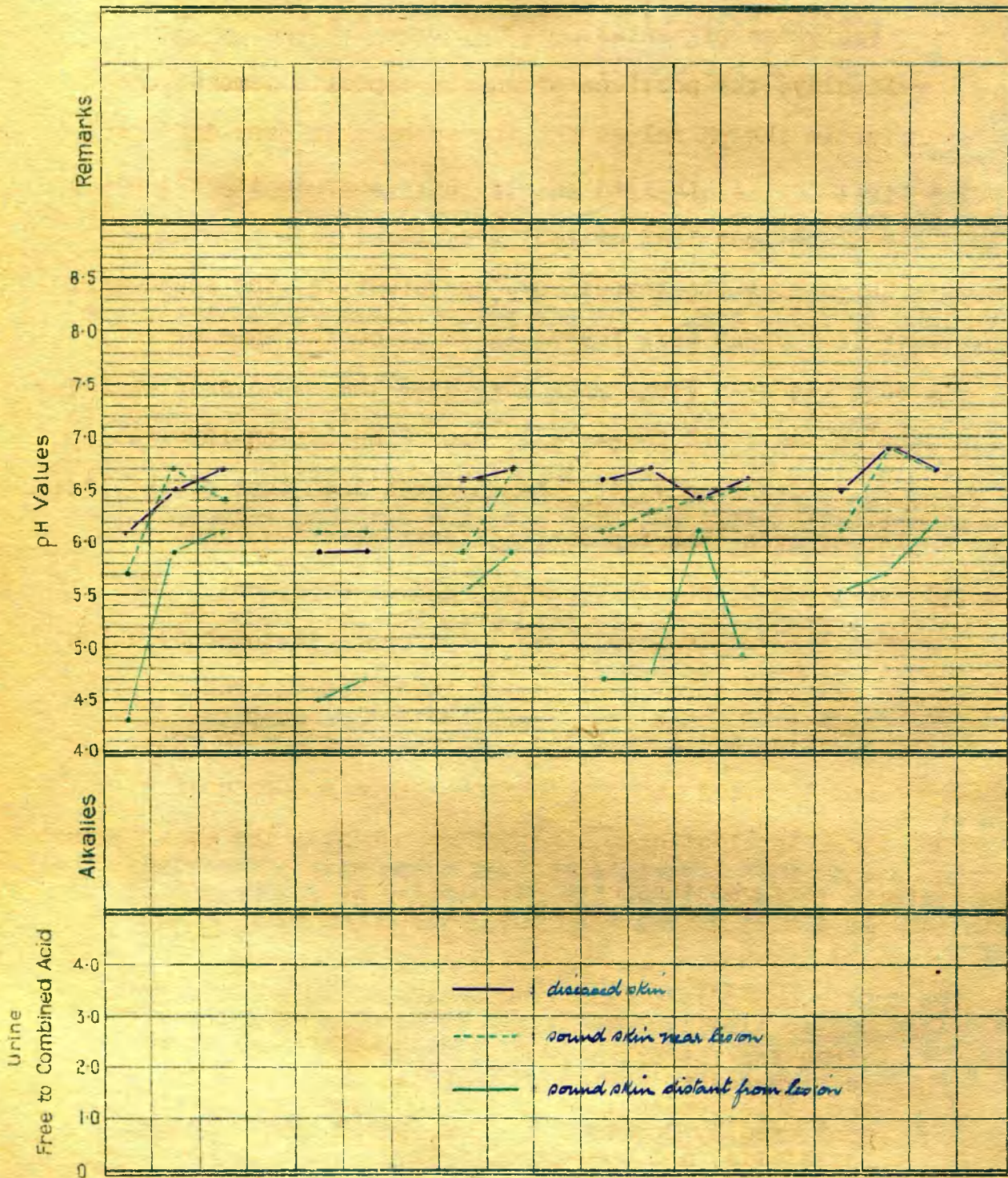
Case 11.

The second chart opposite is from a man with a stocking dermatitis. It is included for the purpose of demonstrating the variations in the pH of the skin which may occur simultaneously over different areas.

The continuous purple line represents the dermatitis area. The dotted purple line represents the sound skin over the knee of that leg. The dotted green line represents the other sound leg, and the continuous green line, a sound arm.

From the chart it is seen:-

- (1) That the pH of the sound skin surrounding the dermatitis area is intermediate in value between that of the dermatitis area and that of the sound skin well away from the lesion.
- (2) Values for the pH of the skin over a sound arm and the sound leg fairly closely correspond.



- (3) On recovery pH values for the dermatitis area and sound surrounding skin approximate towards that of the sound skin elsewhere. The dermatitis area on recovery, however, had not quite regained its normal appearance, remaining scaly and pigmented.

Finally, the portions of charts opposite demonstrate discrepancies in the pH values for the sound skin over different areas, the skin nearer the lesion, yet not close to it, often having a lower pH than that distant from it.

Throughout the investigations values for the sound skin over symmetrical areas were found always to be the same or very close to each other. Frequently the pH of the sound skin of the arms and palms was found, especially where the lesion involved the upper half of the body, to be much lower than that of the legs for example, or even than the lesion itself at times, and especially it seemed, as the result of alkali treatment. Most of the case examined had lesions in the upper half of the body, being principally cases of seborrhoeic dermatitis, eczema, rosacea, &c. For the sound skin, areas at a distance from the lesion were generally used to avoid possible contamination and error from traces of local applications. As far as possible the same control spot was used throughout repeated examinations.

SUMMARY and CONCLUSIONS.

- (1) Values for the urinary pH in dermatoses tend to be higher than normal. Among the dermatoses in whom this tendency seems more constant are those mentioned by Doble, viz. acne, seborrhoeic dermatitis, and cheiropompholyx.
- (2) From our controls the range for the urinary pH in average normal individuals would seem to be much wider, in the acid direction, than that of 6.4 - 6.8, given by Doble.

- (3) The ratio of the free to the combined acid in the urine bears no constant relationship to the urinary pH.
- (4) In some cases this ratio would seem to give a better indication than the urinary pH of the patient's need for alkali treatment.
- (5) Alkalis seemed undoubtedly to help most cases of acne, seborrhoeic dermatitis, and cheiropompholyx, and there was a tendency to relapse in many of the cases on pushing the urinary pH beyond 6.8. In other dermatoses, cases were at times benefited by alkali treatment, but not so constantly.
- (6) The following was found to be the most satisfactory method of treatment by means of alkalis:-
- To begin with a mixture of Pot.Bicarb. and Pot.Cit., of each 20 grs., and later, if indicated, to increase the dose to 60 grs. - 30 grs. of each. Even larger doses were on occasions used.
- The mixture as a rule was given three times a day between meals.
- (7) Alterations in the pH of the diseased skin in dermatoses would seem to depend not so much on the nature of the dermatosis, as on the presence, and degree, or absence, of exudation in the lesions.
- (8) Alkali treatment in some of the cases seemed through time to have a lowering effect on the pH of the sound skin.
- (9) Although values for the sound skin over symmetrical areas of the body invariably closely corresponded, there was a tendency for the pH of the sound skin nearer the lesion to be lower than that at a distance, and this seemed to be more noticeable during alkali treatment.

REFERENCES

1. Doble, F.C. - "Lancet", 1925, i, 272.
2. Ellis, H.A. - "Medical Press", 1925, CLXX, 353.

GASTRIC ANALYSES by the FRACTIONAL METHOD.

Mention must now be made of the part played by fractional gastric analyses in the investigation of dermatoses. Information on this subject was derived from an article by Dr. Brown¹., entitled "Some Observations on the Fractional Method of Gastric Analysis in Diseases of the Skin". Gastric analyses were shown to be of importance in dermatology, and particularly in rosacea, where a subacidity was to be found in more than 50% of the cases. That this finding was of significance also was shown by the striking improvement which followed at times the administration of large doses of HCl to such cases: these had been the findings also of Ryle and Barber².. In other dermatoses a hypochlorhydria was not so frequently to be found, and in acute widespread dermatoses a hyperchlorhydria seemed to be the rule. The following were terms used arbitrarily to denote varying ranges in the amount of free HCl present:-

(1) Complete achlorhydria.	Complete absence of free HCl.
(2) Marked hypochlorhydria	Free HCl under 20.
(3) Slight hypochlorhydria	Free HCl from 20 - 30.
(4) Normal acidity	Free HCl from 30 - 45.
(5) Hyperchlorhydria	Free HCl from 55, upwards.

This classification will be used later in the description of cases.

In addition to ordinary determinations for free HCl and total acidity, simultaneous chloride curves had been done in many of the cases. It had been shown by Bolton³., that in the chloride curve only was a true index of the actual amount of juice secreted to be obtained, variations in the amount of free HCl depending often upon varying degrees of neutralisation of the juice by

alkaline duodenal salts: a hypochlorhydria, or an achlorhydria, might very frequently be due, not to hyosecretion, but to excessive neutralisation of a normal juice, the pylorus being hypotonic and permitting of regurgitation to an abnormal extent.

Only sixteen cases have been examined, five of whom belong to the rosacea group. Of the sixteen, however, only four show a normal acidity. The findings are given in summary form in the following Table:-

S U M M A R Y

Condition	No. of cases	Achlor- :hydria	Hypochlor- :hydria.	Normal Acidity.	Hyperchlor- :hydria.
Rosacea.....	5	1	2	2	nil
Prurigo.....	2	1	1	nil	nil
Lupus Erythematosus	2	nil	2	nil	nil
Hydroa Aestivale..	2	nil	2	nil	nil
Pruritus Vulvae ..	1	nil	1	nil	nil
Urticaria	1	1	nil	nil	nil
Angioneurotic Oedema	1	nil	nil	1	nil
Seborrhoeic Dermatitis	1	nil	nil	1	nil
Multiple Boils ..	1	nil	nil	nil	1

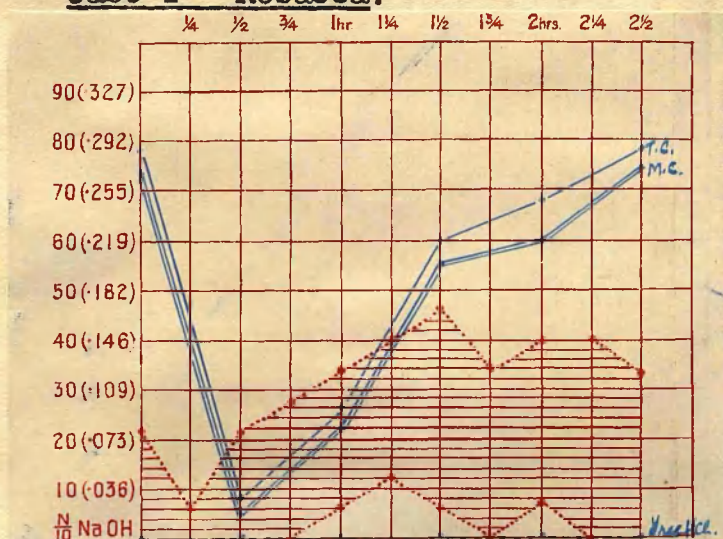
Here also, in the rosacea cases, a subacidity is present in more than 50%: two show a hypochlorhydria and one an achlorhydria, i.e. 60% have a subacidity. The two remaining cases of the group are normal. The only one of the sixteen showing a slight hyperchlorhydria might be said to belong to the class of acute widespread dermatoses, having suffered from multiple recurrent boils for a month. The other cases are of a more chronic nature and in them a subacidity would seem to be the more common finding.

A simultaneous examination of the urine has been made in some of the cases as in 1925 an article by F.D. Ackman⁴. appeared in a **Canadian** Journal demonstrating the gastric origin of the alkaline

tide in the urine. It was shown that normally the urinary acidity varied inversely with the gastric acidity: that in hyperchlorhydria a marked alkaline tide developed, and that in achlorhydria or hypochlorhydria, as a rule, no tide developed. An alkaline tide was said to have developed if there was a fall of 1 pH in any of the hourly specimens after a meal, or of .5 pH in any two specimens, this being the definition of Hubbard and Munford. It was the opinion of the author that in cases where for any reason the gastric secretory activity could not be studied directly a fair conception might be obtained from an examination of the urine alone.

Only a few of the following cases have been examined in this manner, but in them it will be seen whether a urinary examination alone might have given fairly reliable information regarding the secretory activity of the stomach.

Case 1 - Rosacea.



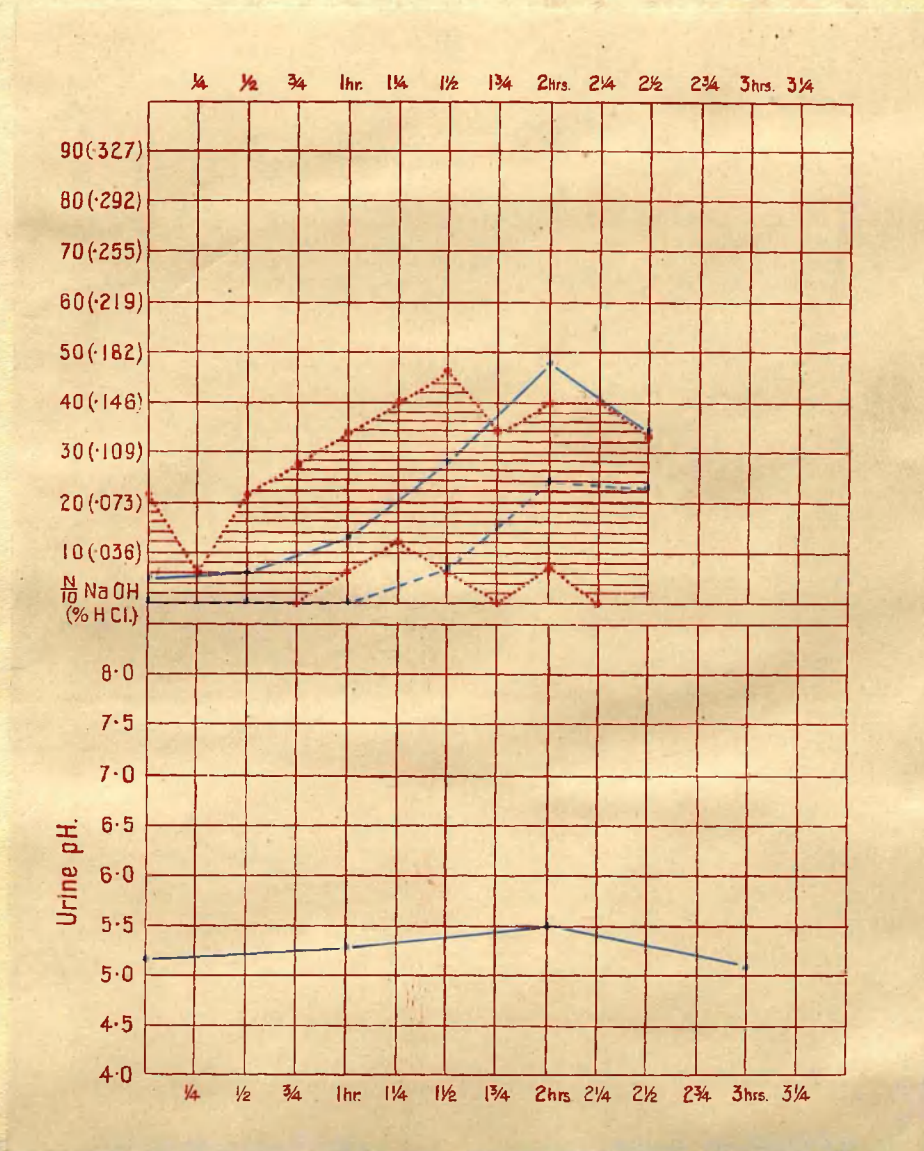
She had been treated for rosacea three years before, being completely cured. An achlorhydria had been present then, also, but by the time of her recovery slight amounts of free HCl had begun to make their appearance. Now she remains well notwithstanding the return to a complete achlorhydria.

Complete achlorhydria.

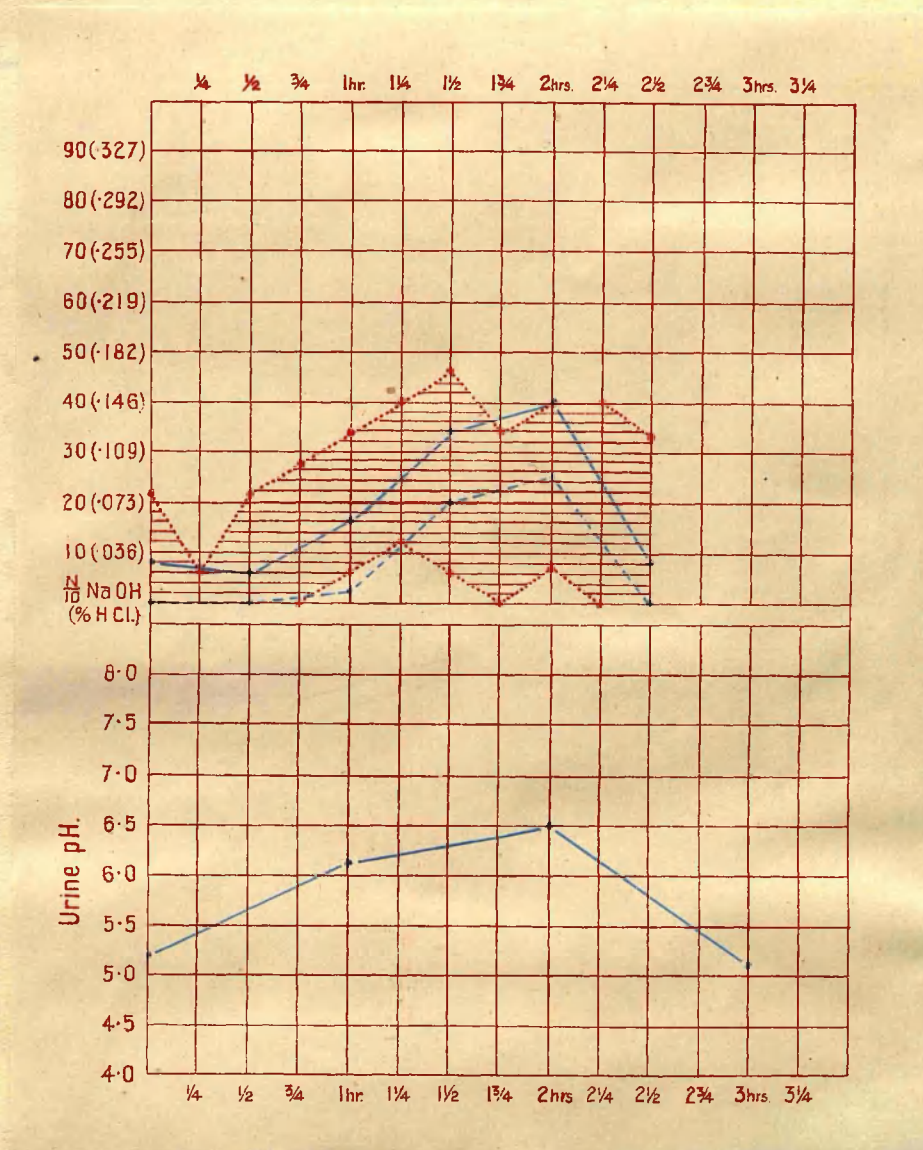
The secretory activity of the stomach is seen to be normal here, the total chlorides rising to the normal 60-90. The mineral chloride curve on the other hand is too high, approximating closely to that for the total.

The achlorhydria then is due, not to hyposecretion, but to excessive neutralisation.

This case by the time of the examination was completely well.

Case 2 - Rosacea.Slight hypochlorhydria.Alkaline tide absent.

This case would seem to bear out the finding that in hypochlorhydria there is an absence of any alkaline tide. There is a fall of only .3 in the urinary pH here.

Case 3 - Rosacea.developed Slight hypochlorhydria. Alkaline tide present.

Here an alkaline tide is present with a degree of hypochlorhydria scarcely any less than that of the previous case. There is a fall of at least 1 pH in the two hours' specimen of urine.

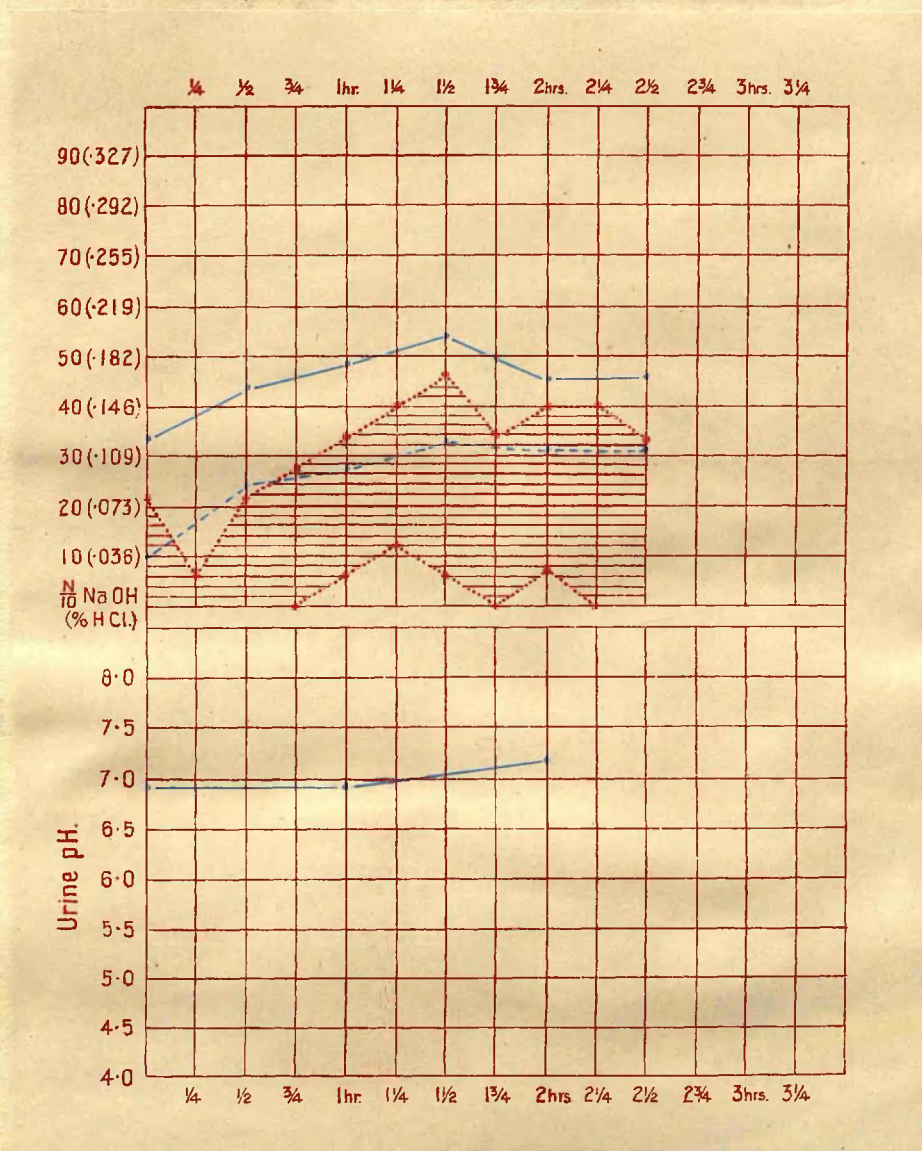
A more pronounced alkaline tide was said to be obtained if, before a test, the urine were definitely acid. In the following case the urine became definitely alkaline after the meal; the actual fall in the pH was, however, not marked, as before the test the urinary pH was already to the low side of normal. Since the urine became

actually alkaline after the meal a tide may be said to have developed.

Case 4 - Rosacea.

Normal acidity.

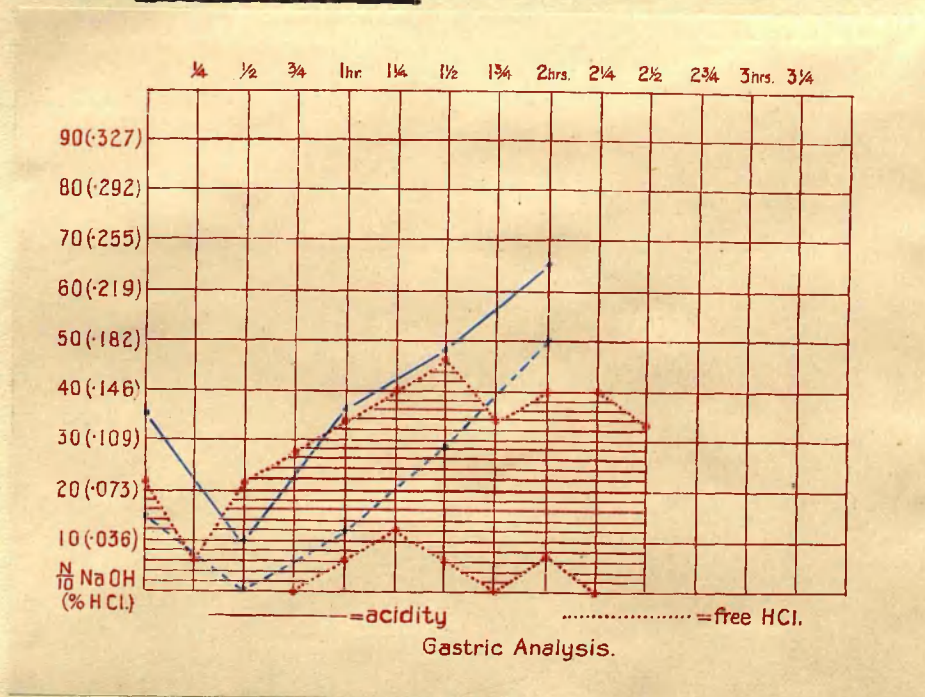
Alkaline tide present.



From the fasting stomach of this patient 7 ozs. of juice were able to be withdrawn, an amount larger than the average; in the juice starch and fat were detected. Here may lie an explanation of the abnormally low urinary pH before the test.

Case 5 - Rosacea

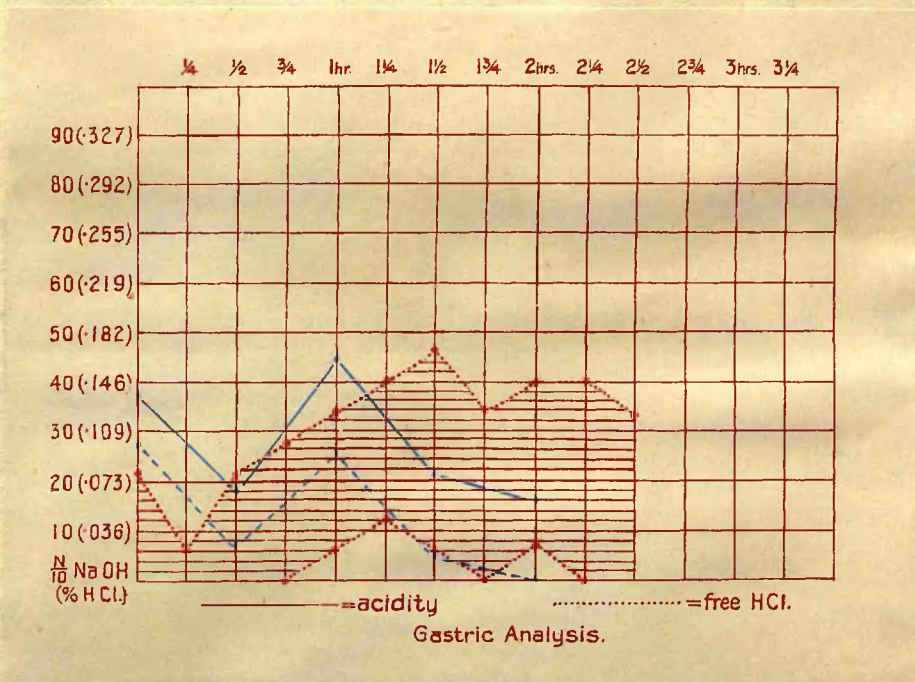
Normal acidity.

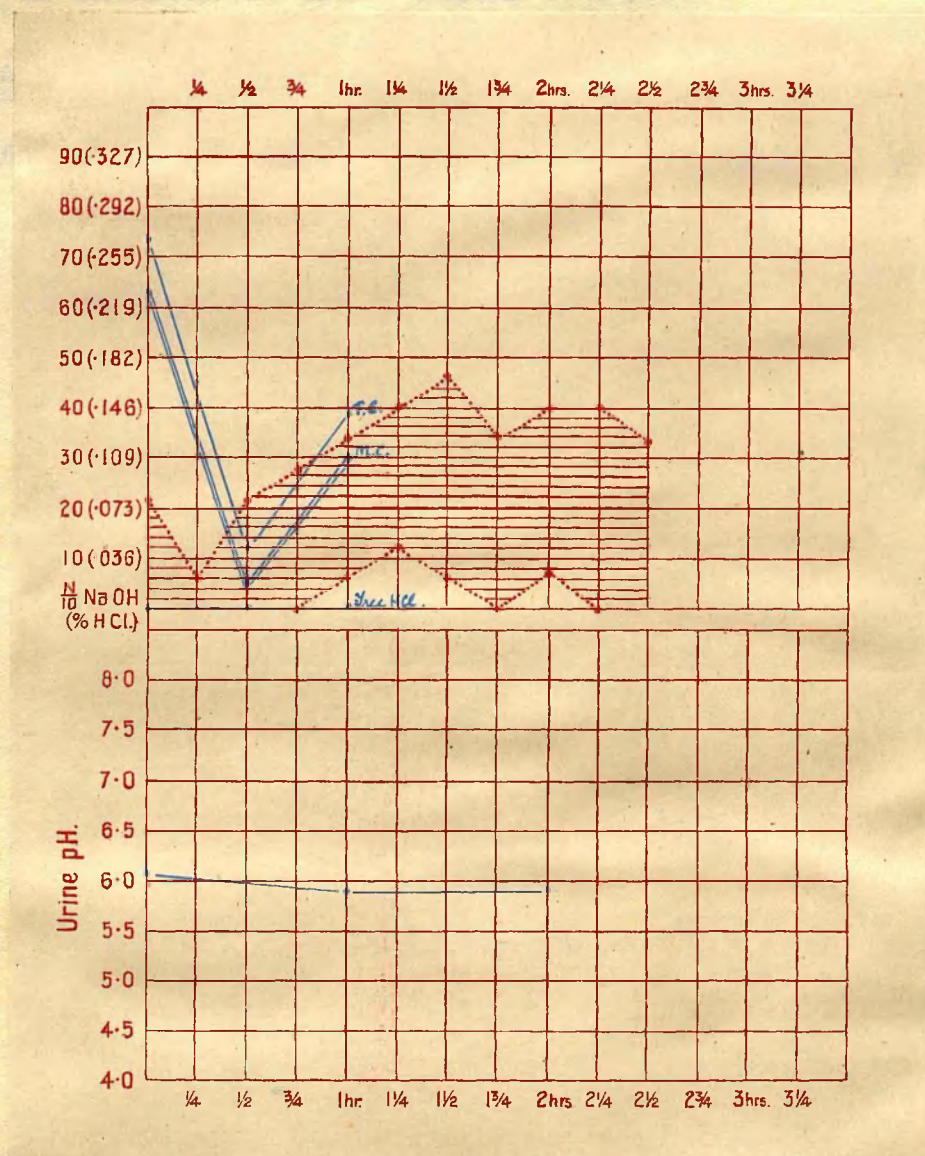


This completes the number of rosacea cases. The next group, of prurigo, consists of two cases:-

Case 6 - Prurigo.

Slight Hypochlorhydria.



Case 7 - Prurigo.Complete achlorhydria. Absence of any alkaline tide.

This is an example of an achlorhydria in whom no alkaline tide develops.

The achlorhydria in this case is due, partly to hyposecretion, the total chlorides not rising to 60, and partly to excessive neutralisation, the mineral chloride curve being almost as high as the total.

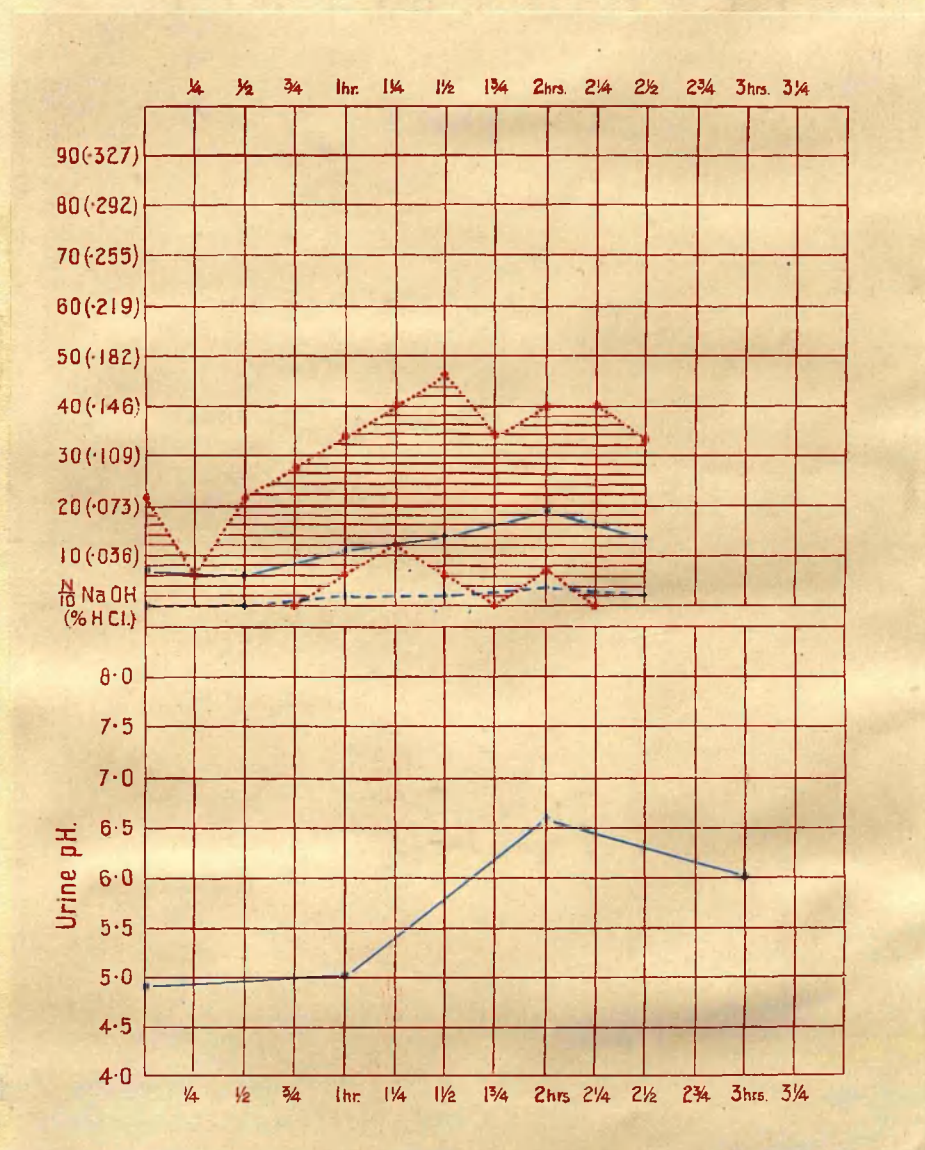
The urine, instead of becoming more alkaline, becomes actually more acid after the meal.

On the two occasions also on which gastric analyses were done on this man a year ago, a complete achlorhydria was found.

The next group consists of two cases of lupus erythematosus. In the first, two determinations were made, there being an interval of three months between.

Case 8 - Lupus Erythematosus.

(A) Marked hypochlorhydria. Definite alkaline tide.



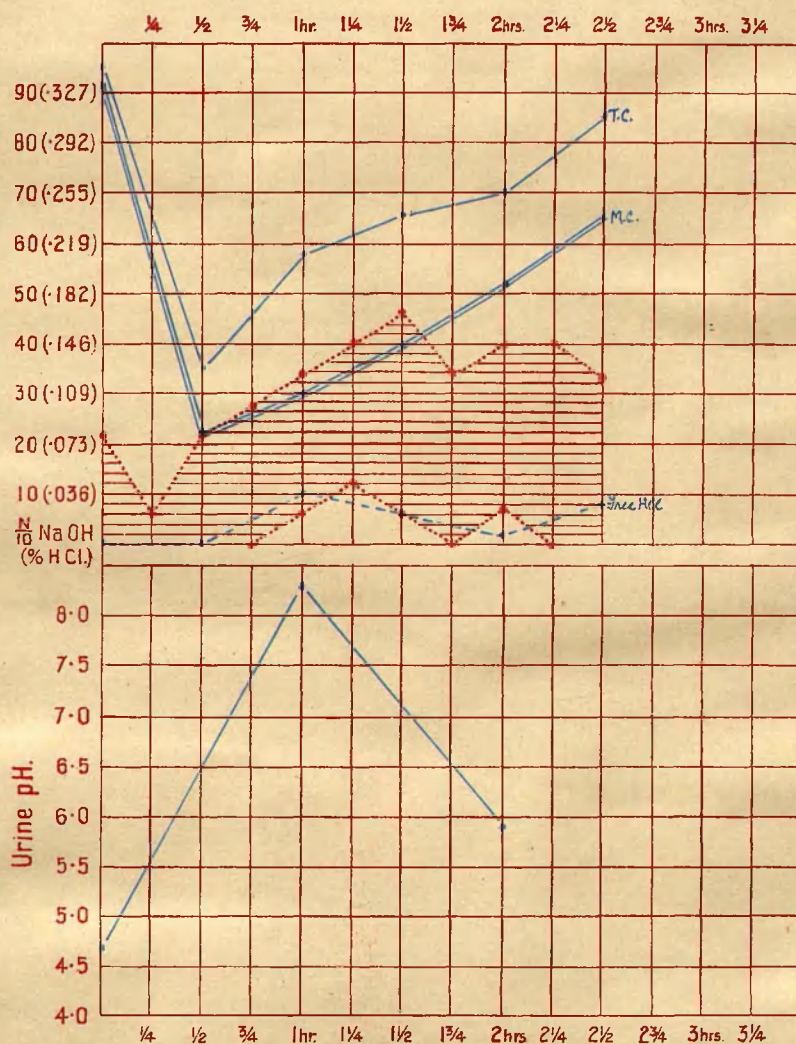
Here the hypochlorhydria amounts almost to an achlorhydria, yet the alkaline tide is very distinct. This is a striking exception then to the rule.

The next curve taken three months later shows the same

main features, the hypochlorhydria, however, is not quite so marked.

Case 8 - Lupus Erythematosus

(B) Marked hypochlorhydria. Pronounced alkaline tide.



The chloride curve would seem here to afford an explanation of the pronounced alkaline tide.

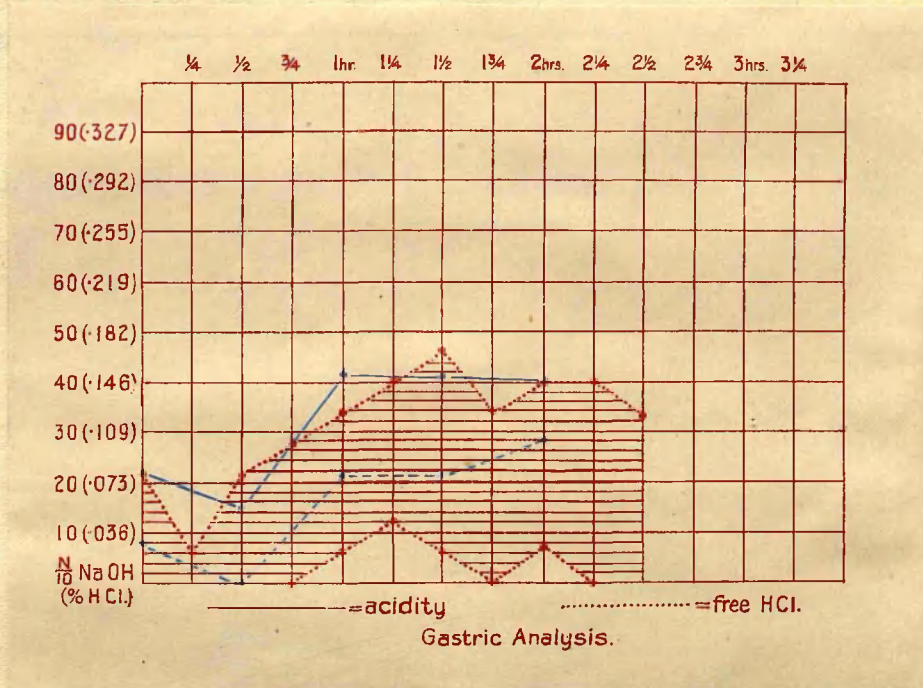
This curve shows the secretory activity of the stomach to be normal in spite of the hypochlorhydria, excessive neutralisation accounting for the latter.

This finding suggest as a possibility, that on the chloride curve only, is the alkaline tide dependant, and not on the curve for free HCl. This would seem reasonable and might account

for apparent discrepancies already encountered.

Case 9 - Lupus Erythematosus.

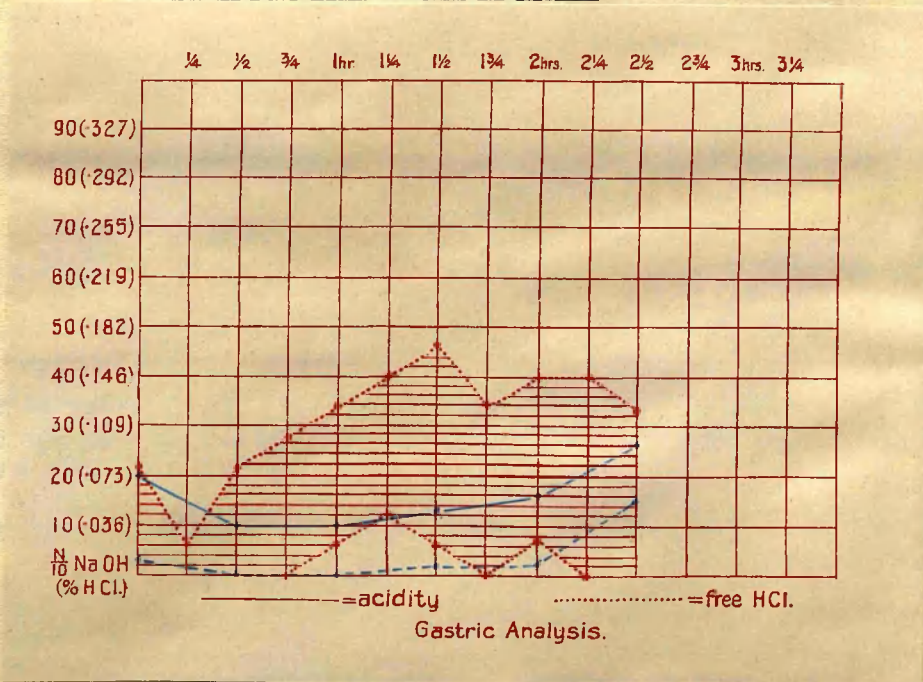
Slight hypochlorhydria.



The next group consists of two cases of hydroa aestivale:-

Case 10 - Hydroa Aestivale.

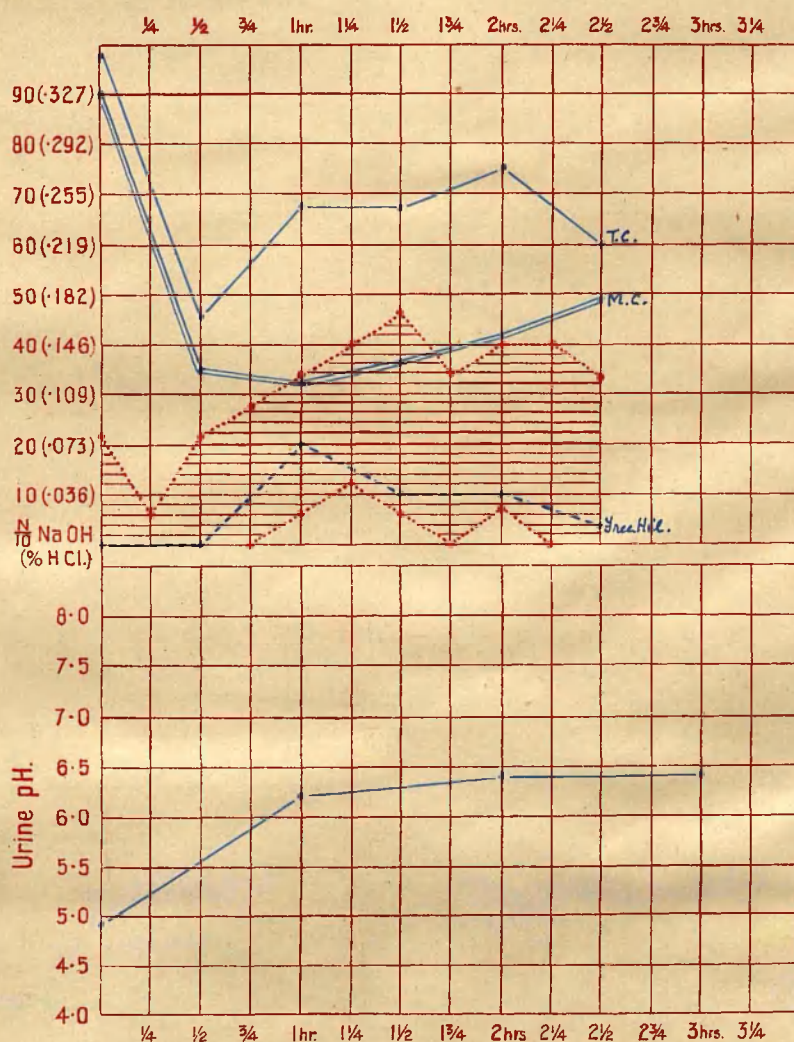
Marked hypochlorhydria.



Four analyses were made in the next case of hydroa aestivale, but, as the two cases will be described in detail later, only one example will be given just now. A hypochlorhydria was present throughout all the examinations.

Case 11 - Hydroa Aestivale.

Slight hypochlorhydria. Definite alkaline tide.



The secretory activity of the stomach is seen to be normal from the chloride curve and the hypochlorhydria to be due to excessive neutralisation.

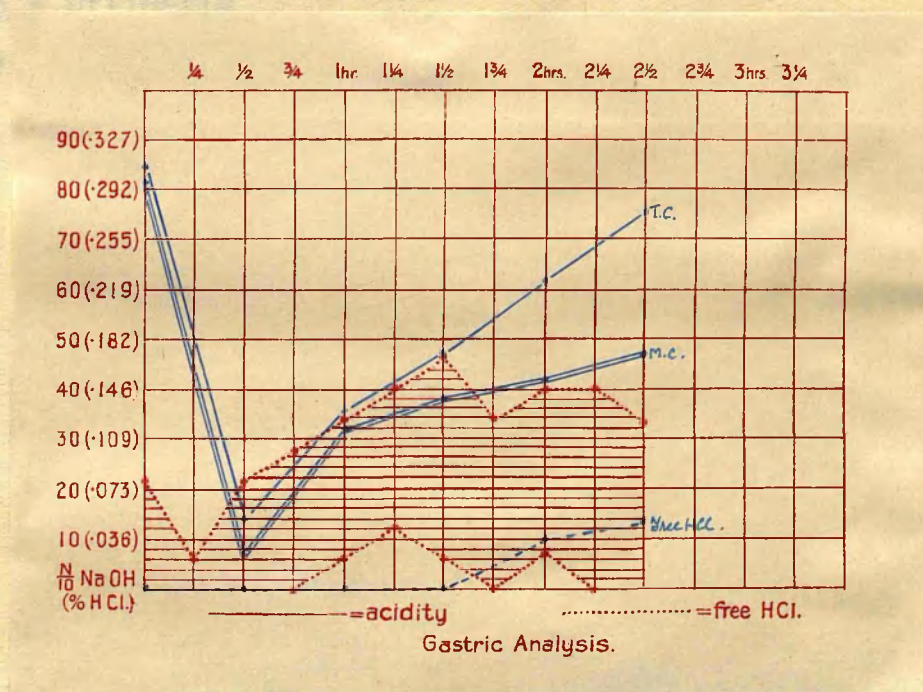
The normal chloride curve might account for the definite

alkaline tide. The chloride curve in this case is not so high as in the previous case of lupus erythematosus and the alkaline tide is not so marked.

The next is a case of pruritus vulvae in whom it was thought that some degree of suprarenal insufficiency might be present. This patient complained of gastric symptoms; these were relieved by large doses of HCl, but the pruritus remained unaffected.

Case 12 - Pruritus Vulvae.

Marked hypochlorhydria.



The hypochlorhydria is seen to be due to excessive neutralisation, not to hyposecretion.

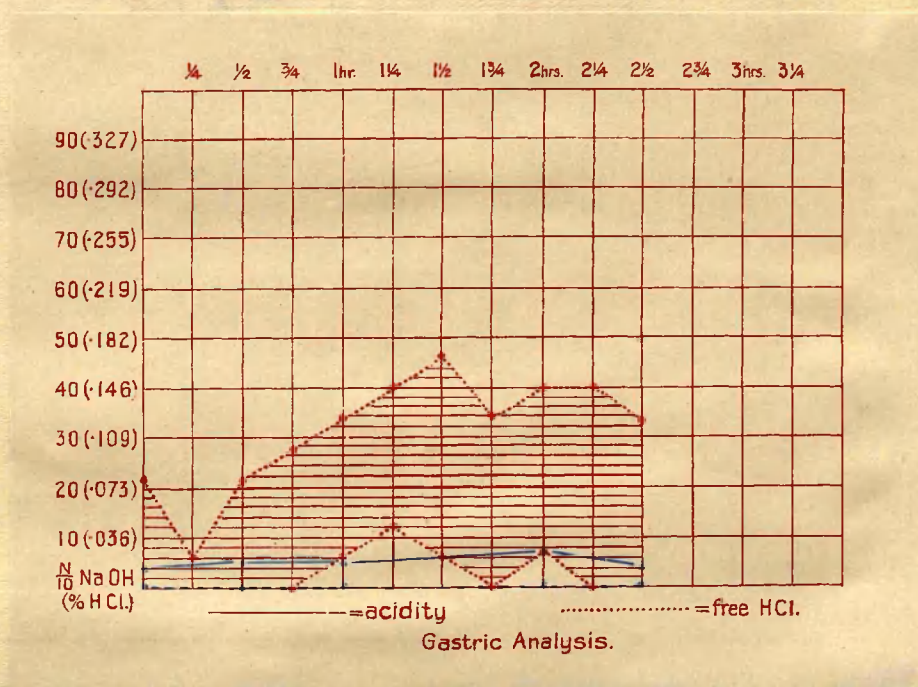
This finding then is quite in keeping with the theory of a suprarenal insufficiency. The excessive neutralisation would indicate a poor maintenance of tone at the pylorus. Sympathetic fibres maintain the contraction of the pyloric sphincter, and these fibres are stimulated by adrenalin: in a suprarenal insufficiency, therefore, it might be expected that there would be

some relaxation of the pyloric sphincter.

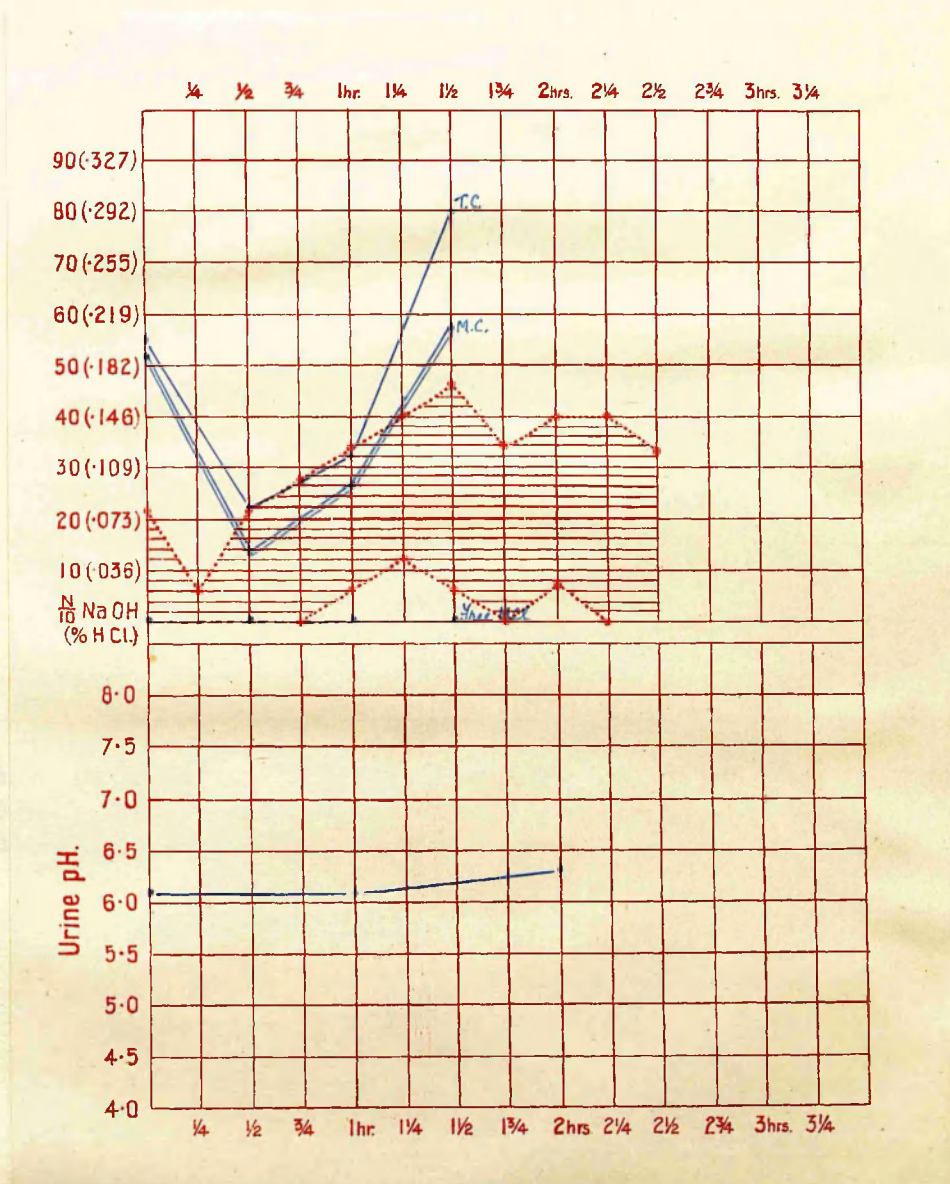
In the following case of urticaria three analyses were made at intervals of two months and one month respectively. In spite of large doses of HCl and clinical improvement, the achlorhydria originally present persisted. The case gave also at first an abnormally high and prolonged sugar tolerance curve; this, with treatment, became rectified. The following are the curves:-

Case 13 - Urticaria

(a) Complete achlorhydria

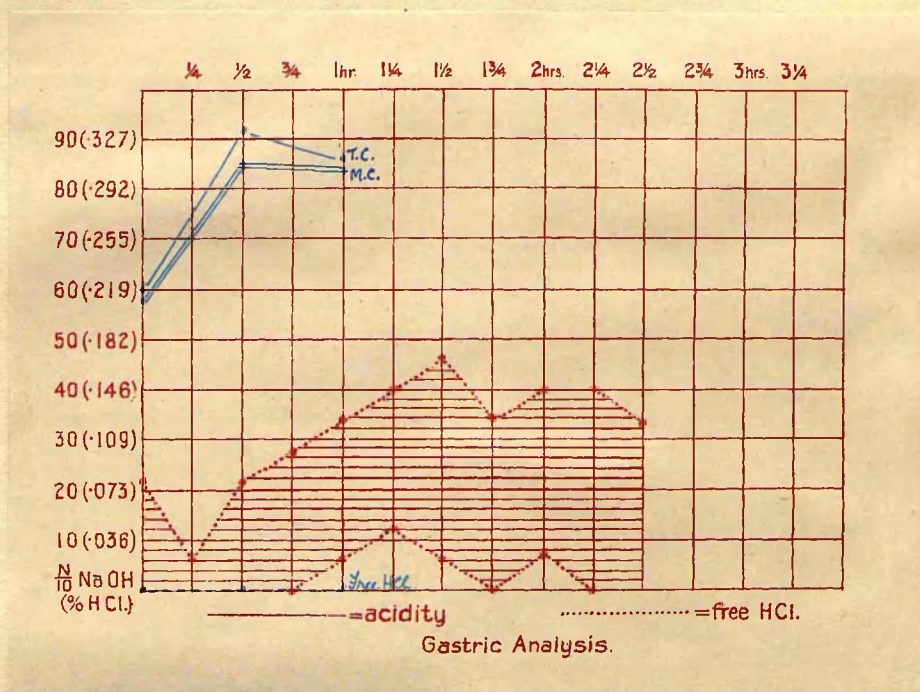


The next curve was taken after two months' treatment with large doses of HCl, improvement being marked by now.

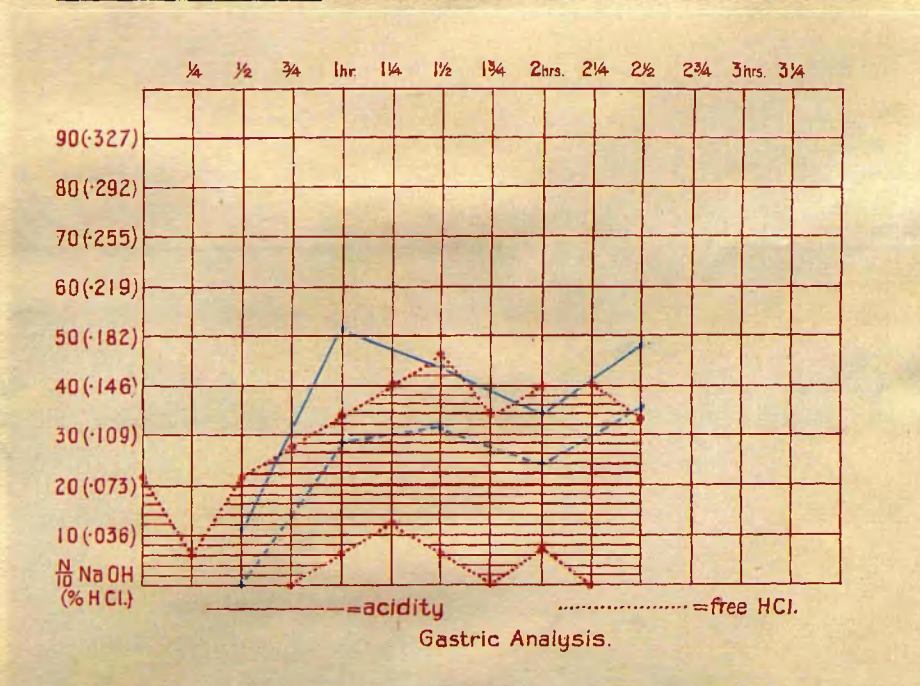
Case 13 - Urticaria.(b) Complete achlorhydria. Absence of any alkaline tide.

Here again in a complete achlorhydria there is an absence, so far, of any alkaline tide.

In this case there is a normal gastric secretory activity, excessive neutralisation accounting for the achlorhydria. This would upset the theory of the dependance of the alkaline tide upon the chloride curve only, had not, unfortunately, an examination of the urine three hours after the meal been omitted. In such a specimen the tendency to a fall already seen in the urinary pH might have been slightly augmented, producing a tide.

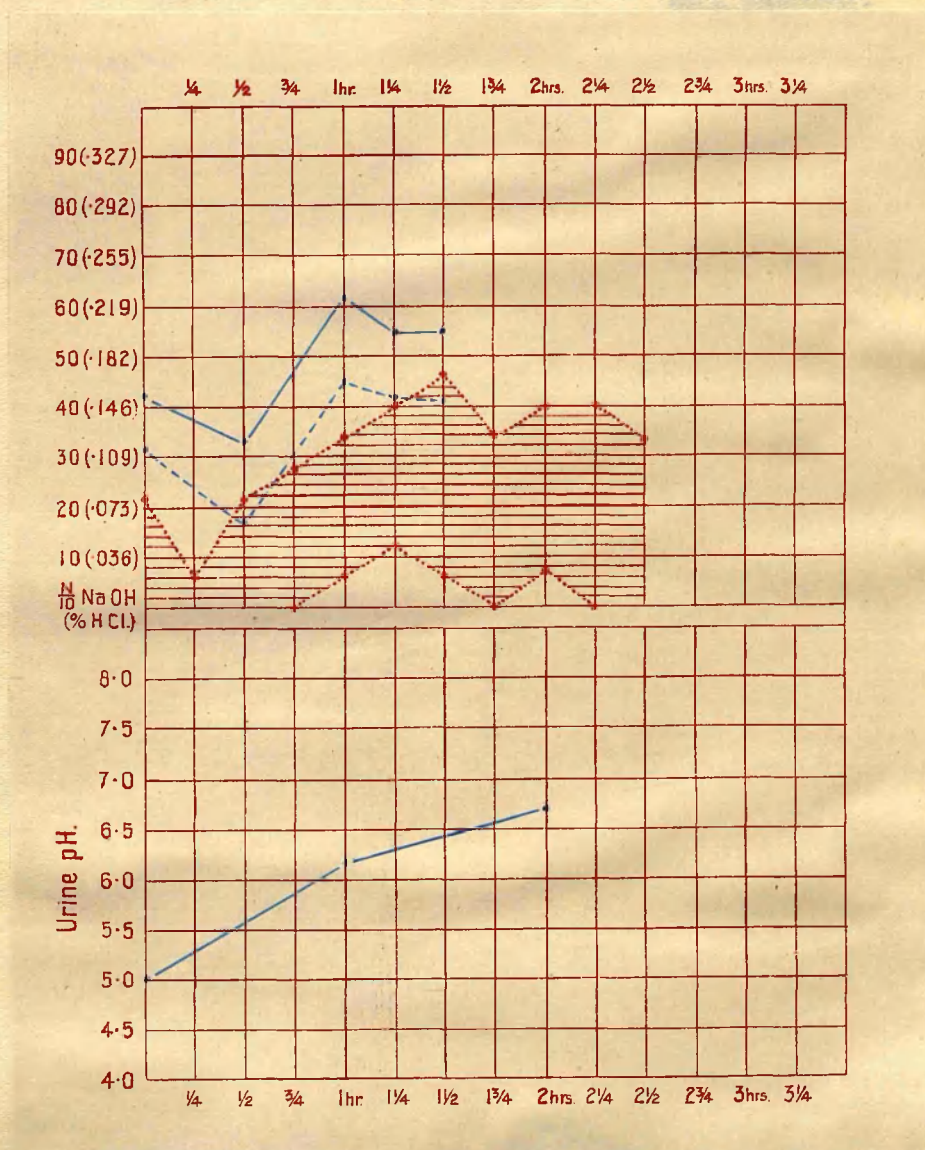
Case 13 - Urticaria(c) Complete achlorhydria.

There is seen here to be a heightening of the chloride or secretory curve as the result of, by now, three months' treatment with large doses of HCl.

Case 14 - Angioneurotic Oedema.Normal acidity.

Case 15 - Seborrhoeic Dermatitis.

Normal acidity. Definite alkaline tide.

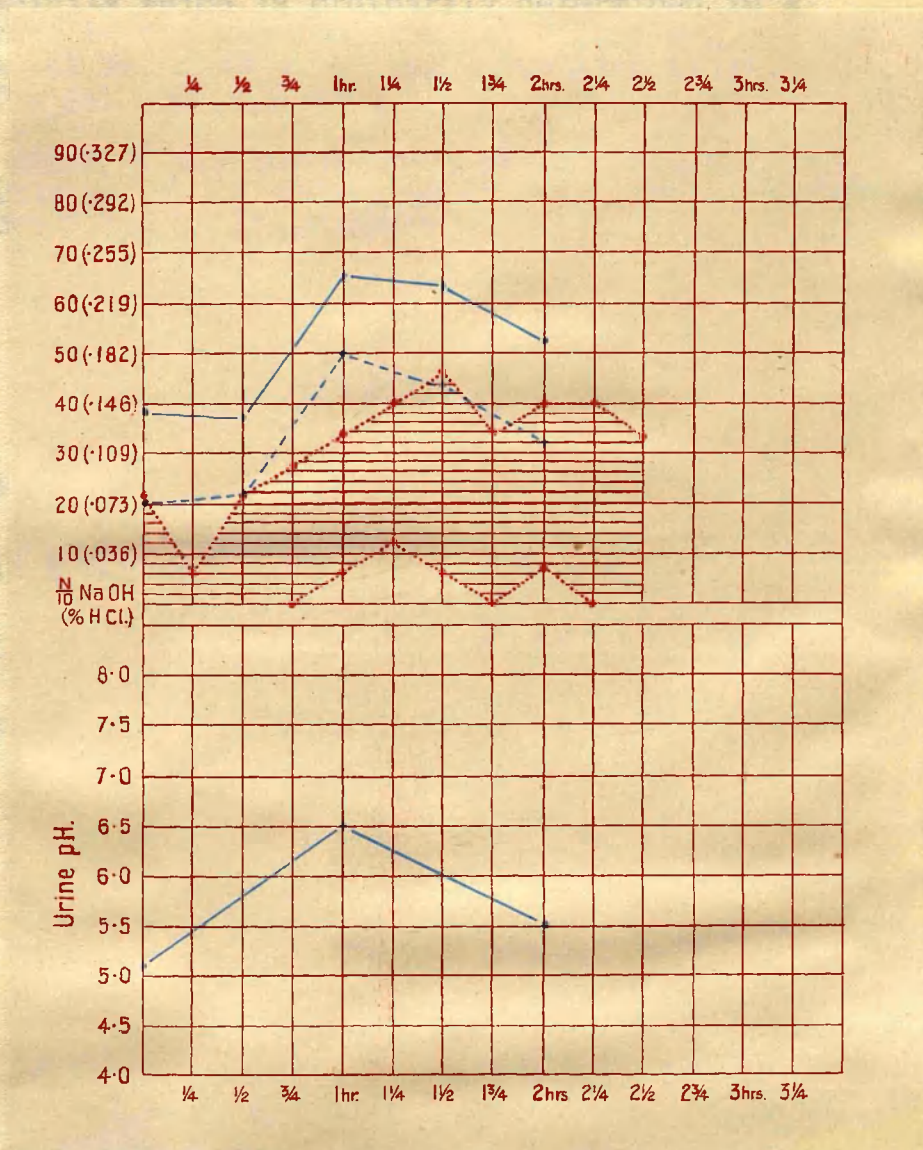


The alkaline tide here is more marked than in the next case, notwithstanding the slight hyperchlorhydria of the next case.

Case 16 - Multiple Boils.

Slight hyperchlorhydria.

Alkaline tide definite, but not marked.



C O N C L U S I O N .

- (1) In these cases the urinary pH bears no constant relationship to the curve for free HCl.
- (2) Since it is the curve for free HCl and total acidity which is ordinarily determined in a routine gastric analysis, a urinary examination alone would be of little value as a substitute for such an analysis.
- (3) In spite of the persistence of an achlorhydria in some of the cases, these cases were undoubtedly benefited by large doses of HCl.

R E F E R E N C E S

1. Brown, W.H. "Brit.Journ.Derm.and Syph.", 1925, XXXVII, 213.
 2. Ryle & Barber .. "Lancet", 1920, II, 1195.
 3. Bolton, "Brit.Med.Journal", August 18th, 1923.
 4. Ackman, F.D. .. "Canad.Med.Assoc. Journ.", 1925, 15, 1099.
-



HYDROA AESTIVALE - two cases.

Two cases of hydroa aestivale - sisters, remain to be described in detail. It was possible in the elder to repeat some of the tests several times; as the younger, however, was only 9 years of age, the majority of the tests in her case were done on only one occasion.

In the photographs the marked pigmentation of the face is seen, and the scarring, which was particularly marked round the mouth and over the nose.

The clinical laboratory findings in both were strikingly similar and are given in detail in the next few pages. In both, the urine and faeces were examined for haematoporphyrin, with negative results. In the blood films of both, one feature was very prominent, viz. the striking excess in the number of platelets. This feature was constant in all the films, but to a varying extent. In the later counts there was a tendency to a relative diminution in the number of platelets, and, from an examination of the dates, this diminution will be seen to be coincident with the approach of winter: from day to day, also, there was ^{an} evident variation in the number of platelets. As a cause for this, varying degrees of exposure to the sun suggests itself.

In a case recorded by A.M.H. Gray¹., however, of haematoporphyria congenita, in whom also there was an excess of platelets, the excess seemed always to be present, not in the summer months but in the winter, according to the tables given. This would seem to be against the light theory. In the films of Gray's case, polychromasia and punctate basophilia were present,

and occasional normoblasts. In our cases, however, the cells were quite normal in appearance. In his case, there was a positive indirect van den Bergh; in ours the van den Bergh was quite negative. This difference as regards the van den Bergh in the two findings is associated possibly with the different staining properties in the cells of both, and with the presence of haematoporphyrin in the urine and faeces of the one case, not present in the others. Fragility tests also were done in our cases, and were found to be normal.

The variations in the number of leucocytes present on different days, in our two cases, suggested the testing for the presence of a haemoclastic crisis. The reaction unexpectedly was found to be positive, and in both cases, being constantly so on the two occasions on which it was done in the elder girl. As has already been shown in a previous section, the sugar tolerance curves in both were abnormally low, suggesting, on taking into account the marked pigmentation of the skin, the presence of some degree of suprarenal insufficiency. The presence of a haemoclastic crisis in both, therefore, is in support of this theory. The gastric findings, also, are in support of a theory of suprarenal insufficiency: here, a marked hypochlorhydria is seen to be caused by a want of tone at the pylorus permitting of excessive regurgitation, and neutralization of the stomach contents. It has already been suggested that a relaxation of the pyloric sphincter is in keeping with a suprarenal insufficiency contraction of the sphincter being maintained by sympathetic fibres which are stimulated by adrenalin. In Addison's disease also an achlorhydria is found.

In conclusion, the following three extracts from a paper by Rasch². are of interest:-

- (1) "It must also here be remembered that there is no light sensibility in persons with porphyrinuria caused by taking sulphonal and trional. Perhaps the truth is that porphyrinuria is not the real cause at all, but the disease is due to an unknown 'x' (probably of an endocrine nature) and that porphyrinuria, sensitiveness to light and trophic lesions of the fingers occur among the symptoms".
- (2) "I have myself once seen a symmetrical gangrene of the ears in association with suprarenal disease caused by congenital syphilis".

and

- (3) "In Schultz's case (1874) the patient was a man, aged 33, with porphyrinuria from childhood and a rash of large blebs;
 At the autopsy a small, hard, cirrhotic liver was found and very considerable enlargement of the spleen. One suprarenal was atrophic. All the cranial bones were dark brown".

Plate I

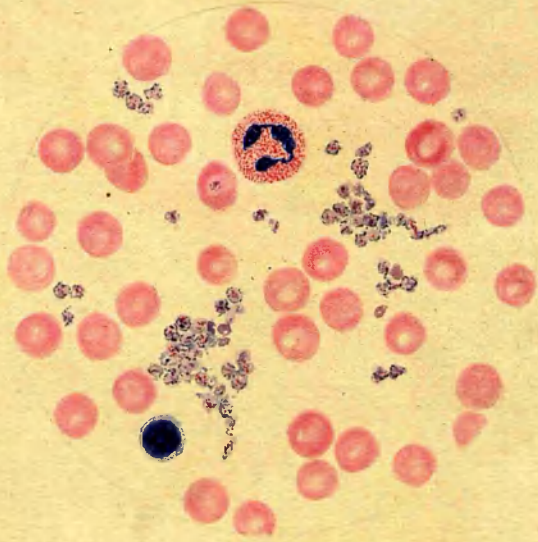
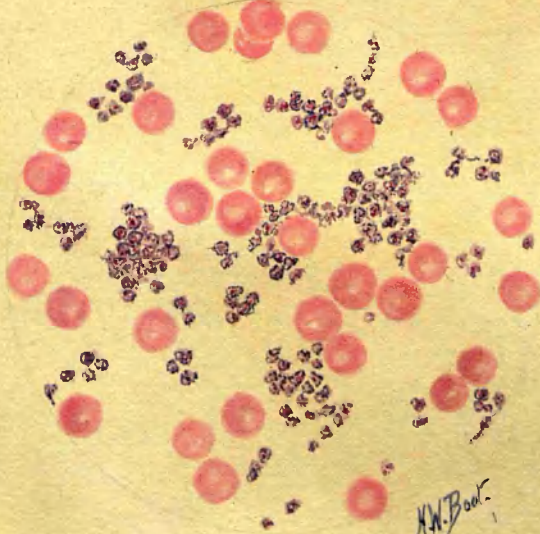


Plate II



N.W. Boer

Case 1 - aet 9 years.

EXAMINATION of URINE Pale amber in colour, acid, Sp. Gr. 1012.
 No haematoporphyrin detected.
 A trace of albumin present, but urea
 concentration test normal:-
 1.5% urea in the urine 1 hour after urea.
 4.0% " " " " 2 hours " "

EXAMINATION of FAECES No haematoporphyrin detected.

EXAMINATION of BLOOD

(a) Blood Counts

13th August, 1926

Hb.		77%.	
Reds	4,490,000.		
Whites	18,000.		
C.I.8	
Blood Platelets ..	1,120,000		(Normal 250,000/350,000).

Differential Count

Neut. polymorphs..	73%
Eosin. " ..	2
Lymphocytes	19
Transitionals ...	6

The cells are of good size and shape, staining well.
 No nucleated reds are seen, but numerous platelets
 are present in clumps.

23rd August, 1926

Hb.		80%.	
Reds	4,830,000.		
Whites	11,000.		
C.I.8	
Blood Platelets ..	966,000.		

Differential Count

Neut. polymorphs..	72.2%
Eosin. " ..	.2
Lymphocytes	20.6
Transitionals ...	6.0
Large Mononuclears	1.0

11th November, 1926

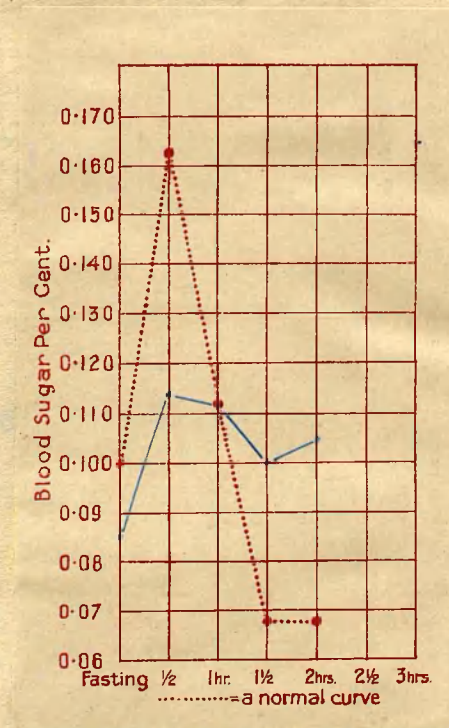
Blood Platelets ..	705,111.
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Plate 1 is a good example of platelets found in an
 average field (x 1000).

Plate 2 illustrates an occasional finding in the
 films, platelets occupying two-thirds of the
 field (x 1000).

EXAMINATION of BLOOD (contd.)

- (b) Fragility Test Normal, haemolysis beginning with .45% saline.
- (c) Van den Bergh Test. Negative reaction.
- (d) Coagulation Time. Shortened 3 mins.5 secs. by Wright's method.
- (e) Haemoclastic Crisis. Positive reaction.
- Leucocyte Count while fasting 9,600
 " " ½ hour after milk ... 8,600
- (f) Sugar Tolerance Curve Very low.



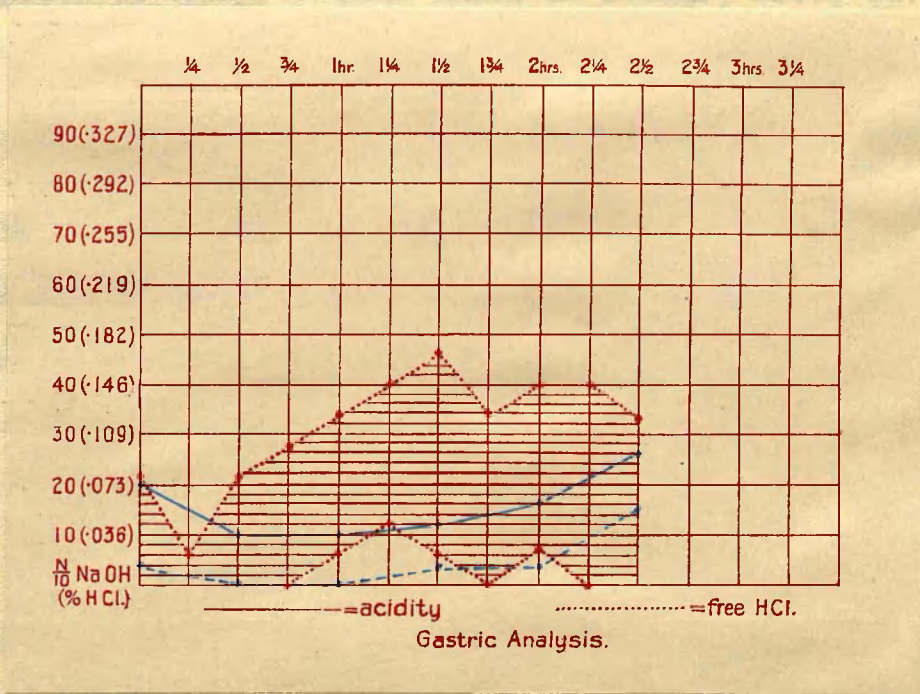
The Blood Sugar after the ingestion of 50 gms. of glucose rises to only 0.113% instead of, as normally, to 0.15% - 0.18%.

- (g) Uric Acid Content of Blood Normal 2.7 mg. per 100 c.c's.

GASTRIC ANALYSIS

Shows a marked hypochlorhydria.

GASTRIC ANALYSIS (contd.)



Marked hypochlorhydria.

Case 2 - aet 19 years.

EXAMINATION of URINE

Pale amber in colour, acid, Sp. Gr. 1015.

No haematoporphyrin detected.

A haze of albumin present, but urea concentration test normal:-

1.3% urea in the urine 1 hour after the test.
3.7% " " " " 2 hours " " "

EXAMINATION of FAECES

No haematoporphyrin detected.

EXAMINATION of BLOOD

(a) Blood Counts

12th August, 1926

Hb.	80 %.	
Reds	4,380,000.	
Whites	9,000.	
C.I.	9	
Blood Platelets	673,846.	(Normal 250,000/350,000)

Differential Count

Neut. polymorphs.	65 %.
Eosin. "	1
Lymphocytes	28
Transitionals	6

The cells are of good size and shape, staining well.
No nucleated reds are seen, but platelets are present in large numbers.

22nd August, 1926

Hb.	68 %.
Reds	4,160,000.
Whites	12,000.
C.I.	8
Blood Platelets	594,285.

Differential Count

Neut. polymorphs. ...	73 %
Eosin. "4
Basophil " ..	.4
Lymphocytes	20.8
Transitionals	5.4

(b) Fragility Test Normal, haemolysis beginning with .45% saline.

(c) Van den Bergh Test Negative reaction.

(d) Coagulation Time

24th August, 1926	Lengthened 4 mins. 20 secs. by Wright's method.
2nd September, 1926	" " 4 mins. 20 secs. " " "
11th November, 1926	Shortened 3 mins. by Wright's method.
8th December, 1926	Normal .. 3 mins. 30 secs. by Wright's method.

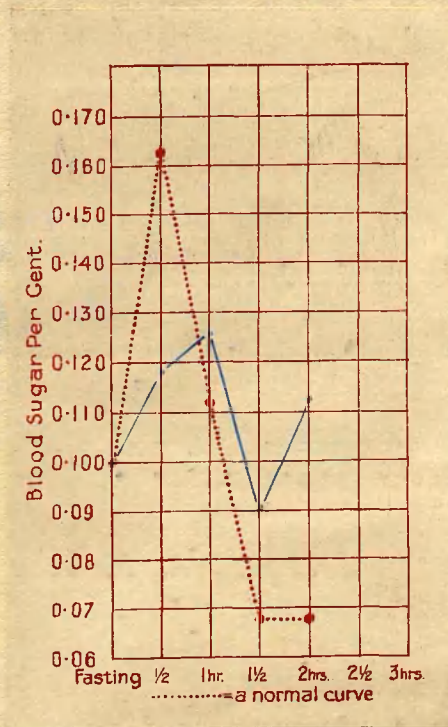
(e) Haemoclastic Crisis - Positive reaction.

3rd September, 1926,	Leucocyte Count while fasting	14,400
" "	20 mins. after milk	13,000
" "	40 " "	14,200
" "	60 " "	14,800
" "	90 " "	14,200

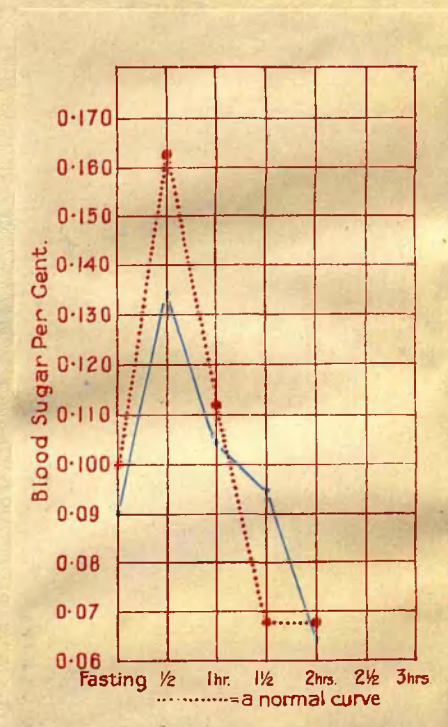
12th November, 1926,	Leucocyte Count while fasting	10,600
" "	30 mins. after milk	8,600

(f) Sugar Tolerance Curves - Both low.

12th August, 1926



25th August, 1926

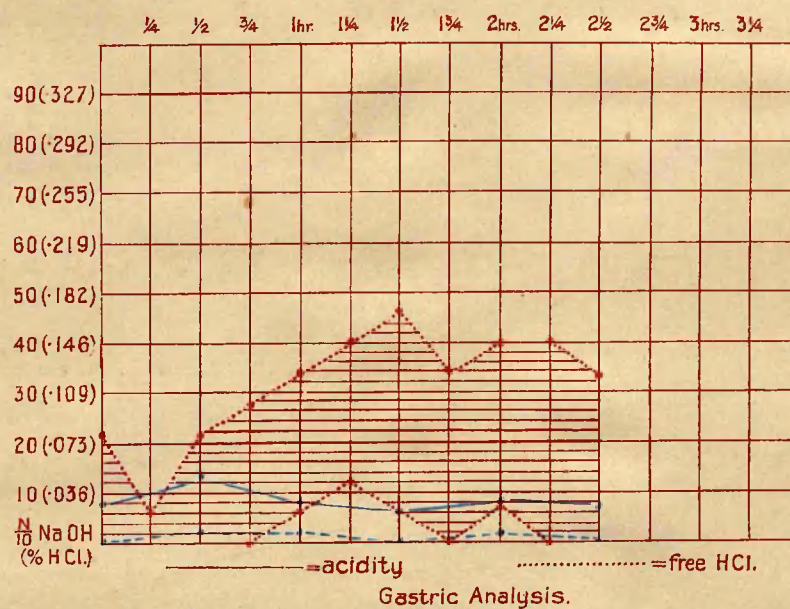


(g) Uric Acid Content of Blood Normal 2.7 mg. per 100 c.c.'s.

GASTRIC ANALYSES

Show a constant marked hypochlorhydria and a practically complete achlorhydria in the first two instances.

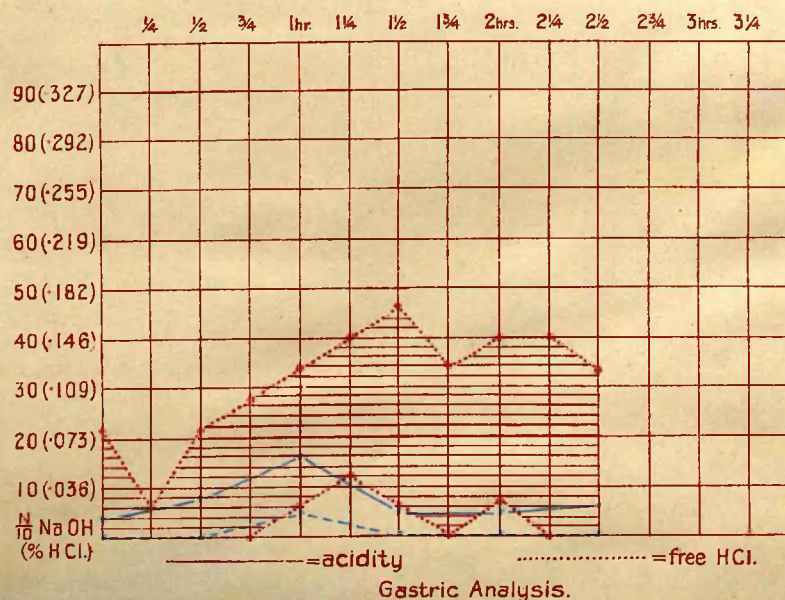
14th August. 1926



Extreme hypochlorhydria, practically an achlorhydria with the presence of bile throughout.

N.B. The patient had a sore throat, with enlarged congested tonsils, and a temperature of 101.4°.

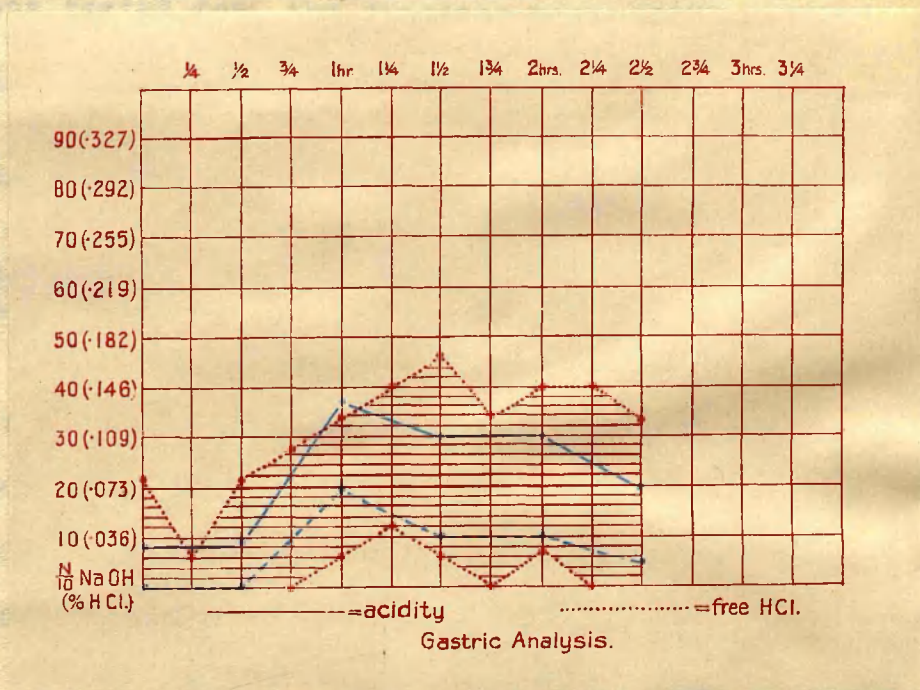
27th August. 1926



Extreme hypochlorhydria practically unchanged.

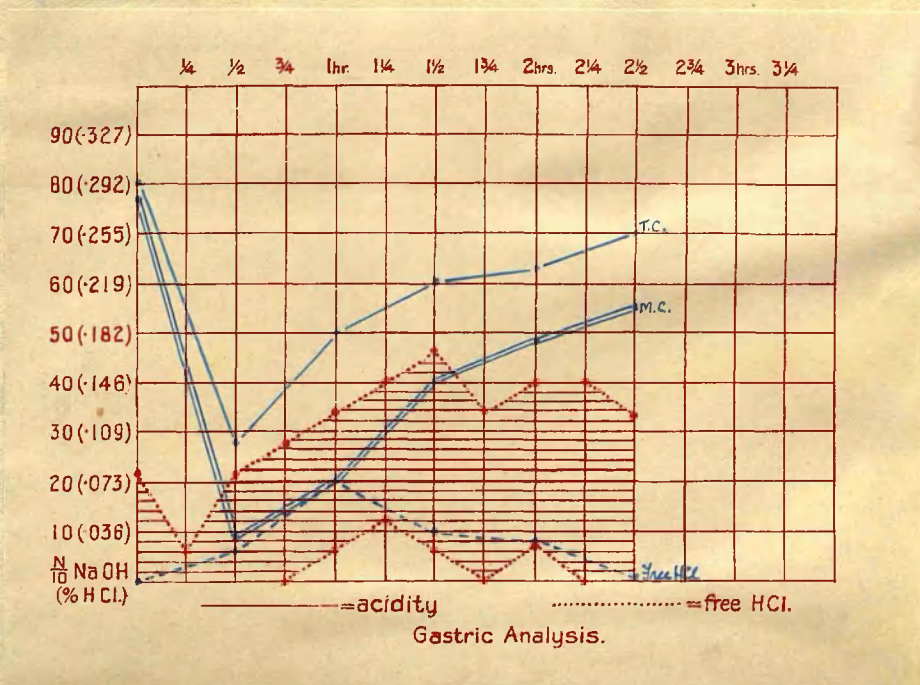
GASTRIC ANALYSES (contd.)

11th September, 1926



Hypochlorhydria is now less marked.

1st October, 1926



Hypochlorhydria unchanged from above, and from the chloride curve is seen to be due to excessive neutralization

Some general medical cases will now be included as controls. In the following three cases, in which a haemoclastic crisis was tested for, the reaction was negative:-

(1) <u>Rhinorrhoea</u>	Leucocyte Count	before milk	6,200
	"	"	$\frac{1}{2}$ hour after milk ..	10,800
(2) <u>Rhinorrhoea</u>	Leucocyte Count	before milk	3,000
	"	"	$\frac{1}{2}$ hour after milk ..	3,600
(3) <u>Raynaud's Disease.</u>	Leucocyte Count	before milk	8,000
	"	"	$\frac{1}{2}$ hour after milk...	15,000

It is worthy of mention that in this case of Raynaud's disease the calcium content of the blood serum was normal, being 10 mg. per 100 c.c's. Also the fragility of the red cells was increased, haemolysis beginning with .5% saline, whereas haemolysis in the control began as usual with .45% saline.

Fragility tests were carried out also on three cases of haemolytic jaundice - a brother and two sisters. Splenectomy was performed on the two sisters, and since operation they have remained free from jaundice.

The following are the findings for the three cases:-

M. aet 29 - 24th August, 1926.

Fragility Test ... Haemolysis began with .65% saline.
 In the control " " " " .45% "

Van den Bergh Test. Biphaseic reaction.

F. aet 27 -

Before Splenectomy - 16th June, 1925 -

Fragility Test .. Haemolysis began with .65% saline.
Van den Bergh Test. Delayed direct reaction.

A year after Splenectomy - 25th August, 1926 -

Fragility Test ... Haemolysis began with .55% saline.
Van den Bergh Test. Indirect reaction.

F. aet 18 -Before Splenectomy - 5th January, 1925 -

Fragility Test ... Haemolysis began with .7% saline.
Van den Bergh Test Delayed direct reaction.

About ten days after Splenectomy - 16th June, 1925 -

Fragility Test ... Haemolysis began with .5% saline.

More than a year after Splenectomy - 25th August, 1926 -

Fragility Test ... Haemolysis began with .5% saline.
Van den Bergh Test Indirect reaction.

Some authors state that after splenectomy in acholuric family jaundice, the increase in the fragility of the red cells disappears. The findings in these two cases do not bear out this statement. Certainly, immediately after splenectomy there was a very striking decrease in the fragility, which became almost normal, but with the passage of time the fragility of the red cells would seem to be very gradually increasing again, possibly owing to a compensatory development of the reticulo-endothelial system in other sites.

The following are control blood platelet counts obtained in purpura cases. The coagulation time in each, by Wright's method, is also given; little reliance, however, can be placed on these results, so many fallacies tend to shorten the coagulation time; where the coagulation time is delayed, however, some significance may be attached to the finding.

M. aet 58 - Marked Gingivitis with purpura of the legs.
 There was no dietetic history pointing to scurvy.

Platelet Count .. 594, 285 (normal 250,000/350,000)
 Coagulation Time.. 3 mins.10 secs. (normal 3 mins.30 secs.)

In this case the number of platelets is above normal and the coagulation time is shortened.

M. aet 9 years - Chronic Purpura - possibly Scurvy.

Platelet Count .. 313,571 (normal)
Coagulation Time. 1 min.46 secs. (markedly shortened)

He had been having calcium for a day or two up to admission. His blood was examined on the day after admission.

F. aet 50 years or more - Purpura - possibly Scurvy.

Platelet Count .. 293,000 (normal).
Coagulation Time. 3 mins.50 secs.(slightly delayed)

F. aet 9 years - Chronic Purpura.

Platelet Count .. 250,000 (normal).
Coagulation Time. 4 mins.15 secs. (definitely delayed)

F. aet 38 years - Purpura complicating a Terminal Nephritis.

Platelet Count .. 127,000 (lower than normal).
Coagulation Time. 5 mins.15 secs. (markedly delayed)

Anaemia was extreme in this case, -

Hb.	30 %.
Reds	1,650,000.
C.I.9
Whites	9,200

Differential Count

Neut. Polymorphs.	85 %
Basophil "	1.5 %
Eosinophil "	.5
Lymphocytes ...	11.0
Large Hyalines.	2.0

Slight anisocytoses and poikilocytosis was present, with occasional polychromasia and punctate basophilia. Some "giant" platelets were seen.

M. aet 50 years - Purpura - Aplastic Anaemia.

4th December, 1926

Platelet Count .. No platelets seen.
Coagulation Time.. 3 min.40 secs. (slight delay).
Bleeding Time ... Normal.

Anaemia was extreme, -

Hb.34%
Reds	1,191,000.
C.I.	1.5
Whites	1,200

The red cells were large, very regular in shape and size on the whole, and stained deeply. No leucocytes or platelets were seen on looking over two ordinary films on coverslips.

8th December, 1926

Whites 2,400.

Differential Count

Neut. Polymorphs.	68 %
Eosin. "	1 %
Lymphocytes	26.5 %
Myelocytes	4.5 %

More leucocytes were seen in this film and an occasional platelet. There was slight anisocytosis and poikilocytosis, and the cells did not stain so deeply. Very occasional ploychromasia was present, and two nucleated reds were seen on counting 200 leucocytes.

The calcium content of the blood serum was normal, viz. 10 mg. per 100 c.c's., and the reaction to the van den Bergh test was quite negative.

According to Tidy³. a reduction in the number of platelets may occur in any form of purpura and is not a criterion for the separation of a special type. A reduction in the number of platelets is, in his opinion, a secondary phenomenon, depending on the degree of severity of the illness. This would seem to offer the best interpretation of the results obtained in the six cases just recorded.

At first sight here the coagulation time would seem to become more and more delayed as the number of platelets diminishes; in the last case, however, in which no platelets were found, the coagulation time was almost normal.

R E F E R E N C E S .

1. Gray, A.M.H. "Quart. Journ. Med. ", 1926, 75, 381.
2. Rasch, C.... "Proc. Roy. Soc. Med."., Vol.XX; No.1, 11.
3. Tidy, H.L... "Lancet", August 21st, 1926.

FINAL SUMMARY and CONCLUSION.

The striking results recorded by McGlasson as the result of dieting in cases with a high blood sugar have not been obtained in this investigation. We have been unable to confirm the statement that a high fasting content of the blood sugar is frequent in dermatoses, such a finding being obtained in only relatively few cases. A high content of the blood sugar was most constant in the Lichen Simplex Chronicus and Localised Lichenoid Eczema Groups, and in the group of cases of localised and generalized pruritus. In the first two groups 100% gave values to the high side of normal, and in the first group 100% gave definitely abnormal values; the group, however, consisted of only three cases. The Pruritus Group was of interest as in it high values were frequent - occurring in a third of the cases: in the remainder of the group on the other hand, values tended to be on the low side of normal, there being no gradual transition from one type of case into the other.

With sugar tolerance curves, on the other hand, information of much more interest and value was obtained, and principally it seemed, from the possible relation borne by endocrine disturbance to the dermatoses examined. There was a similarity in the findings also for the individual groups, of which the two of perhaps most interest were the group consisting of multiple boils, and the group of pruritus ani and pruritus vulvae. In the group of multiple boils some disorder of the carbohydrate metabolism was constant, a high and prolonged curve being present in two of the cases, and a renal

glycosuria in the third. In the pruritus ani and vulvae group consisting of six cases, 100% gave a markedly low curve. In one of these cases also adrenalin injections seemed to have a marked effect in allaying the itch, There was difficulty in regulating the dosage, however, relapse occurring with over-dosage as evinced by the abnormal rise in the curve, and with too small a dosage, the curve returning to its original low level. For this reason, and since more than one member of the endocrine system is likely to play a part in the etiology, it has been suggested that by the administration by the mouth of a combination of thyroid and suprarenal, the dose might be more easily regulated, and treatment rendered more effective. In this relation, of the endocrine system to diseases of the skin, the case of pemphigus foliaceus is of interest, her curve resembling exactly the peculiar curve obtained from a case of Addison's disease in whom the diagnosis was confirmed post mortem. This case of pemphigus foliaceus improved strikingly with adrenalin administration. A case of dermatitis herpetiformis also seemed to be improving on adrenalin injections, but unfortunately was lost sight of owing to a severe scalding accident: and two cases of hydroa aestivale gave very low curves, adrenalin treatment in their case, however, was not attempted. These were the only bullous types of disease examined in this part.

Of the twenty-three cases whose sugar tolerance curves were done, six only gave normal curves, six, curves which were abnormally high and prolonged, and eleven, abnormally low curves.

Our investigations with regard to the uric acid blood content have not confirmed to any degree those recorded by Schamberg and Brown.

In our series, the eczema group gave the lowest blood uric acid average of all, although it contained the only definitely abnormal figure of all the cases examined. The case from which the high reading was obtained improved steadily with restriction of proteins in the diet while at rest in bed and having local treatment, the blood uric acid gradually returning to normal. During a relapse, however, the blood uric acid remained normal. Confirmation, therefore, was not obtained that in this case the high blood uric acid was the factor of importance in causing the condition.

We are able to agree that alkali treatment has a definitely beneficial effect in acne, seborrhoeic dermatitis, and cheiropompholyx, but find the range for the urinary pH in average healthy individuals to be much wider than that of 6.4 - 6.8 as stated by Doble, a more usual range in our series being from 5.5 - 6.4.

The ratio between the free and combined acid in the urine was found to bear no constant relationship to the urinary pH, and on the whole this ratio seemed to give a better indication than the urinary pH, of the need for alkali treatment.

According to our findings the pH of the diseased skin in dermatoses seems to depend not so much on the nature of the dermatosis as on the amount of exudation taking place in its lesions; this being so, variations in the pH of the diseased skin would seem to be of no significance from the point of view of treatment.

Gastric analyses were found to be of importance in dermatoses, a subacidity occurring frequently in rosacea and treatment with large doses of HCl leading to improvement. It was noted also that in some

of achlorhydria, the achlorhydria persisted notwithstanding the marked clinical improvement with HCl. Most of the dermatoses examined were of a chronic nature and most of them showed some degree of subacidity. The only case of acute widespread dermatosis, on the other hand, showed a hyperacidity. From the chloride curves it was shown that in almost all the cases of subacidity the condition was due not to hyposecretion but to excessive neutralization, the pylorus being hypotonic and permitting of excessive regurgitation. This was found in cases in which it had been thought that some degree of suprarenal insufficiency might exist, and seemed, therefore, to be in support of such a theory.

A urinary examination alone was found to be of little value as a substitute for a routine gastric analysis. There seemed to be a possible relationship between the urinary pH and the chloride or secretory curve, but no constant relationship between the urinary pH and the curve for free HCl.

Two cases of hydroa aestivale have been investigated by means of clinical laboratory tests and results have been obtained which seem, on taking into account the marked pigmentation of the skin, to point to the presence in this condition of some degree of suprarenal insufficiency. The findings in favour of this are:-

- (1) The very low type of sugar tolerance curve.
- (2) The marked hypochlorhydria due to excessive neutralization by alkaline duodenal salts, the pylorus being hypotonic.
- (3) The presence of a haemoclastic crisis.

The most prominent feature in these two cases was the very striking increase in the number of blood platelets.

The problems presenting themselves in the etiology of skin conditions are exceedingly difficult to unravel, but the foregoing observations emphasise the fact that clinical laboratory tests are of undoubted value in the investigation of dermatoses, and it is only by pursuance of careful investigation along these lines that one can hope to make much progress in this branch of medicine. The role that endocrine system plays is a very complex one, but would seem to be a very important one in certain cases.
