THESIS presented by: -----

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An investigation into the incidence and significance of hyperglycemia in certain pathological and physiological conditions.

m. D. 1925.



The metabolism of the carbohydrates of the food is accompanied by the production of a long series of intermediate products. Only two of these are sufficiently stable to allow their presence on accumulation to be calculated by chemical methods. They are glycogen, and glucose, the former accumulating in the tissue cells in colloidal form, the latter dissolved in the circulating fluids of the body.

The increase of glucose in the blood can only be the result of:

(1) Absorption of sugar from the intestine

(2) Following the hydrolysis of glycogen, particularly in the liver

(3) The formation of glucose from 'non-carbohydrate substances, e.g: amino-acids.

The diminution of the glucose content of the blood can be the result of:

(1) Oxidation in the tissues

(2) Excretion by the kidneys

(3) Polymerisation into glycogen

(4) Conversion into non-carbohydrate substances such as fat.

The estimation of blood sugar in health and in conditions arising from disease, throws light on the behaviour of one or other of these processes, but the results can only be of value provided that the processes other than that under investigation are normal.

Since Claude Bernard (1) showed the presence of glucose in the circulating blood, blood sugar estimation has been recognised as all important.

The recognised methods are two:

- (1) TITRIMETRIC METHOD.— The reduction of cupric to cuprous oxide in alkaline solution by the unknown Sugar Solution is determined by titrating the latter, either with ferric Sulphate and permanganate as in Bertrand's (2) method, or with free iodine as in Bang's (3) and MacLean's (4) method and their modifications.
- (2) COLORIMETRIC METHOD.— The development of a red colour due to the reduction by the sugar solution of picric acid to sodium picramate, or of a blue colour due to the action of cuprous oxide on Folin's phenol reagent (tungstic acid) is measured quantitatively by the colorimeter (5, 6, 7, 8). The colorimetric method usually gives a higher reading than the titrimetric.

The following table shows the percentage blood sugar (a) in a normal case, (b) in a case with uraemic convulsions, (c) in a diabetic patient as calculated by the two methods:

METHOD

PERCENTAGE GLUCOSE

Titrimetric - Bang's (a)0.097(b)0.118(c)0.154 Colorimetric - Benedict's (a)0.118(b)0.151(c)0.198

The Blood Sugar curve after ingestion of glucose and its variations in the normal subject must be understood before we can claim deviations from it in disease.

Bang (3) was the first to show that the sugar of the blood taken from the vein of a rabbit was increased after the introduction into a starving animal of 2-10 gms. of glucose or starch by stomach tube. The maximum was reached in about one hour, and it took about three hours to reach starvation level.

Bandouin (9) in 1908 and Frank (10) in 1910 estimated the blood sugar in the human subject before and one hour after 100 gms. glucose. They found it raised in some cases and unaltered in others.

Jachau (11) in 1911 made further observations on healthy cases and also in cases of diabetes, chronic nephritis, and jaundice. He estimated the blood sugar at hourly intervals after 100 gms. of glucose. He failed to detect a rise and concluded there was not any in healthy people. He got a rise in diabetics after one hour.

Rolly and Oppermann (12), Bing and Jacobsen (13) found inconsistent results as they did not realise the importance of frequent estimations. Jacobsen (14) using Bang's method of blood sugar estimations pointed out that the blood sugar began to rise ten minutes after the ingestion of a meal of carbohydrates, reaching its maximum within thirty minutes. The hyperglycemia passed off in many cases by the end of the first hour. Considering these results it is now evident that if the blood sugar curve is to be accurately plotted and used as a test of sugar tolerance, or as an indication of the functional activity of the carbohydrate storage mechanism, attention must be given to three points:

(a) The dose of sugar must be sufficient to provoke the maximum rise

(b) The estimation of the blood sugar must be made at frequent intervals so that the highest point can be detected

(c) Estimations must be continued until the blood sugar returns to its normal or fasting level.

Sakaguchi's (15) work covered this ground. Using Bang's method he estimated the blood sugar at intervals of ten minutes for two hours, after the ingestion of 100 gms. of glucose in healthy young adults. His results are very similar to those of Jacobsen (14). His rise was appreciable in ten minutes, reaching its maximum in twenty to forty min-

utes and rapidly falling to its fasting level in fifty to ninety minutes. He found that the highest point of the curve varied between .133 per cent and .191 per cent., but the rapid subsidence after reaching this point was constant.

In four of his cases it reached only .12 per cent. or .13 per cent., whereas in eight other cases it reached between .17 per cent. and .23 per cent. This rapid fall is a point of great importance.

In eight cases examined by Hopkins (16), the maximum stood between .11 per cent. and .156 per cent., and in six cases examined by Haumman and Hirschmann (17), between .1 per cent. and .14 per cent.

Similarly considerable irregularity is observed in the time at which the maximum reading occurred and in the duration of the hyperglycemia.

In Jacobson's (14) cases the maximum was reached in about half-an-hour in those cases in which the maximum only reached a low level, but in the cases in which the maximum was high it might be delayed for one to one-and-a-half hours.

Cummings and Piness (18) examined the blood sugar in 58 normal subjects before, one hour and two hours after giving 100 gms. of glucose, and they emphasise the fact that the rise in blood sugar attained its maximum (at about 50 per cent. above normal) during the first hour and drops to about half that value during the second hour.

In Haumman and Hirschmann's (17) observations, the maximum was reached in twenty minutes to one-and-a-half hours, and the duration of the hyperglycemia varied between forty-five minutes and three-and-a-half hours, a proportion existing more or less between the height of the maximum and the time of the continuance of the hyperglycemia.

It has been shown conclusively that normal urine contains sugar which becomes altered in amount under conditions which are known to cause a change in the blood sugar. Bailey (19) and others by a combination of blood and urine estimations were the first to show the relation between hyperglycemia and glucosuria. There is substantial evidence in their work that the normal sugar threshold of the kidney is reached when the blood sugar rises to the level of .17 per cent. and that active secretion of sugar takes place above that level. This knowledge enabled cases of "renal diabetes" and "diabetes innocens" to be examined. Graham (20) and Goto (21) reported cases of this type.

Epstein (22) and Woodyatt (23) have emphasised the necessity of considering besides the concentration of blood sugar, the blood volume, i.e., the increase or decrease in water. Epstein came to the conclusion that it is the total amount of the sugar in the blood rather than its percentage that is the factor which determines the escape of sugar by the urine.

Woodyatt (23) found that in laboratory animals and in man, glucose could be injected continuously into the venous blood by means of a special injection apparatus at the rate of about 0.85 gm. per kilo per hour, without causing glucosuria. Beyond this tolerance limit and up to 2.0 gms. per kilo per hour, a certain fraction of the sugar appeared in the urine varying in different individuals and in the same individual with different rates of injection. Variations in the amount of water but constant rate of injection of glucose per unit of time did not affect the rate of utilisation or excretion of glucose.

MacLean and de Wesselow (24) described the use of the determination of the blood sugar curve as a chemical test. They compared the curve of normal individuals with diabetics and determined the response to various carbohydrates using glucose, cane sugar, laevulose, lactose, galactore, maltose and potatoes. All of these

caused a similar rise except laevulose, which has no effect on the blood sugar. They showed that 25 gms. of glucose was sufficient to test sugar tolerance, the only effect of larger doses being to prolong the fall to the fasting level. If the blood sugar fails to return to the normal level in one-and-a-half hours then they consider there is an error in storage.

This sudden drop to the normal level is thought by them to be due to the intervention of a storage mechanism which abstracts the sugar from the blood more quickly than it enters.

Hatmman (25) tried to throw light on this point by administering a second dose of sugar immediately after the reaction of the blood to an earlier dose. He found that this second dose did not cause a proportionate rise. The difference between the first and second rise was slight but was constant in all nine cases published. He assumed that the first dose of glucose stimulated a mechanism of carbohydrate disposal which was still acting when the second dose was administered, so producing a lessmarked hyperglycemia.

Fisher and Wishart (26) think this sudden fall due to a change in blood volume, the osmotic effect of an increased blood sugar content being to produce a dilution of the blood.

Bailey (27) investigated this point in a subsequent work. He found only a slight change in the blood volume, using the haemoglobin estimation as a measure of blood volume.

Strouse (28) attempted to alter the blood volume by altering the water intake and by administering Cathartics. He found these measures had no effect on the blood sugar level. Both Bailey and Strouse concluded that the sudden fall in blood sugar content is not due to an alteration in blood volume.

Leaving aside theories, in the average

young or middle-aged healthy person, the blood sugar concentration usually rises from the basal figure of .1 per cent. to a maximum of .16 per cent. or .17 per cent., this maximum being reached in thirty to sixty minutes or so after the ingestion of glucose and falls to the basal figure within one-and-a-half to two hours.

Variations from the normal type of curve are got in certain diseases, other than diabetes.

I. <u>NEPHRITIS</u>. Nephritis may be associated with the diabetic type of curve with a raised renal threshold for sugar.

Cases have been reported of chronic interstitial nephritis with a fasting blood sugar percentage of .12 per cent. or .16 per cent. rising to 0.2 per cent. or 0.25 per cent. and subsiding to the original level slowly in about three hours.

Williams and Humphreys (29) consider that the blood sugar curve is high when the nitrogenous metabolites are excessively high and when uraemia is imminent.

On the other hand Tackau (30) examined five cases and found normal blood sugar in three of them. In the other two the blood sugar was still raised to 0.2 per cent. one hour after 100 gms. of sugar.

Hopkins (31) using Bang's method found a moderate hyperglycemia in many of the twenty-six cases of nephritis he investigated. Some of the cases had a normal blood sugar. On the other hand Bailey (21) using Benedict and Lewis' method noted that hyperglycemia was most marked in those cases of diabetes with chronic interstitial nephritis.

Haumman and Hirschmann (17) studied the blood sugar curve in six cases of nephritis. The blood sugar was still raised two-and-a-half hours after 100 gms. of glucose.

de Wesselow (32) by comparing the picric acid test of Lewis and Benedict with MacLean's

method showed that the former may give readings forty to fifty per cent. too high, and that this may be the result of the retained Creatinin in the blood. Under the conditions of the estimation it gives a similar colour to that produced by glucose in presence of picric acid.

Cowie and Parsons (34) confirmed this work and they state that epinephrin, acetone, diacetic acid and creatinin when presect in the blood will vitiate the results given by the Lewis Benedict method. Consequently in cases of nephritis with creatinin retention, the Lewis Benedict method will show an apparent rather than real hyperglycemia.

Neubauer (35) offered the theory that excessive activity of the suprarenals associated with hypertension was the underlying factor.

O'Hare (36) suggested that sclerosis of the arteries of the pancreas, being part of a general arteriosclerosis might be the pathological background of the condition.

Pearce and Keith (37) suggested that owing to the diseased condition of the kidney, it is unable to utilise the ordinary amount of sugar brought to it by the blood and consequently diminished sugar consumption resulted in an accumulation of this substance in the blood.

Myers and Killian (38) noted an increase in the diastatic activity of the blood and they expressed the idea that this might account for the hyperglycemia often noted in these cases of chronic nephritis.

Herrick (39) found hyperglycemia in ten to thirty per cent. of his cases showing arterial hypertension. This was especially so if raised blood pressure was associated with obvious disease of the kidney. He considers that the prolonged hyperglycemia enhanced the hypertension and general arteriosclerosis. He found that by lowering the blood sugar the blood pressure fell. He considered the cutting out of sugar from the diet of these patients with hypertension, more important than the cutting out of proteins.

On the other hand Ajello (40) found no parallelism between glycemia and hypertension. He thinks hyperglycemia is associated with the retention of nitrogen.

Iwai or Lowy (41) also found in pure hypertension a normal glycemia and alimentary reaction to twenty gms. of glucose. It was only the azotemic patients that showed increased blood sugar and a diabetic alimentary curve.

Rotky (42) also got hyperglycemia marked in oliguric patients.

II. DISEASES OF THE DUCTLESS GLANDS. Results here are indefinite and contradictory. Croser Griffith (43) reported a case of hypopituitarism of Frohlich with increased blood sugar tolerance. One hour after 100 gms. of glucose the blood sugar was .104 per cent. and there was no glucosuria. After two months' treatment with pituitary extract the sugar tolerance diminished and after 100 gms. of sugar the curve rose to .18 per cent. in one hour and sugar was passed in the urine.

Janney and Isaacson (44) have reported a case of acromegaly with a prolonged curve of the diabetic type. They also investigated cases of myxoedema, exopthalmic goitre and cretinism. From their work and the work of Janney and Henderson (45) it seemed impossible to demonstrate any constant relation between the functional activity of the thyroid gland and sugar tolerance.

Schwab (46) in doing routine blood sugar determinations, found a high frequency of abnormally elevated curves, in the psychoses associated with melancholia and depressed states, and also in those patients who were depressed and in the habit of worrying excessively.

Kovy (47) reported a hyperglycemia in nineteen cases of melancholia and four cases of neurasthenia and psychasthenia and occasionally in general paresis and dementia praecox.

a basis of seventy blood sugar estimations, said there was a hyperglycemia in cancer. He was unable to observe a similar change in sarcomatous patients. He suggested that a blood sugar estimation might be used as an aid in the diagnosis between the two conditions.

Trinkler (49) investigated 109 cases, including cases of cancer, typhoid, pneumonia, and tuberculosis. He found a greater hyperglycemia in cancer than in the other diseases and thought that it was more marked in cancer of the internal organs. Cachexia he considered played no part in the production of this hyperglycemia.

Rohdenberg, Bernhard and Krehbiel (50) made a fasting blood sugar estimation, and also at 45 minutes and 120 minutes after 100 gms. glucose. They found that cancer patients have a normal fasting level, which rises steadily in forty-five minutes to .18 or .2 per cent. and continues to rise or remain stationary for 120 minutes.

In some cases the blood sugar level reached .28 per cent. or even .35 per cent., then gradually fell reaching the normal level in one hundred and eighty-five to two hundred and forty minutes. They found this type of curve in twenty-four cases of cancer and one of sarcoma. The site of the cancer did not appear to alter the type of the curve.

Benedict and Lewis (51) investigating fifty-three cases of cancer found that in ten of them the blood sugar was still raised three-and-a-half hours after a carbohydrate meal. Thirty-six per cent. of their cases showed a fasting blood sugar ranging from .12 per cent. to .16 per cent. They also noted a steady increase in the blood sugar as the disease progressed, reaching its maximum just prior to death. They think that this hyperglycemia may be due to the constant call of the tumour for carbohydrate. Cammidge (52) also calls atten-

tion to the hyperglycemia present in cancer, believing it to be due to a faulty function of the endocrine glands from comparing the type of curve with that got in hyperthyroidism and exopthalmic goitre.

Rohdenberg, Bernhard, and Krehbiel (50) made an elaborate investigation on two hundred and twenty-eight cases including cases of cancer, syphilis, tuberculosis and nephritis. They found that three different types of reaction were given after the ingestion of 100 gms. of dextrose in 300 cc of black coffee, the readings being taken before, forty-five and one-hundred-and-twenty minutes after the meal.

- TYPE I. The blood sugar at forty-five minute intervals rises above the zero hour figure and at the one hundred and twenty minute interval is as high or higher than the forty-five minute interval.
- TYPE II. The rise at forty-five minute intervals is as in type I, but at one hundred-and-twenty minute intervals shows a return to the original zero figure.
- TYPE III. The initial sugar concentration is higher than or the same as that at forty-five minutes and the one hundred-and-twenty minutes interval shows a return to the original figure, more or less, sometimes going higher.

61 per cent. of his gastric cancer cases and 50 per cent. of the intestinal cancer cases belonged to Type I.

They conclude that any condition associated with an increase of cell growth tends to give a curve of type I character.

Fredenwald and Grove (53) using Epstein's

method and giving 100 gms. of dextrose investigated thirty-two cases of gastric intestinal cancer. They found a high initial rise which after forty-five minutes was 0.24 per cent. or higher, and remained at that. level for at least two hours. This they termed the cancer curve. The fasting blood sugar value lay between .14 per cent. and .17 per cent. In eleven cases the blood sugar rose above .25 per cent. and yet only one had gylcosuria. They considered the blood sugar estimation of diagnostic help in carcinoma. In a second paper they find a normal blood sugar curve in fifty per cent. of cases and conclude that no type of curve is characteristic of cancer.

Le Noir and his workers (54) disagree with the American workers. In twenty-six cases of cancer of the gastro-intestinal tract fifteen cases had a normal blood sugar figure. They think with the developing of cachexia, the blood sugar tends to fall. They do not consider the blood sugar value of any use in diagnosis, but it might be of prognostic value.

Spence (55) using MacLean's method investigated five cases of ages between 30 and 54 years. Two showed a normal curve, and one showed a delayed hyperglycemic curve of the mild diabetic type. He considers that there is no type of curve diagnostic of cancer.

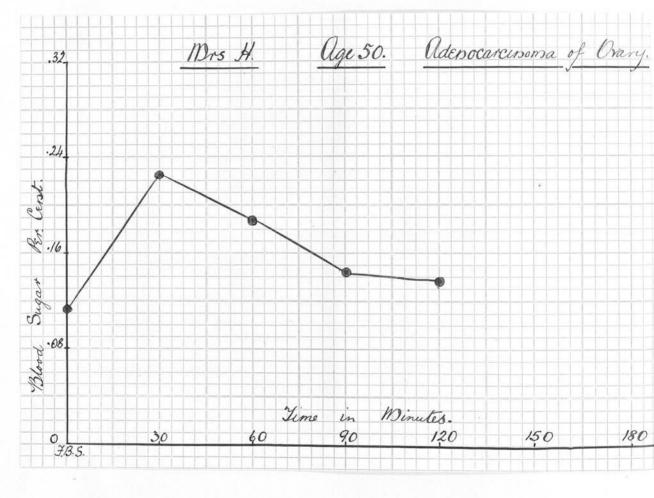
Benedict and Lewis (56) found that by feeding rats with transplantable sarcoma on a carbohydrate free diet, they showed an increased resistance to tumour growth. As soon as they were put on a carbohydrate rich diet, the tumour grew luxuriantly. Benedict working on phloridzinized rats with sarcoma found that after phloridzin the tumour softened and broke down and finally disappeared and after death no sign of malignant tumour was found. During the experiment the rats were kept on a carbohydrate free diet.

The blood sugar estimations in the series of cases investigated by me were made by MacLean's method. The fasting blood sugar was estimated either early in the morning before breakfast, or four hours after a meal.

The patient passed water and the fasting blood sugar was estimated. Then 50 gms. of glucose in 200 cc of water were given and blood sugar estimations were made at half-hourly intervals. Urine was again passed one hour and two hours after the glucose was given.

To act as a control, the blood sugar was estimated in three healthy young adults, after ingestion of 50 gms. of glucose.

Fasting Blood Sugar .1 per cent	$\frac{1}{2}$ hour .135%		1½ hours	2 hours
C.D. Age 19 Years Fasting Blood Sugar .095%	hour .16%			2 hours
E.F. Age 35 Years Fasting Blood Sugar .093%		1 hour .17%	1½ hours	



Blood Sugar Estimations were made in the following twenty cases of Cancer.

MRS. H. Age 50 years. Admitted with ascites and loss of weight. Paracentesis abdominis was done and the right ovary was then found to be enlarged. At a subsequent laparotomy, the enlarged ovary was removed. Secondary deposits were found in the peritoneum but not in the liver.

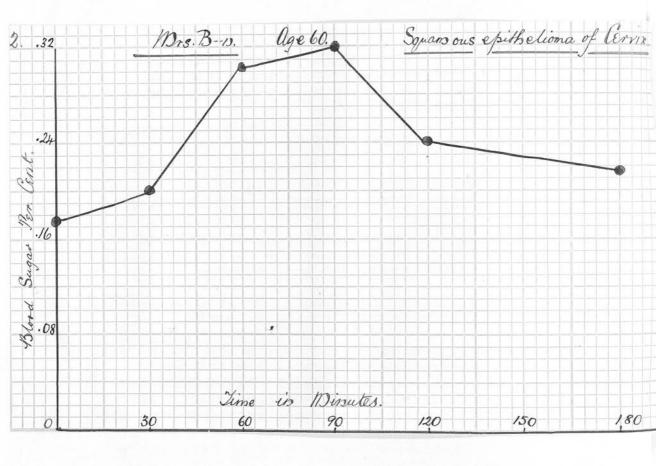
Paracentesis was performed again about three weeks following the operation and the patient was then discharged home.

There was considerable loss of weight but she was not cachetic.

The urine was sugar and albumen free on frequent examination.

On Section the growth of the ovary was shown to be an adeno carcinoma.

Fasting Blood 45 mins. $1\frac{1}{2}$ hours $2\frac{1}{4}$ hours Sugar .112% .225% .143% .137%



MRS. B--N. Age 60 years. Admitted complaining of irregular vaginal haemmorrhage.

The patient was markedly emaciated and had suffered much pain, with subsequent loss of sleep.

ON EXAMINATION a large growth infiltrating the supra vaginal cervix was felt. This later ulcerated through into the bladder and rectum with the formation of a double fistula.

The blood sugar estimations were made one month before death.

Fasting Blood & hour 1 hour 1 hours 2 hours 3 hours Sugar .175% .2% .312% .32% .24% .215%

Sugar was passed in the third specimen of urine. There was pus (Bacillus Coli infection) during the last month.

POST MORTEM FINDINGS. The loss of flesh and subcutaneous fat was general.

PELVIS ORGANS. The vagina was filled with an ulcerating malignant mass making it difficult to distinguish vagina from cer-The slightly enlarged uterus was fixed to the bladder and rectum by the infiltrated tissue in the broad ligaments. A ragged perforation was found between the vagina and bladder and a smaller one between the vagina and rectum. The bladder showed signs of chronic infection of the mucous membrane with a recent ascending suppurative nephritis. Both kidneys on section showed the formation of small abscesses, especially in the cortex, some of which broke open on stripping the capsule. The pelvis in both cases was dilated. The inguinal glands on both sides were enlarged and a secondary deposit was found in one of the larger glands.

CARDIOVASCULAR SYSTEM beyond some general arteriosclerosic changes in the vessels with some recent aortitis there was no marked pathological change. The myocardium was fairly healthy and the valves were healthy.

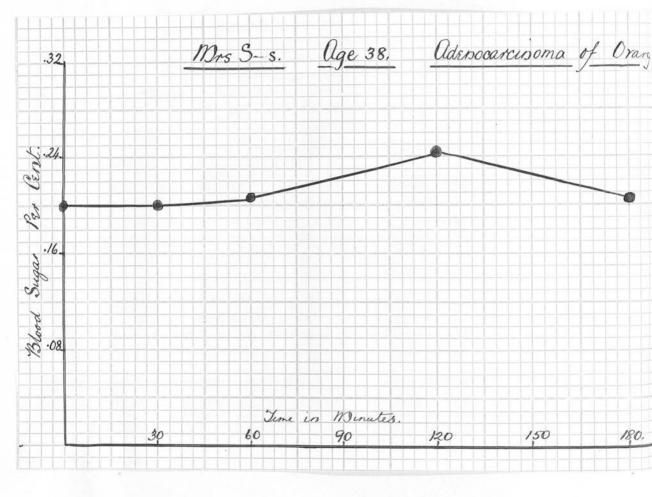
LUNGS showed some old scarring at the right apex but were otherwise healthy.

There was no enlargement of the mediastinal glands.

ALIMENTARY TRACT healthy.

The liver was not enlarged, and there was no secondary deposits seen. It showed some fatty degeneration. The pancreas appeared healthy as did the spleen.

The microscopic appearance of the growth showed it to be a squamous epithelioma of the cervix.



MRS. S----T. Age 38 years. Admitted complaining of swelling of the left leg, loss of appetite, and breathlessness. The patient showed a marked loss of weight.

There was an enlargement of the supraclaviculer glands, especially on the left side, with a general enlargement of the axillary, retromammary and inguinal glands. There was considerable oedema of the left leg. Fluid was present in both pleural cavities and X-ray examination showed a broadening of the mediastinal shadow.

The abdomen was distended with fluid. On pelvic examination a mass which was separate from the uterus was felt in the pouch of Douglas. The uterus was not enlarged. There was an infiltration and thickening of the left broad ligament. The liver was not enlarged.

As the conditions progressed the right leg became swollen and oedematous. The chest and abdomen were frequently tapped.

A section of one of the excised axillary glands showed the primary growth to be an adeno carcinoma probably of the ovary.

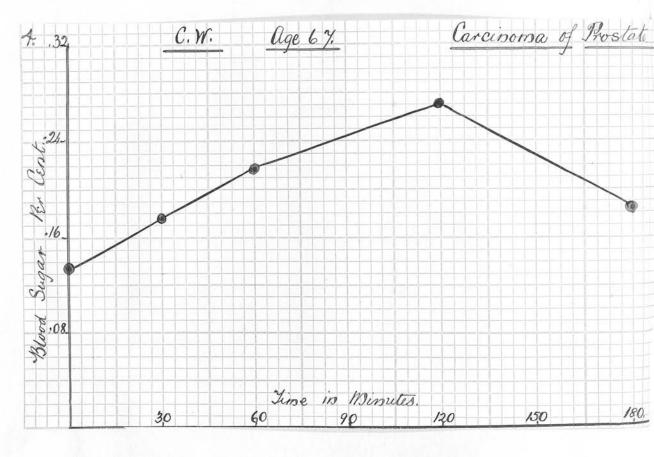
The blood sugar estimation was made two months before death.

Fasting Blood 1 hour 1 hour 2 hours 3 hours Sugar .2% .2% .206% .243% .206%

The urine was sugar free. There was a trace of albumen present.

The Wassermann Reaction was strongly positive.

A post-mortem examination was refused.



C.W. Age 67 Years. He was admitted with carcinoma of the prostate with secondary growths in the lumbar region of the cord with consequent paralysis of the lower limbs and incontinence of urine. He showed marked cachexia. The urine was sugar-free but contained pus due to a bacillus coli infection.

The Wassermann Reaction was negative.

Fasting Blood & hour 1 hour 2 hours 3 hours Sugar .133% .175% .218% .27% .181%

POST MORTEM FINDINGS. There was a small adeno carcinoma found in the prostate. The bladder wall was thickened and there was considerable infection of the mucous membrane.

The kidneys were slightly enlarged and showed signs of ascending pyelonephritis with some dilatation of the pelvis on both sides.

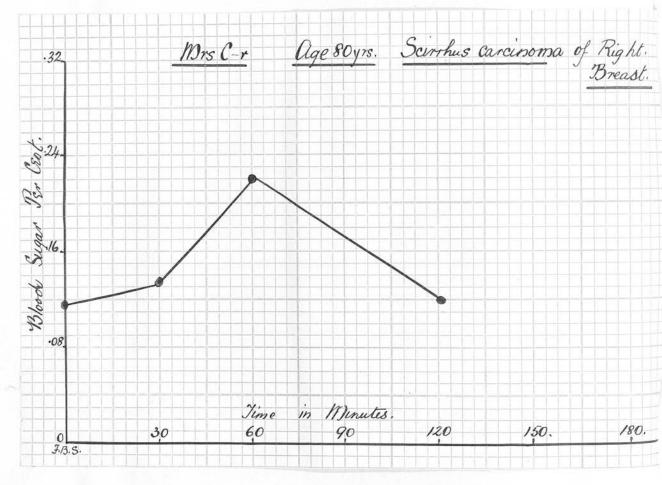
The cancellous tissue of the third and fourth lumbar vertebrae was replaced by a tumour mass which had stimulated a new formation of dense bone, and by pressure caused the spinal symptoms mentioned.

The gastro intestinal tract was normal.

There was no liver enlargement and no mediastinal involvement.

The heart showed some myocarditis, especially round the pulmonary artery orifice and the papillary muscles of the left venticle.

The aorta showed some arteriosclerotic plaques.



MRS. C--R. Age 80 Years. Admitted with a history of having had a scirrhus carcinoma of the right breast for five years at least, and with chronic bronchitis. Her general condition was fairly good. She died one year after admission.

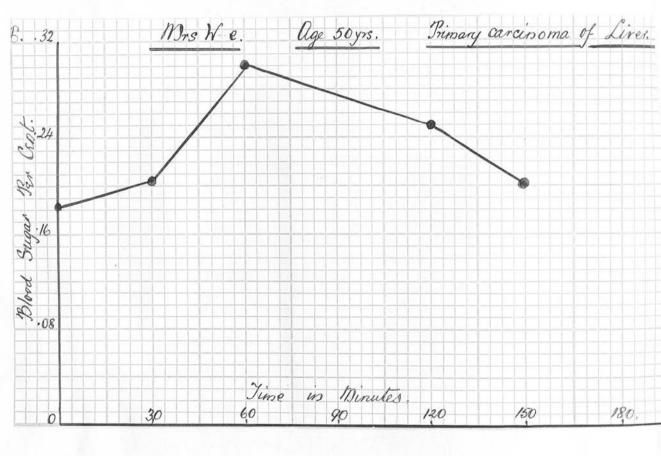
Fasting Blood & hour 1 hour 2 hours Sugar .112% .134% .22% .12%

POST MORTEM FINDINGS. A large atrophic scirrhus carcinoma which had ulcerated through the skin was involving the lateral two thirds of the right bresst. The growth had infiltrated the paramammary and retromammary areolar tissue and subjacent pectoral fascia and muscles, right down to the ribs, to which the pleura was adherent. The axillary glands were considerably enlarged and showed secondary deposits. The mediastinal glands also were enlarged with secondary deposits visible on section. The heart showed some atheromatous changes in the coronary arteries with some fibrous tissue overgrowth of the myocardium. similar fibrotic change was seen in the papillary muscles and columnae carneae. The aorta showed calcareous deposits with old aortitis.

There was old scarring at the right apex with small areas of old-standing collapse at the free edge of the base.

ALIMENTARY TRACT normal. There was no liverenlargement and no secondary growths were found.

KIDNEYS healthy.



MRS. W----E. Age 50 Years. On admission complained of shortness of breath and jaundice. She died two weeks after admission, with enlargement of the liver.

Fasting Blood & hour 1 hour 2 hours 3 hours Sugar .181% .206% .3% .25% .2%

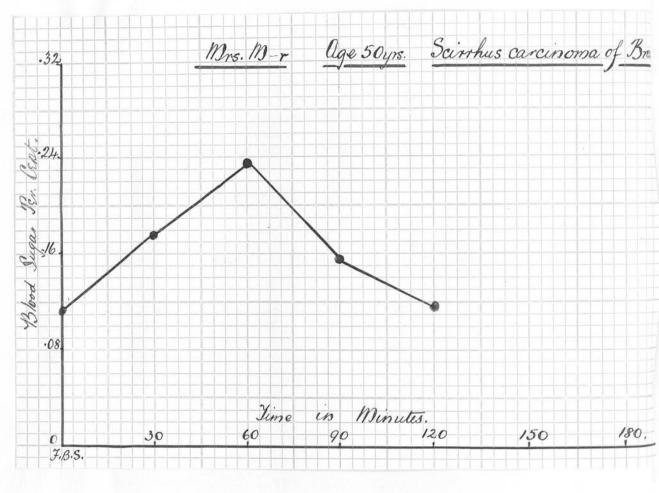
The urine was sugar-free.

The Wassermann Reaction was negative. On section the tumour was seen to be in primary carcinoma of the liver.

POST MORTEM FINDINGS. The body was emaciated and generally deeply jaundiced. There was a large collection of fluid in the abdominal cavity. The liver was very much enlarged, weighing twenty lbs. and was studded with greyish rounded masses showing central necrosis. It showed no signs of any previously existing cirrhosis. There were no metastatic growths found.

The Alimentary tract was normal.

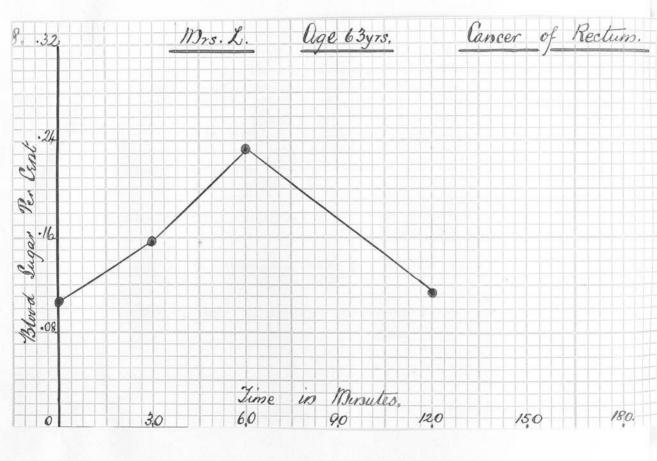
The Cardio-vascular remal system showed changes in keeping with secondary anaemia. The lungs were healthy. The pelvic organs were healthy.



MRS. M----R. Age 50 years. Admitted with an adeno carcinoma the size of a walnut in the upper and outer quadrant of the right breast of at least six months' duration. Two of the atxillary glands were enlarged to the size of a pea.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{2}$ hours 2 hours Sugar .112% .175% .235% .156% .118%

No sugar was passed in the urine.

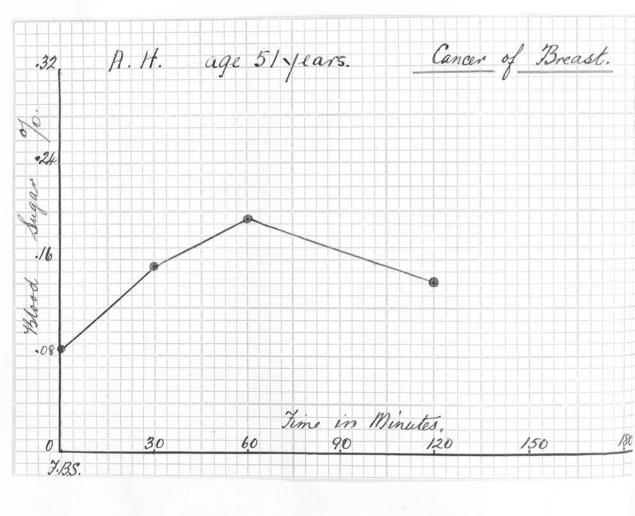


MRS. L - Age 63 Years. Admitted with inoperable carcinoma of the rectum.
She gave a history of two-and-ahalf years' duration, colostomy
having been necessary six months
before admission. She showed
marked cachexia and she complained
of much pain. The inguinal glands
on the left side were enlarged.

There was no enlargement or growth of the liver.

Fasting Blood & hour 1 hour 2 hours Sugar .106% .156% .231% .112%

No sugar was passed in the urine.



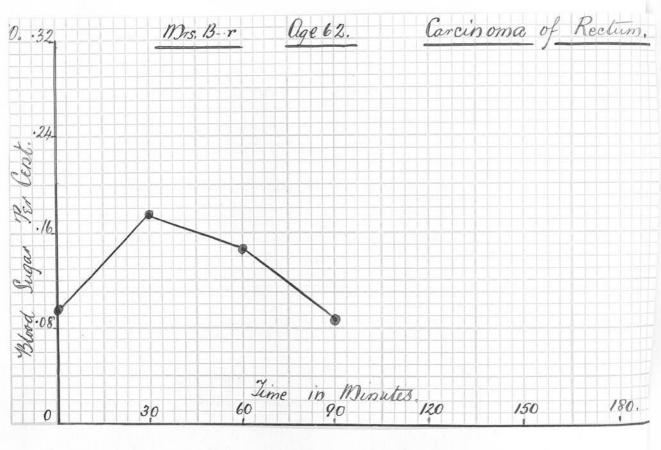
Age 51 Years. Her history was that in September, 1923, she had a radical operation for removal of right breast for scirrhus carcinoma.

She was re-admitted in February, 1925, with recurrent growths in the old operation scar.

Her general condition was good, and no other secondary growths were found on examination.

No sugar was passed in the urine.

Fasting Blood $\frac{1}{2}$ hour 1 hour 2 hours 3 hours Sugar .086% .143% .2% .225% .131%

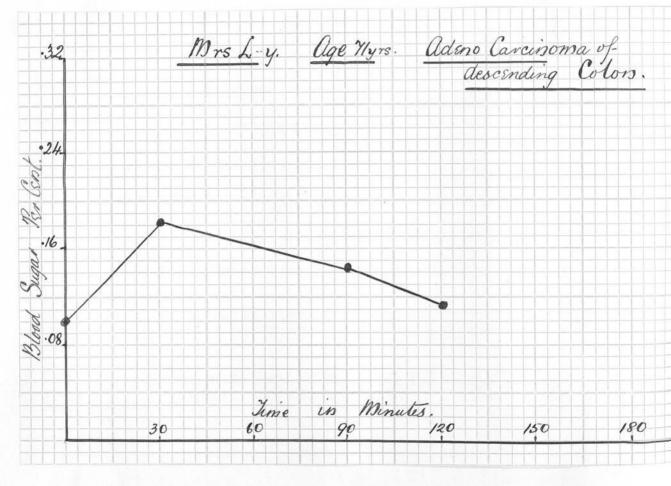


MRS. B----R. Age 62 Years. Admitted
with carcinoma of rectum of threeand-a-half years' duration with
previous history of constipation and
bleeding piles. Colostomy was performed in December, 1924.

ON ADMISSION she showed considerable emaciation with loss of appetite.

ON EXAMINATION a large ring carcinoma was felt in the upper reaches of the rectum. There was some enlargement of the iliac and inguinal glands.

She had a mild B. Coli cystitis - there was no sugar in the urine.



mRS. L---Y. Age 71 Years. Admitted

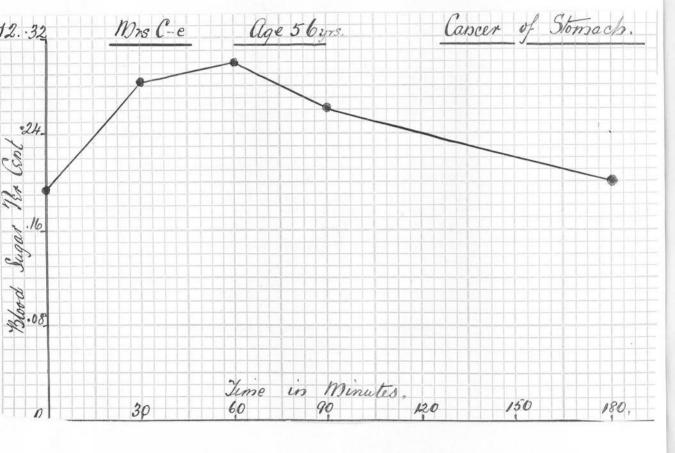
complaining of swelling of the left
leg and weakness. Examination
showed considerable loss of flesh.
There was a mass felt in left iliac
fossa with enlargement of the left
inguinal glands. The liver was
not enlarged.

Microscopic section of one of the smaller inguinal glands revealed an adenocarcimona probably of descending colon.

The urine was sugar and albumen free. The Wassermann Reaction was negative.

Fasting Blood $\frac{3}{4}$ hour $1\frac{1}{6}$ hours 2 hours Sugar .1% .181% .143% .114%

This patient went home to die.



MRS. C----E. Age 56 Years. She was admitted complaining of loss of appetite.

She gave a history of jaundice in July, 1924, which she thought was due to the shock of finding her husband dead in bed just previously.

ON ADMISSION she showed general carcinomatosis of the abdomen with a fixed mass in the pouch of Douglas.

A test meal showed absence of free hydrochloric acid, but a Bismuth meal with X-ray examination showed a normal stomach outline and no delay in emptying. She developed some ascites before death with swelling of both legs.

The urine was free of sugar.

The blood sugar was examined one month before death.

Fasting Blood $\frac{3}{4}$ hour 1 hour $1\frac{1}{2}$ hours 3 hours Sugar .193% .281% .3% .26% .2%

The Wassermann Reaction was negative.

POST MORTEM FINDINGS. There was general emaciation.

The stomach was full of a large blood cloth. A solid carcinoma of the sessile type with thick ulcerated edges was found occupying about two-thirds of the lesser

curvature of the stomach in the neighbourhood of the pyloris. The stomach was firmly adherent to the pancreas. Metastatic nodules were found in the pyloric lymph glands which were enlarged.

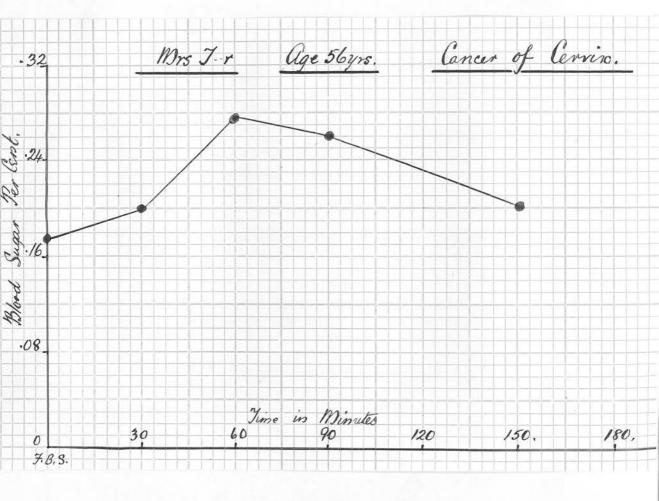
The ovary on both sides and especially the right had become the seat of a large secondary growth undergoing cystic degeneration in parts. These tumours occupied the greater part of the abdominal cavity.

The uterus was healthy.

The liver was not enlarged but showed three translucent secondary deposits about the size of a shilling. They appeared to be fairly recent. There was some degree of fatty degeneration in the liver.

There were several secondary deposits appearing 45 minute lenticular flecks of grey transparent tissue scattered over the lungs. The mediastinal glands were not enlarged. The spleen showed some fibrosis.

The myocardium was degenerated with some atheroma of the coronary arteries. The valves were healthy and competent.



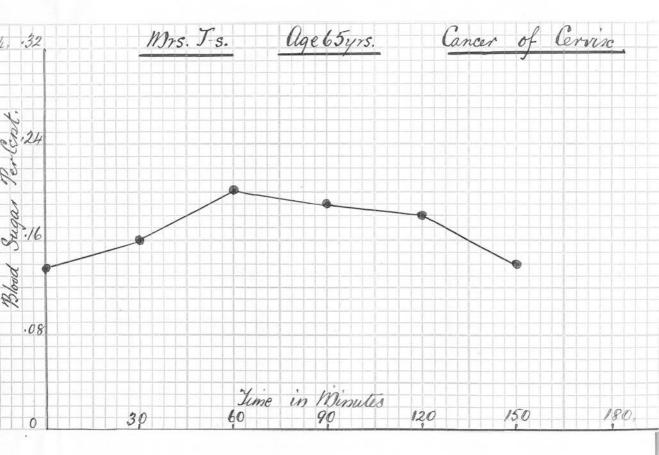
MRS. T----R. Age 56 Years. Was transferred from another hospital with
a large ulcerating carcinomatous
cervical mass protruding from the
vulva with profuse offensive discharge. She showed marked cachexia and died four days after admission from vaginal haemorrhage.

The liver was not enlarged and no enlarged abdominal glands could be felt.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{2}$ hours $2\frac{1}{2}$ hours Sugar .175% .2% .278% .26% .2%

The urine was sugar free, but the woman had a mild B. Coli infection of the bladder.

A Postmortem examination was refused.



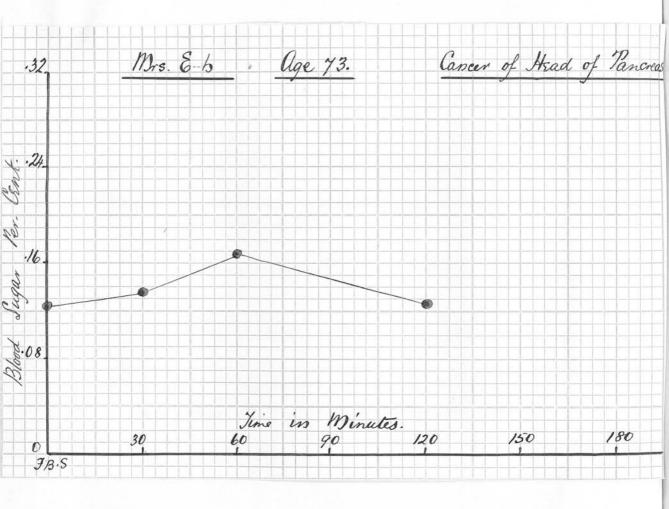
MRS. J----S. Age 65 Years. She was transferred from another hospital with a history of irregular vaginal haemorrhage for a year previous to a hysterectomy in December, 1924, for malignant growth of the body of the uterus.

On admission she showed a considerable degree of cachexia and she died a month after admission.

Blood sugar estimations were made three weeks before death.

Fasting Blood $\frac{1}{2}$ hr. 1 hr. 1 $\frac{1}{2}$ hrs. 2 hrs. 3 hrs. Sugar .137% .16% .2% .19% .18% .14%

POST MORTEM FINDINGS. A total hysterestomy had been performed. There were a few secondary deposits found scattered over the peritoneum. There were five secondary growths found in the under-surface of the liver. The other organs appeared healthy.



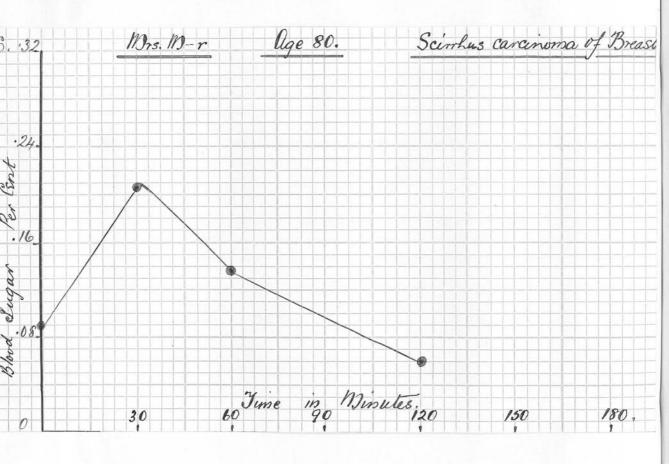
P----H. Age 73 Years. Admitted complaining of loss of appetite and vomitting after food. She was very emaciated and deeply jaundiced. Examination showed a growth of the pyloric with secondary deposits in the liver which was enlarged. The patient died three weeks after admission.

Fasting Blood $\frac{1}{2}$ hour 1 hour 2 hours Sugar .125% .137% .168% .125%

The urine was sugar free.

The Wassermann Reaction was negative.

A post mortem examination was refused.

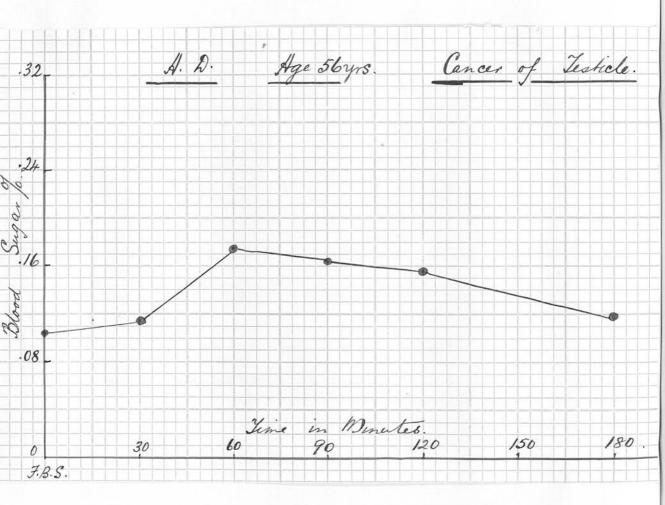


MRS. M---R. Age 80 Years. She was admitted suffering from senile changes following a general arterial degeneration. On routine examination it was found that she had a scirrhus carcinoma about the size of a small tangerine orange occupying the outer and lower quadrant of the right breast.

She had known of its existence for three to four years. There was no enlargement of the axillary glands.

Fasting Blood 45 mins. 1 hour 2 hours Sugar .09% .206% .137% .062%

The urine was sugar free.



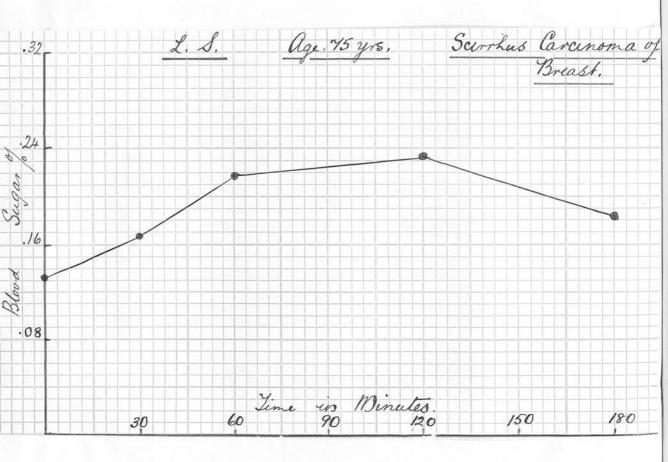
mitted with ascites and general cachexia. The history showed that the right testicle was removed for cancer two years previous to admission. After paracent sis a mass of enlarged glands was felt in the pelvis. The liver was not enlarged and no secondary growths were felt.

There was no sugar in the urine.

Fasting Blood & hr. 1 hr. 1 hrs. 2 hrs. 3 hrs. Sugar .103% .114% .175% .162% .156% .118%

The Wassermann Reaction was negative.

A post mortem examination was not allowed in this case.

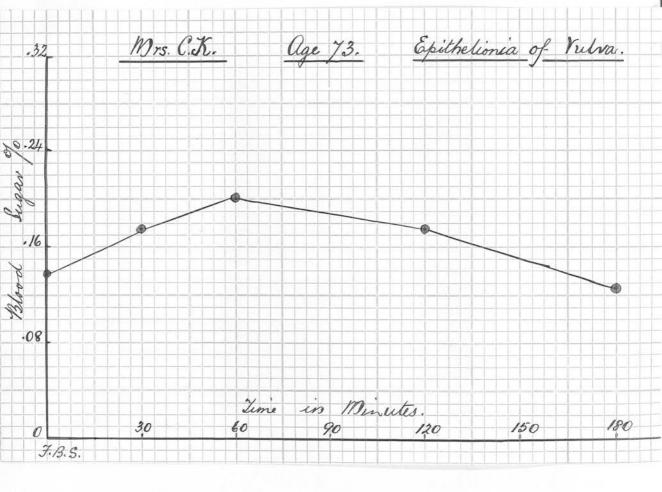


L. S----Y. Age 75 Years. She was admitted with well-marked arterial changes and with myocarditis.
Routine examination showed a scirrhus carcinoma of the right beagt, which occupied the outer two-thirds of the gland. It was firmly adherent to the skin and to the ribs below. The axillary glands were enlarged. It gave rise to no symptoms. The patient thought she had had it for about three years.

There was no sugar or albumen in the urine and renal function appeared good.

The Wassermann Reaction was negative.

Fasting Blood & hour 1 hour 2 hours 3 hours Sugar .131% .168% .218% .231% .181%



MRS. C----K. Age 73 Years. She was admitted with Epithelions of vulva.

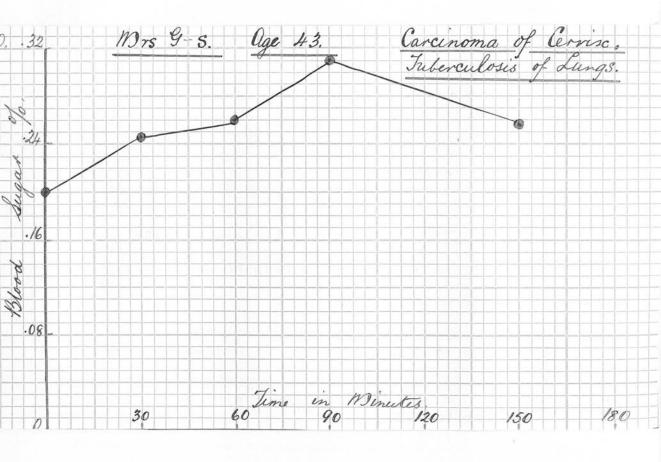
The ulcerated tumour with hard everted edges replaced the greater part of the right labium majus extending up towards the urethra, causing some disturbance of micturition.

The right inguinal glands were enlarged probably due to the septic condition on admission. The ybecame smaller as the local condition was made healthier.

There was no sugar or albumen in the urine.

The Wassermann Reaction was negative.

Fasting Blood & hour 1 hour 2 hours 3 hours Sugar .137% .175% .20% .175% .125%



MRS. C----S. Age 43 Years. Admitted with advanced tuberculosis of both lungs, (T.B. present in the sputum) and with cancer of the cervix of one year's duration. She had been troubled with a winter cough for past ten years but for past three years it had become much worse.

The Wassermann Reaction was negative.

The sugar estimations were made three months before death.

Fasting Blood & hour 1 hour 1 hours 2 hours Sugar .2% .245% .26% .32% .256%

There was sugar in the third specimen of urine collected, and she had a trace of albumen and pus in the urine during the last month.

POST MORTEM FINDINGS. A large fungating extra cervical carcinoma was found practically filling the vagina and spreading backwards into the utero sacral ligaments and the peritoneum of the pouch of Douglas.

The external iliac and inguinal glands were enlarged and some showed signs of secondary growth.

There were several secondary deposits in the liver, which was not enlarged. There were no deposits in the peritoneum.

THORAX. The pleura of both lungs was thickened and covered with fibrous exudate with some dense adhesions attaching a large cavity in the upper lobe to the thoracic wall. The cavity opened widely into a bronchus and was surrounded by consolidated fibrous lung tissue studded with caseos foci. A large area of pneumonic consolidation occupied both basal lobes and in the left lung this was softening in one area, with cavity formation. The hilum lymphatic glands were enlarged and caseous.

HEART. Showed some degenerative changes in the myocardium. The valves were healthy.

AORTA. No marked change.

ABDOMEN. No deposits in peritoneum. Alimentary tract healthy. The pancress appeared normal.

URINARY SYSTEM. On the right side some cancerous infiltration partially blocked the ureters with the formation of hydro ureter and hydronephrosis. There was some cancerous infiltration of the base of the bladder.

A Fasting Blood Sugar Estimation was made on the follow-ing Cases of Cancer.

NAME	AGE	SITUATION OF CANCER	FASTING BLOOD SUGAR	GENERAL CONDITION
		poulta in 1100		
Mrs.	48	Adeno carcinoma of right overy	.112%	Fairly Good
Mrs. C.	50	Cancer of Cervix. T.B. lungs	.2%	Cachexia marked
Mrs. D.	62	Cancer of Cervix (ulcerated)	.175%	Cachexia marked
W.S.	65	Cancer of tonsil with secondary glands of neck, which had ulcerated	.2%	Cachexia marked
		through skin		
Mrs.	50	Melanosis	.137%	Cachexia marked
W.B.	65	Cancer of rectum. Secondary deposits in glands of groin	.143%	Fairly Good
		and iliac glands		
S.C.	79	Cancer of left breast ulcerated	.153%	Fairly Good
		through skin		
R.B.	86	Cancer of left breast ulcerated through skin	.166%	Fairly Good
Mrs.	79	Cancer of left breast. Secondary deposits in left groin and brain	.162%	Cachexia marked.
M.H.	50	Cancer of stomach. Laparotomy done and incision septic	.175%	Cachexia marked

NAME	AGE	SITUATION OF CANCER	FASTING BLOOD SUGAR	GENERAL CONDITION
Mrs.	60	Sarcoma of ileum with secondary de-	.2%	Cachexia marked
		posits in liver		
Mrs.	48	Cancer of cervix. Vesico-vaginal fis- tula - Cystitis	.2%	Cachexia marked
Mrs. B.	53	Cancer of stomach with secondaries in spine	.168%	Cachexia marked
G.H.	69	Cancer of left ton- sil secondary in cervical glands	.1%	Fairly Good
R.F.	69	Cancer of stomach	.093%	Fairly Good
J.C.	78	Cancer of rectum with secondary in	.1%	Fairly Good
		iliac glands		
R.S.	78	Cancer of prostate. Cystitis	.131%	Fairly Good
J.S.	69	Cancer of stomach (Two years)	.131%	Cachexia marked
Mrs.	56	Cancer of cervix (ulcerated)	.143%	Cachexia marked
Mrs. G.	49	Cancer of rectum with Colostomy (Two years' duration)	.143%	Fairly Good
Mrs. S.	66	Cancer of right breast (ulcerated through skin) with	.143%	Fairly Good
		secondaries in ax- illary glands		
Mrs. D.	58	Cancer of cervix (Two years' duration	.108%	Poor

NAME	AGE	SITUATION OF CANCER	FASTING BLOOD SUGAR	GENERAL CONDITION
Mrs.	80	Cancer of descending colon	.09%	Poor
A.B.	69	Cancer of rectum. Colostomy two years ago. Recto_vesical fistula	.1%	Poor
T.K.	73	Cancer of floor of mouth involving alveolus	.093%	Poor
J.B.	79	Cancer of umbilious with secondaries in liver	.137%	Fairly Good
M.S.	38	Adeno carcinoma of ovary with second- aries in axillary glands	.2%	Cachexia marked
E.B.	62	Cancer of rectum. Three years' dur- ation. Colostomy	.095%	Fairly Good
E.L.	71	Cancer of descending colon	.1%	Fairly Good
E.C.	54	Cancer of stomach with secondaries in the abdominal glands	.193%	Cachexia marked
K.T.	65	Cancer of body of uterus - hysterectomy - recurrence in ab- dominal glands	.137%	Cachexia marked
Mrs. F.	73	Cancer of pylorus	.125%	Cachexia marked
<u>A.H.</u>	51	Cancer of breast (recurrence in scar after operation)	.086%	Good

NAME	AGE	SITUATION OF CANCER	FASTING BLOOD SUGAR	GENERAL CONDITION
C.W.	67	Cancer of prostate with secondaries in spine	.1337	Cachexia marked
Mrs.	50	Cancer of stomach with secondaries in liver	.181%	Cachexia marked
Mrs.	S.	as above	.187%	tr
Mrs.	63	Cancer of rectum (inoperable)	.112%	Poor
Mrs.		Cancer of breast	.156%	Fairly Good
Mrs. E.	50	Cancer of cervix (early)	.146%	Fairly Good
Mrs. G.	68	Cancer of stomach. Secondary growths in liver	.153%	Cachexia marked
Mrs.	80	Cancer of breast - ulcerated not septic	.134%	Poor
Mrs.	u	Cancer of breast Six years	.09%	Fairly Good
A.D.	56	Cancer of testicle with secondary growths in abdominal glands - ascites	.103%	Cachexia marked
Mrs. S.	73	Scirrhus cancer of right heart. Ax-illary glands in-volved. Duration five years	.131%	Poor
Mrs.	73	Epithelioma of Vulva	.137%	Fairly Good

SUMMARY.- Taking the average of the percentage readings in four cases of cancer of the cervix, the following results are obtained:

Fasting Blood & hour 1 hour 2 hours Sugar .172% .207% .262% .24%

Taking the average of the percentage readings in two cases of cancer of the ovary the following values are obtained:

Fasting Blood & hour 1 hour 2 hours Sugar .156% .212% .196% .190%

Taking the average of the percentage readings in five cases of cancer of the breast the following values are obtained:

Fasting Blood t hour 1 hour 2 hours Sugar .084% .154% .194% .142%

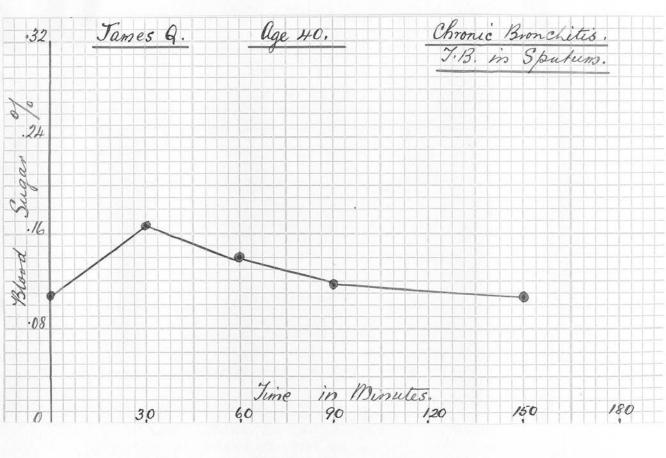
The average fasting blood sugar in forty-five cases of cancer was .139%. The average fasting blood sugar in seven cases of cancer of the cervix was .16%. The average fasting blood sugar in nine cases of cancer of the breast was .135%. The average fasting blood sugar in eight cases of cancer of the stomach was .15%. The average fasting blood sugar in six cases of cancer of the rectum was .115% and in two cases of cancer of the colon was .095%.

Eight of the twenty cases in which sugar tolerance tests were done showed a normal reaction; three cases showed a slight variation from the normal.

Nine of the twenty cases showed a raised fasting blood sugar and a raised maximum with the lag type of curve described by Rohdenberg, Bernhard and Krehbiel, taking three hours to return to the fasting level.

Keeping in mind the tendency for the fasting blood sugar level to rise above .1% with advancing years (the average age in my cases was 65 years), it would still appear that in some cases of cancer a hyperglycemia does exist accompanied by a raised renal threshold. Factors associated with this hyperglycemia appear to be:

- (i) The Type of Cancer. The slow growing avirulent cancers of the elderly patients did not appear to raise the blood sugar percentage to the same degree as some of the more virulent cancers of the younger patients.
- (ii) Secondary Infection. The ulcerated cancers of the cervix and of the breast, the cancers of the prostate and uterus with a superimposed cystitis, showed a considerable departure from the normal blood sugar levels.
- (iii) The Development of Cachexia. It would appear that the sugar level of the blood tended to rise with the development of marked cachexia except in cases of cancer of the colon and rectum.
- CONCLUSION. No type of curve is typical of cancer. Consequently an estimation of the blood sugar is not of value in diagnosis. In my series certain rapidly growing cancers in younger patients and those associated with secondary infection and cachexia showed a varying degree of hyperglycemia associated in some cases with a raised renal threshold for sugar.



IV. TUBERCULOSIS. Trinkler (49) in his investigation of one hundred and nine cases including some cases of tuberculosis found a hyperglycemia. In the series of cases investigated by Rohdenberg and his co-workers (50) he found that sixty per cent of his tuberculosis cases showed a hyperglycemia and that in two hours after 100 gms. dextrose, the fasting level was not reached.

Ten cases of tuberculosis of varying ages and with varying degrees of infection were examined. The results are as follows:

James Q. Age 40 Years. This patient had "always had a cough," which becomes worse in the winter. His occupation (a dustman) tended to make this worse.

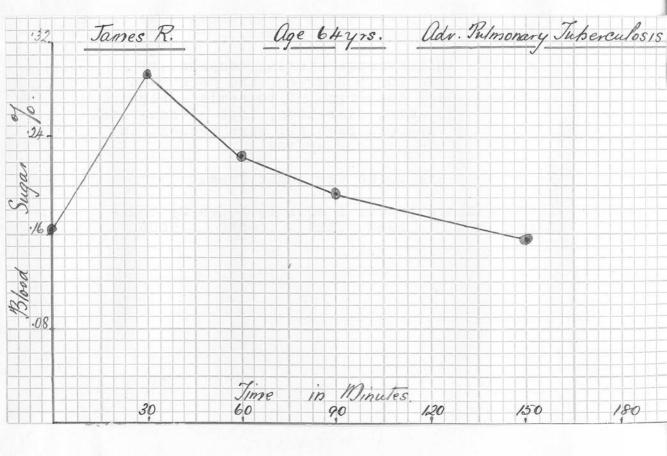
He showed signs of chronic bronchitis and emphysema with tubercular involvement of base of the right lung. The tubercle bacillus was found in the sputum.

His average evening temperature is 99 degrees.

His condition was improving under open-air treatment.

No sugar was passed in the urine.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{2}$ hours $2\frac{1}{2}$ hours Sugar .11% .165% .14% .12% .15%

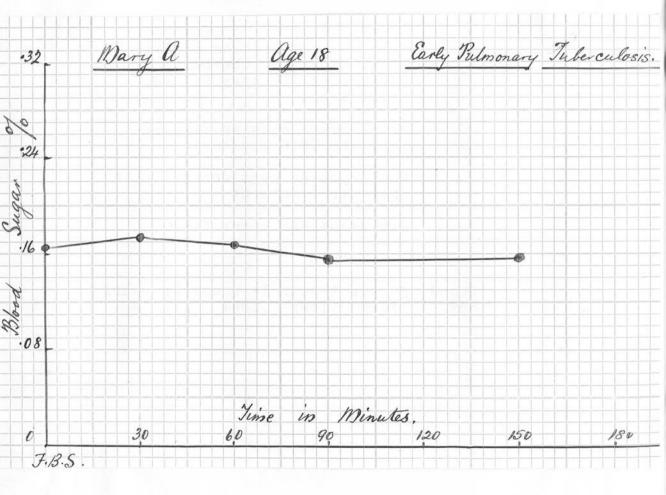


James R. Age 64 years. This patient had been treated for pulmonary tuberculosis in Sanatoria and Hospitals for the past twenty years. He was admitted to this hospital (in a dying condition) after a severe haemoptysis.

His average evening temperature was 100.5 degrees, and he showed all the signs of toxaemia - night sweats, diarrhoea, loss of appetite. Tubercle baccilli were present in his copious sputum.

His urine was sugar free.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{2}$ hours $2\frac{1}{2}$ hours Sugar .16% .295% .22% .195% .156%



Elizabeth A.

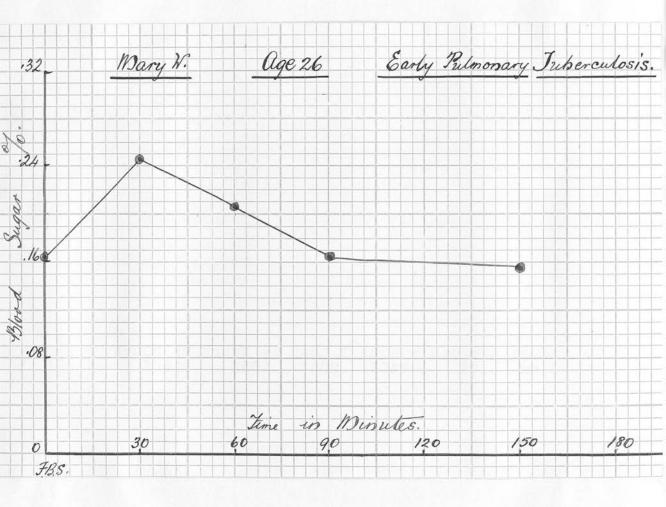
Age 18 Years. She was admitted following a haemoptysis. Examination showed signs of early tubercular infection of the apex of the right lung.

Her average evening temperature was 98.6 degrees.

She improved considerably with open-air treatment.

Her urine was sugar free.

Fasting Blood & hour 1 hour 1 hours 2 hours Sugar .166% .175% .168% .156% .156%

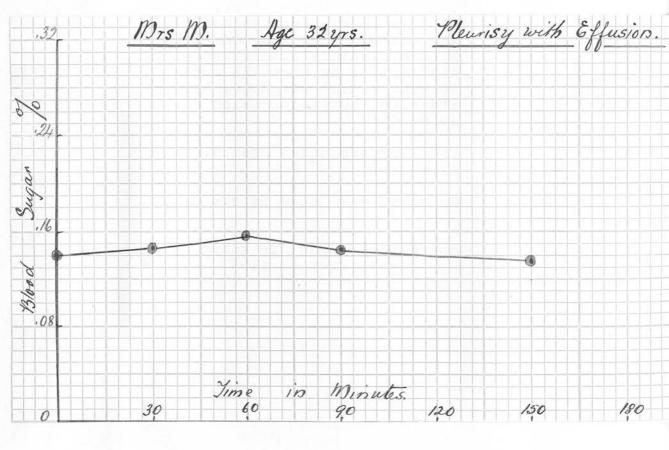


Mary W. Age 26 Years. This patient was admitted because of a cough which had become worse since the birth of her child. Three months previously she showed an early involvement of the right apex. The tubercle bacillus was present in the sputum.

Her average evening temperature was 98.4 degrees.

She was gaining weight and she had less cough and sputum after three months in hospital.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{2}$ hours $2\frac{1}{2}$ hours Sugar .16% .246% .206% .165% .156%



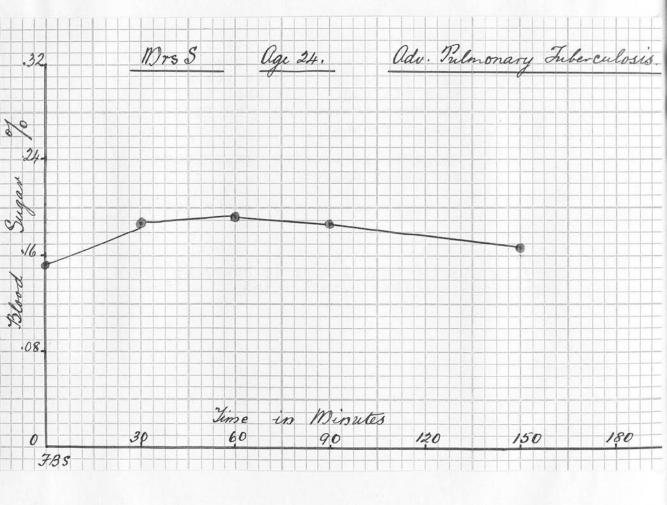
Mrs. M.

Age 32 Years. A laparotomy was performed a year beforead-mission for abdominal pain. Plastic tubercular peritonitis was found. She was admitted with a pleurisy with effusion of the right lung when the sugar tolerance test was done, her abdominal condition being quiescent.

She improved under open-air treatment.

No sugar was found in the urine.

Fasting Blood & hour 1 hour 12 hours 22 hours Sugar • 14% .145% .16% .143% .136%

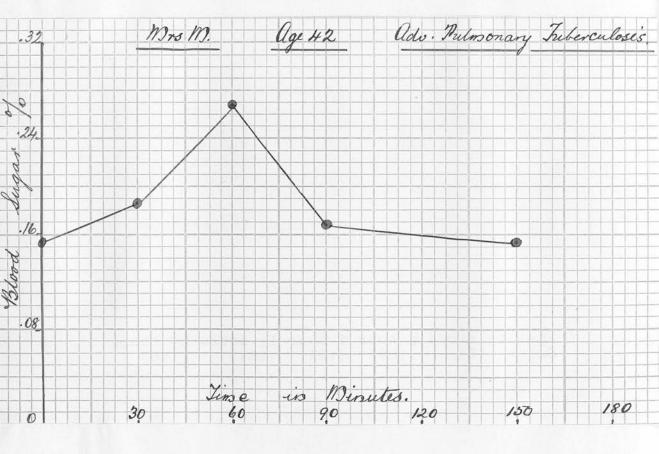


Mrs. S. Age 24 Years. She gave a history of pulmonary tuber-culosis for past three years. When the sugar tolerance test was done the patient was fast losing ground.

Her average evening temperature was 101.6 degrees.

No sugar was passed in the urine.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{2}$ hours $2\frac{1}{2}$ hours Sugar .15% .184% .193% .185% .168%

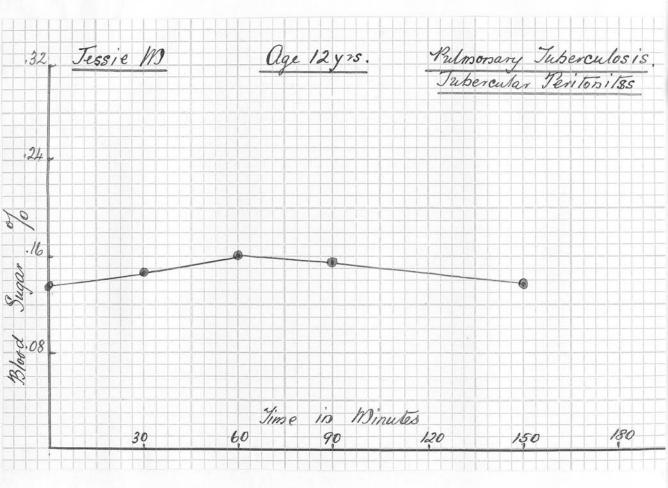


Mrs. M. Age 42 Years. She gave a history of influenza in October, 1918, which left her with a cough. She had a severe haemoptysis in May, 1924, and has gone rapidly downhill since then. Examination showed advanced tubercular infection of both lungs.

The average evening temperature was 100 degrees.

No sugar was passed in the urine.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{2}$ hours $2\frac{1}{2}$ hours Sugar .15% .187% .19% .184% .156%



Jessie M. Age 12 Years. This patient had measles and whooping cough when aged four years. She has never been robust since. Two years ago she was treated for one-and-a-half years at a Sanatorium for tubercular peritonitis. The home conditions were poor and on returning there she began to lose weight and developed a cough.

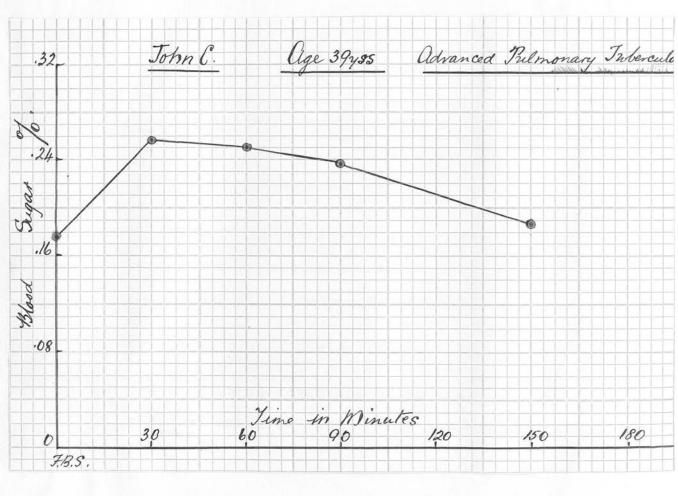
She showed involvement of the basal lobes of both lungs and the abdominal infection was also active with the formation of ascites.

Her general condition was very poor.

Her evening temperature was 99.2 degrees.

No sugar was passed in the urine.

Fasting Blood & hour 1 hour 1 hours 2 hours Sugar .135% .148% .16% .156% .137%



John C. Age 39 Years. This patient's wife had suffered from tuberculosis for four years. She had been nursed at home by him. In February, 1925, three months after his wife's death, he had a haemoptysis.

He showed considerable involvement of both lungs, with loss of appetite, cough, night sweats.

His evening temperature was 99 degrees.

His condition was slowly improving under hospital treatment.

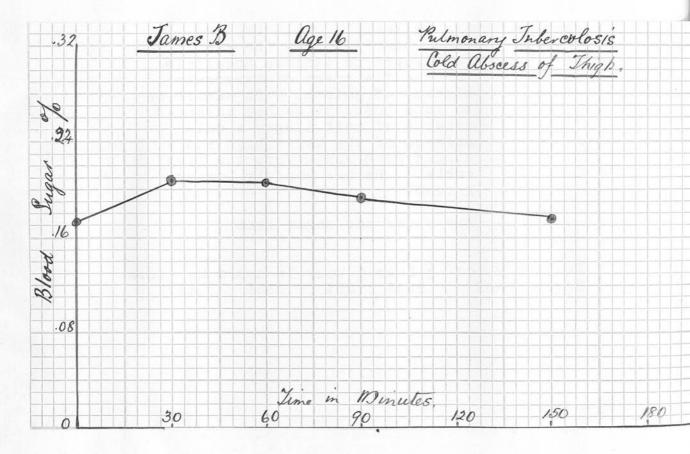
His urine was sugar free.

Fasting Blood & hour 1 hour 1 hours 2 hours Sugar .168% .256% .25% .235% .187%



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James B. Age 16 Years. This boy had spent his life from the age of four years in various hospitals for the treatment of tubercular disease of joints. On admission to this hospital he had advanced disease of both lungs, a cold abscess of the left thigh and a discharging sinus from the right ankle. He was rapidly losing ground.

His urine was sugar free.

Fasting Blood & hour 1 hour 1 hours 2 hours Sugar .168% .266% .25% .195% .187%

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CONCLUSION.— It would appear that in certain cases of tuberculosis there is a hyperglycemia and that the common factor in these cases, of the ten cases of tuberculosis investigated, was the progressive state of the disease.

A sugar tolerance test, therefore, might be of prognostic value in cases of tuberculosis.

V. OLD AGE.- It has been known for some time that the blood sugar percentage tends to rise with advancing age.

Spence (55) in investigating five cases found that only two showed a normal fasting blood, the others lying between .149 per cent and .158 per cent. Four showed a persistent hyperglycemia.

The fasting blood sugar was estimated in ten elderly patients.

No. of Case	Α	ge	F	esting Blood Suga
1.	88	years		.168 per cent
2.	78	11		.093 per cent
3.	82			.137 per cent
4.	74	11		.1 per cent
5.	88	11		.093 per cent
6.	88	Ħ		.15 per cent
7.	70	11		.143 per cent
8.	79	11		.143 per cent
9.	80	11		.112 per cent
10.	85	11		.168 per cent

Average age = 81 years. Average Fasting Blood Sugar = 1.306 per cent

It would appear that the fasting blood sugar level tends to rise with advancing age.

VI. PREGNANCY. Most of the early work done on sugar content of the blood during pregnancy and in the puerperium has been done by foreigners using methods other than Benedict's method.

The chief workers are Schirokauer (5%), Bergsma (58), Benthin (57), Neubauer and Novak (59), Morris (60), Slemons (61). Schiller (62), Killian and Sherwin (63), Guy (64) and Caldwell with others (65), have contributed to the literature more recently. The following table as given by Rowley (68), shows the comparative values as found by these workers:

		PREG- NANCY	STAGE LABOUR	PERIUM	OVALD	IN- FANCY	VALUE IN OP- ERATIVE LABOUR	THETIC	
Bergsma		.09		.09	.11			Chloro-	
Morriss Sedgwick & Zeigler (会)	ė		0.13			0.08	0.17	form	
Schiller Caldwell &		0.10							
Lyle Killian & Sherwin		0.11		0.09		0.09			
buy fuy		0.11				0.07			
Rowley		0.11		0.14	0.09			Ether	

NORMAL FIRST SECOND PUER- CORD EARLY FOETAL

BERGSMA (58) used Frank-Moeckel plasma method which propably gives slightly lower results than Benedict's method. He found a maximum value of .136 per cent and a mean value of .09 per cent during the later months of pregnancy. Blood from the cord had an average blood sugar content of .11 per cent.

The figures given by Morriss (60) show a mean value of .10 per cent during the latter part of pregnancy, the average rangebeing from 0.09 per cent to .11 per cent.

The blood sugar content of the mother's blood at the end of the second stage of labour was .13 per cent and of the umbilical blood was .12 per cent. Morriss' percentage figures show that the foetal blood sugar content is higher than the maternal blood values during pregnancy.

He found that factors causing an increase in the mother's blood sugar value, e.g., prolonged second stage, anaesthesia or operative delivery caused a variation in the value of the foetal blood sugar. The mean cord value in these cases was .17 per cent as compared with .13 per cent in the normal.

SCHILLER (62) found values within the normal range for blood sugar concentration during pregnancy.

KILLIAN and SHERWIN (63) gave an average blood sugar content during pregnancy of .11 per cent.

CALDWELL and LYLE (65) give an average value of .09 per cent at the end of a normal labour.

MORRISS (60) showed that there was a greater blood sugar concentration at the end of labour in primipara than in multipara. He thought that this might be due to the increased voluntary effort and prolonged labour.

McGUIGAN and ROSS (66) STEWART and ROGOFF (67) have shown that anaesthesia is a definite factor in the production of hyperglycemia.

ROWLEY (68) working on fifty-three patients during normal pregnancy found an average blood sugar content of .11 per cent, that is the mean average in normal pregnancy approximates to the upper limit of the general average = 0.09 per cent to .11 per cent. His maximum value was .25 per cent.

The average percentage in twenty-two umbilical cord estimations was .09 per cent.

In thirty-two blood sugar estimations made on the umbilical cord blood the highest was .15 per cent, and here the child was delivered by low forceps, the indications being asphyxia to the child. Ether was the anaesthetic employed.

The post partem calculations were made on the morning of the second day of the puerperium. In twenty-two cases the average blood sugar content in the mother was .14 per cent.

In twenty cases it was possible to obtain consecutive observations on the blood sugar during pregnancy, on the child from the cord blood and on the mother in the second day of the puerperium.

These results he divided into three groups:

- GROUP I. Patients whose blood sugar concentration was augmented during the puerperium.
- GROUP II. Patients whose blood sugar concentration was decreased during the puerperium.
- GROUP III. Patients whose blood sugar concentration remained constant.
- Average blood sugar = .10 per cent

 Average blood post partem = .14 per

 cent.

 Average blood from cord = .08 per

 cent.

These findings agree with those of Morriss, whose mean value was based on the value at the end of labour.

Rowley does not consider that age, parity, change in body weight influence the concentration of sugar in the blood. Reduction of blood volume due to excessive postpartem haemorrhage, or long labour are not altering factors.

He thought that the increase of blood sugar post partem might be due to the rapid loss of weight plus the elimination of fluids from the tissue causing a concentration of the blood sugar values in the body fluids generally, immediately post partem.

GROUP II. Contained four cases where the blood sugar concentration was diminished during the puerperium.

GROUP III. Four cases in which the blood sugar was the same during and after pregnancy. The maternal blood sugar concentration was in all cases higher than the foetal blood sugar content.

In eleven cases there was excessive nausea and vomiting during pregnancy. The average blood sugar content in these cases was .12 per cent.

KILLIAN and SHERWIN (63) also showed a raised blood sugar content (average .13 per cent.) in cases with nephritis toxaemia and .12 per cent. in cases which showed hepatic toxaemia.

SLEMONS (61) found normal values in preeclamptic toxaemia but convulsions give rise to
increased blood sugar percentage. Rowley thinks
that the hyperglycemia of the puerperium is
probably due to metabolic changes associated with
a general process of involution and that the endocrine system shares to some unknown degree in
this.

A study of the fasting blood sugar in advanced pregnancy during labour and in the early and late puerperium was made on fifty-one cases.

The fasting blood sugar was taken as near the end of pregnancy as possible.

The umbilical cord blood was taken after the child had been tied off, and then the mother's blood was taken. The third fasting blood sugar estimation was made on the morning of the second day of the puerperium, and in some cases again

about the fourteenth day of the puerperium, before discharge home.

The patients were kept on carbohydrate free diet, all during labour in the case of multiparae, and from the end of the first stage in primiparae - beef tea, soda-water, tea and coffee without milk or sugar being allowed.

The results are shown in a tabulated form, giving age, parity, weight of child and character of labour, blood lost post partem as given by Rowley (68).

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FURTHER NOTES ON CASES .-

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		Parity				Blood lost		Weight	Health during			ugar Estimation:	
Case	Years	B. 1000, 1774, 1000, 1000, 1001, 1000, 100		2nd e Stage Hrs.		post partem	thetic	of Child in lbs	Pregnancy	Late preg-	- Umbilical cord	L End of Second Stage	l Second day of puerperium
1.	35	2nd	91	1호	45	Normal	-	82	Good	.095%	.139%	.16%	.146%
2.	19	lst	15	11	70	Normal	Chloroform	7-5/16	Good	.086%	.181%	.206%	.106%
3.	39	9th	91	34	10	Normal	-	9-6/16	Good	.112%	.134%	.168%	.106%
4.	35	2nd	7	21/4	30	Normal	Chloroform	91	Asthmatic Attks	.1%	.15%	.16%	.125%
5-	45	13th	Preci	ipitate	5	Normal	_	6홍	Good	.1%	.146%	.177%	.114%
6.	23	lst	121	21/2	10	Normal		68	Good		.153%	.166%	.128%
7.	21	1st	23	54	30	Normal	_	82	Good	.09%	.14%	.176%	.146%
8.	21	1st	5	7	10	Normal	-	6-5/16	Good	.09%	.187%	.24%	.187%
9.	26	2nd	4½	21	10	Normal	Chloroform	8	Good	.09%	.187%	.206%	.186%
10.	36	4th	7	1	20	Normal	_	6 8	Good	.1%	.131%	.131%	.137%
11.	22	1st	9	4	20	Normal	-	8	Good	.1%	.156%	.156%	.133%
12.	24	2nd	18	1 20m.	10 10	Normal Normal	=======================================	67 58	Good Good	.12%	(.134% (.146%	.158%	.187%
13.	42	14th	12	41/2	40	Normal	_	5-13/16	6 "		.162%	.171%	.14%
14.	38	7th	Caesa			Good	Chloroform and Ether		6 " Central Pla- centa praevia	.168%	.157%	.253%	.163%
15	21	1st	29	142	5	Somewhat excessive	-	6-6/16	Good	.114%	.181%	.2%	.1%
16.	23	1st	5	2	15	Normal		6		.1%	.187%	.246%	.134%
17.	32	3rd	4	1	30	Normal		7-10/16	6 "	.112%	.172%	.187%	.134%
18.	38	1st	7	92	1	Normal		6-10/18	6 "	Admitted in labour	.161%	.171%	.164%
19.	25	1st	1.5	21/2	45	Normal	-	5-3/16	3 Premature	Admitted in labour	.143%	.156%	181%

No.of Case	Age in Years	Parity	1st Stage	2nd Stage Hrs.	3rd Stage	Blood lost post partem	Anses- thetic		Health during pregnancy	Late preg-		r Estimations End of Second Stage	Second day puerperium
20	23	1st	8	1날	$4\frac{3}{4}$ hours	s Normal	-	7-7/16	Epileptic Fits	.09%	.181%	.206%	.118%
21	40	2nd	10	3	5 mins	Normal	Chloroform 1/4 hour	7-10/16	Good	-09%	.143%	.143%	.14%
22	33	5th	7	12	10 .	Normal	_	6-6/16	Good	Admitted in labour	.181%	.21%	.137%
23	45	14th	12	9	15	Normal	Chloroform 20 mins.	8-8/16	Good	.1%	.134%	.181%	.118%
24	21	1st	10	$27\frac{3}{4}$	5	Normal	_		Excessive morn- ing sickness - albumen in urine		.14%	.2%	.134%
25	34	3rd	91/2	1	10	Normal	_	6-13/16	Good	Admitted in	.156%	.156%	.175%
26	36	10th	24	23	5	Normal		6-6/16	Good	.09%	.134%	.16%	.2%
27	18	1st	4	1	5	Normal	_	5-3/16	Good	.09%	.162%	.168%	.156%
28	30	2nd	3	1 2	10	Normal	-	6-3/16	Good		.158%	.264%	.131%
29		1st	40	1	15	Normal	_	8	Good	.112%	.112%	.175%	.14%
30	26	1st	30½	23/4	5	Normal	_	7-8/16	Good	In labour	.2%	.256%	.146%
31	25	1st	7	1	10	Normal	_	2-14/16	Good	In labour	.134%	.181%	.146%
32	32	8th	10	200	10	Normal			Wassermann	.1%	.137%	.221%	.14%
33		3rd	11	11	15	Normal	-	8-3/16	positive Good	In labour		.175%	.112%
34	26	1st	11	22	30	Free loss	_	6-12/16	Good		.153%	.153%	.146%
35						Normal			Good	, and the sec. Now the self and you self this sec the	.193%	.225%	.153%
36	26	2nd	8	1	15					And the same has the same and the same than the	.1%	.181%	.131%
37	29	3rd	26	2	10	Normal			Good	.118%	.15%	.16%	.125%
38	26	2nd	734	13	30	Normal		6-9/16	Good	.09%	.175%	.175%	.143%
39	30	2nd	18	1	15	Normal		8-13/16	Good		.109%	.122%	

		Parity				r Blood lost	Anaes-	Weight Health during	Blood Sugar Estimations				
Case	Years		1st Stage	2nd Stage Hrs.	3rd Stage		thetic	of pregnancy Child in lbs			End of Second Stage		
40	44	13th	9	1	5	Normal	_	Wassermann 2-4/16 positive		.112%	.167%	.14%	
41	41	13th	2	2)	15	Free loss	-	8-8/16 "		.125%	.134%	.153%	
42	27	2nd	5	3	15	Free loss	-	6-15/16 "	.1%	.125%	.162%	.131%	
43	38	4th	72	14	25	Normal	_	8 Good	.09%	.156%	.262%	.159%	
44	33	7th	į	ż	15	Normal	-	5-5/16 Good	.1%	.15%	.172%	.162%	
45	44	19th	274	23	20	Normal	-	7-6/16 Good ·	.135%	.172%	.202%	.162%	
46	26	2nd	8	1호	20	Normal	_	6-15/16 "	.09%	.114%	.134%	.14%	
47	33	6th	2½	Ž	20	Normal	-	6-3/16 Good	.115%	.134%	.168%	.14%	
48	26	3rd	21支	20m	10	Normal	-	8-2/16 Good	.1%	.146%	.16%	.146%	
49	26	2nd	6	2	20	Normal		6-14/16 "	In labour	.118%	.162%	.158%	
50	25	1st	15	3	20	Normal	_	7-9/16 Good	In labour	.146%	.181%	.143%	
51	26	3rd	14	2	10	Normal	-	9-3/16 Good	.134%	.134%	.137%	.146%	
		~ ~ ~ ~ ~ ~ ~		(46, 50, 104, 50, 54, 40,									

FURTHER NOTES ON CASES .- Case II .

The chloroform anaesthesia at the end of labour would be a factor in raising the blood sugar. Sugar was passed in the urine for twenty-four hours after labour.

- <u>Case 4.</u> This patient was a chronic asthmatic. Immediately following labour she developed an acute attack which lasted forty-eight hours.
- Case 8. Sugar was passed in the urine for forty-eight hours after labour. She developed a mild B. Coli cystitis and ran a temperature (average evening temperature 99 degrees) for the first four days of the puerperium. This may account for the raised fasting blood sugar value on the second day. On discharge on the fourteenth day her fasting blood sugar was .118%.
- Case 9. This patient also passed sugar in the urine for two days after labour. Her breasts were engorged.
- Case 12. This patient's fasting blood sugar late in pregnancy was one of the highest. She gave birth to twins. The umbilical cord value of the second twin is slightly higher than that of the first. The raised blood sugar on the second day might be the result of the excessive stimulation of the breasts following the nursing of both babies. This patient passed sugar in the urine for three days after labour. The fasting blood sugar on the fourteenth day of the puerperium was .13%.
- Case 14. This patient was admitted with uterine haemorrhage. Examination showed that she was eight-and-a-half months pregnant and that she was bleeding from a central placenta praevia. Caesarian Section was performed four hours after admission. She was a nervous patient, and the thought of an operation upset her considerably. I think that is a factor in raising the fasting blood sugar to .168%. She had excessive post anaesthetic

vomiting and was passing sugar in the urine for five days after the operation. Her fasting blood sugar on discharge was .1%

- Case 15. This patient had a long labour. It was a breech presentation, and the baby was still-born. Readings taken towards the end of the first stage were .114 per cent, and when the membranes ruptured .162 per cent. The absence of stimulation of the breasts might explain the low fasting blood sugar (.1 per cent.) on the second day of the puerperium.
 - Case 16. Blood sugar readings were taken here after the rupture of the membranes and at the end of the second stage. The results were as follows:-
 - (i) At end of first stage .153 per cent.
 (ii) During second stage .187 per cent.
 Later during second stage .2 per cent.
 - Case 17. At the end of the first stage the blood sugar value was .156 per cent.
 - Case 20. This patient was an epileptic and during the ninth month of pregnancy the fits became more frequent and of greater severity. She was treated with luminal and bromides.
 - Case 22. This patient was admitted in the second stage of labour. She had a contracted pelvis and the face was presenting. Her labour was long and difficult.
 - Case 24. This patient was working all day up to the day labour began. She said she felt quite well and was eating well. The second stage was prolonged and a macerated full-time child was born. Immediately following the birth of the child she had a convulsion and on examining a catheter specimen of urine albumen was found to be present. Her urine was clear in two days. The Wassermann Reaction was negative.

- Case 26. This patient had a prolonged labour due to a breech presentation. She passed sugar in her urine for six days after labour. Her fasting blood sugar on discharge on the fourteenth day of the puerperium was .12 per cent.
- Case 28. This patient was passing sugar in her urine for four days after labour. Milk had to be taken off her breasts by breast pump to prevent over-engorgement. This may have been a factor in raising her fasting level on the second day. Her fasting blood sugar on the fourteenth day was .1 per cent.
- Case 30. This was a brow presentation and consequently a long and difficult labour. She was admitted in labour. The value of the blood sugar at the end of the first stage was .2 per cent., at the end of the second stage it was .256 per cent. 1 cc Pituittrin was given after the placenta was delivered, and in half-an-hour the blood sugar value was .231 per cent.
- Case 32. This patient gave a history of three previous miscarriages. The Wassermann Reaction was positive. This may have been a factor in raising the mother's blood sugar at the end of labour to .221 per cent. There was sugar in the urine for twenty-four hours after labour.
- Case 35. Readings were taken in this case during the first stage of labour. The readings were taken, roughly, at intervals of one hour and were:-
 - (i) .156 per cent. (ii) .156 per cent. (iii) .134 per cent. (iv) .146 per cent.

This patient was passing sugar in the urine for three days after labour. On the fourteenth day of the puerperium the fasting blood sugar was .1 per cent.

Case 36. Labour was induced here (see later).

- Case 36. This patient was admitted in labour, the baby being born twenty minutes after admission. This may account for the value and the umbilical value.
- Case 41. This patient had intractable vomiting for five days following labour.
- Case 43. Sugar was passed in the urine in this case for four days. Her fasting blood sugar on the fourteenth day of the puerperium was .12 per cent.
- Case 44. Sugar was passed in the urine for four days after labour. Her breasts were very engorged and as the baby was premature the milk had to be withdrawn by breast pump. Her fasting blood sugar on discharge was .12 per cent.
- Case 45. This patient passed sugar for three days after labour. Her fasting blood sugar on discharge was .1 per cent.

SUMMARY. Taking the average of thirty-five cases the fasting blood sugar in late pregnancy was .0996 per cent. Taking the average of fifty-two cases the average umbilical cord value was .15 per cent. Taking the average of fifty-one cases the value of the mother's blood sugar at the end of the second stage of labour was .18 per cent. Taking the average of fifty-one cases the fasting blood sugar on the second day of the puerperium was .144 per cent.

That is the average fasting blood sugar in late pregnancy is within the upper reaches of the normal value. With the onset of labour there appears to be a rise in the value of the blood sugar up to the end of the second stage of labour. It gradually falls from then (during the puerperium) to its antepartem value.

The increased muscular effort developed during labour, and especially during the second stage, has been suggested as a cause of this hyperglycemia, and that consequently the values found in primiparae are higher than in multiparae. My results do not bear this out.

In one case of precipitate labour the umbilical cord value was .146 per cent. and the mother's value was .177 per cent. The average values in fifteen primiparae are (i) umbilical cord value = .164 per cent; (ii) mother's value = .181 per cent; (iii) second day of the puerperium = .141 per cent.

These values correspond very closely to the average values in the fifty-one cases examined. Muscular effort therefore does not appear to be the only factor in the production of this hyperglycemia.

Excessive blood lost post partem has also suggested the theory that the hyper-glycemia is part of a general concentration of body fluids. There seems to be no relation between the degree of hyperglycemia and the amount of blood lost post partem in my cases.

In reviewing the various theories put forward as to the causation of labour it would appear that any theory must explain the two factors which seem to produce labour (i) a process which gives rise to an alteration in metabolism (ii) a purely mechanical irritation of the uterus which is not accompanied by What the first factor is has such a change. not yet been determined, but it is probably some substance which enters the circulation and profoundly alters the entire metabolism and at the same time stimulates the uterus to Slemons (69) has shown that the contract. output of nitrogen is considerably diminished for twenty-four hours or so before the onset of labour, and that marked diuresis occurs. He has also found that these changes are less marked when labour is induced. Zangemeister (70) too, has shown that during the last three or four days before labour, the woman loses about 1,000 grammes, instead of gaining 50 to 60 grammes daily as she has been doing up to this time. He says it is possible to say when labour will commence by carefully watching the weight.

All the ductless glands exert directly or indirectly a stimulating or retarding effect upon sexual processes in women, which may become greatly exaggerated during pregnancy.

A moderate degree of hypertrophy of the thyroid is a usual concomitant of normal pregnancy, and it may be recognised clinically in 60 to 90 per cent. of cases. Likewise it is admitted that the parathyroids undergo a considerable hypertrophy, and that their secretion is essential to the normal progress of pregnancy, controlling calcium metabolism. It is now definitely known that the cortex of the suprarenal bodies also undergoes definite hypertrophy.

The researches of Stumme (71), Cushing (72), Mayer (73) and others show definitely that the anterior lobe of the pituitary gland regularly undergoes great hypertrophy during pregnancy and that it returns to its normal size after completion. The significance of this is not clear, but it has been suggested that this increased hypophyseal secretion is to supplement a supposed deficiency in that derived from the ovaries.

Wallace (74) suggests that the intolerance of pregnant women for sugar and a transient glycosuria may be attributed to excessive secretion of the gland.

The posterior or infundibular portion of the gland does not hypertrophy but as well as its known effect on the blood pressure its secretion has the power of markedly stimulating uterine contractions. Whether this is normally concerned in the regulation of uterine contractions is not known, although a substance closely allied to imidazolyithylamin, one of the constituents of ergot has been isolated from it.

Reviewing the results of the blood sugar estimations in the fifty-one cases examined by me, it would appear that there is a certain metabolic change during labour and the early puerperium which influences blood sugar concentration and which is probably controlled by the endocrine system. With a view to finding if it is in any way related to an over-secretion of the pituitary gland, which some authorities suggest is the cause of labour, blood sugar estimations were made on a series of cases before and at half-hourly intervals

after 1 c.cm. Pituitrin was given intramuscularly.

The literature shows that the early results obtained were contradictory. Borchardt (75) said that pituitrin causes the blood sugar to rise, and this was denied by Franchivie (76) and reaffirmed by Cushing (77). Stenstrom (78) showed that infundibular extract depressed or inhibited the adrenaline hyperglycemia and glycosuria of rabbits. This was confirmed by Burn (79) who also found that subcutaneous injections of the posterior lobe of the pituitary gland given simultaneously with insulin diminished or abolished the fall of blood sugar produced by the latter. The doses of pituitary extract given alone do not produce a rise of blood sugar sufficient to account for this inhibition. He also showed that this result is not obtained if extracts of the enterior lobe, or of spleen, thyroid, brain tissue or thymus are substituted.

Since commencing my estimations, Lawrence and Hewlett (80) have shown that subcutaneous injections of 1 c.cm. of posterior
lobe extract (pituitrin) have no appreciable
or constant effect on blood sugar in normal
and diabetic subjects, but that these doses
markedly antagonise the effect of insulin on
blood sugar, both in normal and diabetic
subjects. They suggest that the pituitary
gland like the thyroid is one of the most important factors in producing a normal balance
between anabolism and Katabolism, doing so
primarily by its effect on glycogenic function
and carbohydrate metabolism.

Moehling and Ainslee (81) find that injections of posterior pituitary extract produce # a slight rise in the blood sugar in rabbits. They also find its action is antagonistic to insulin, and they consider that the site of action seems to be in the skeletal muscle metabolism.

As before, the patients fasted for four hours, then the fasting blood sugar was calculated. 1 cc "Infundin" (Burrough and Wellcome's Extract of Pituitary) was then injected intramuscularly and the blood sugar estimated

at half-hourly intervals for two hours.

Case 1., This case and Case 2 were chosen because they gave the highest fasting blood sugars in late pregnancy of my series of cases.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{2}$ hours 2 hours Sugar .137% .143% .137% .136% .14%

Labour was not induced but the patient said she felt pains, like labour pains.

Case 2. Mrs. H. Multipara. Full-time pregnancy.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{2}$ hours 2 hours Sugar .15% .143% .150% .131% .14%

Labour was not induced, and the patient felt no uterine pains.

Case 3. Mrs. B. Age 35. Multipara. Full-time.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{2}$ hours 2 hours Sugar .1% .12% .15% .1% .1%

Labour was not induced.

Case 4. Mrs. H. Age 24. Multipara. Full time.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{2}$ hours 2 hours Sugar .09% .1% .1% .09% .1%

Labour was not induced.

Case 5. Mrs. W. Multipara. Full-time pregnancy. This patient was given five doses of Quinine Sulphate grs. X at intervals during the night and five hours after the last dose was given & cc. Pituitrin at half-hourly intervals until 3 cc had been given. The fasting blood sugar was estimated before the first dose of Pituitrin was given.

Fasting Blood & hour 1 hour 2 hours 3 hours Sugar .118% .131% .121% .109% .1%

Uterine contractions were seen and felt and the patient went into labour six hours after the last injection.

Case 6. Mrs. S. Age 21 years. Primipara. Full-time pregnancy. The quinine sulphate and the pituitrin injections were given as in case 3.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{2}$ hours 2 hours Sugar .12% .125% .131% .131% .12%

Uterine contractions were seen and felt and on examination the external os was 12 inches dilated. The pains passed off and she went into labour seven days later.

Case 7. Mrs. F. Age 28 years. Admitted bleeding from a retained placents, following an incomplete abortion ten days previously. The patient's temperature was 100 degrees and she showed signs of toxic absorption, which probably accounted for the raised fasting blood sugar level. In this case 1 cc Pituitrin was given into the triceps muscle.

Fasting Blood & hour 1 hour 12 hours 2 hours Sugar .168% .187% .168% .168% .153%

Case 8. Mrs. W. Age 25 years. Admitted with haemorrhage following an incomplete abortion three days previously. The placenta was retained. 1 cc Pituitrin was given into triceps.

Fasting Blood & hour 1 hour 12 hours 2 hours Sugar .164% .153% .134% .14% .15%

The placenta had to be removed later.

Case 9. Mrs. B. Age 28 years. Admitted with haemorrhage from an inevitable abortion. The first blood sugar value was taken on the patient's admission. She said she had eaten nothing for five hours previously. The raised fasting level may partly be explained by the excitement of admission to hospital. 1 cc Pituitrin was given on admission.

Fasting Blood hour 1 hour Sugar .181% .162% .153%

A three-and-a-half month's foetus with placenta and membranes was passed half-an-hour after the injection of pituitrin. The fasting blood sugar in forty-eight hours was .09 per cent.

Case 10. Mrs. K. Age 25 years.
Primipara. The blood sugar values here were taken four hours after labour was over. 1 cc Pituitrin was given as above.

Fasting Blood & hour 1 hour 2 hours Sugar .193% .181% .166% .153%

On the morning of the second day of the puerperium this patient's fasting blood sugar value was .14 per cent.

Case 11. Mrs. C. Age 35 years. Multipara. The blood sugar values were taken on the first day of the puerperium. 1 cc Pituitrin was given.

Fasting Blood $\frac{1}{2}$ hour 1 hour 1½ hours 2 hours Sugar .158% .16% .150% .158% .15%

The value at the end of the second stage of labour was .2%, the umbilical cord value being .14 per cent.

Case 12. (Two cases of cancer with a hyperglycemia were also examined).

Mrs. P. Age 56 years. This patient was admitted with a carcinoma which had ulcerated through the upper outer quadrant of the left breast.

Her fasting blood sugar value was taken and also after 1 cc Pituitrin at half-hourly intervals.

Fasting Blood $\frac{1}{2}$ hour 1 hour $1\frac{1}{5}$ hours 2 hours Sugar .175% .175% .18% .175% .168%

Case 13. S.W. Age 69 years. This patient had amputation of the right breast performed three months previously for sarcoma. She was re-admitted with a tense growth of the

left breast and ulceration of the operation scar of the right breast.

Fasting Blood & hour 1 hour 1 hours Sugar .185% .18% .18% .175%

SUMMARY. In seven cases of pregnancy four cases in the early puerperium and two cases of cancer with hyperglycemia, 1 cc of Pituitrin given intramuscularly had no appreciable and constant effect on the blood sugar value; That is the hyperglycemia of labour and the puerperium is not due to an over-secretion of the pituitary acting alone. It may be due to its action in conjunction with other ductless glands.

Whether or not involution of the uterus has a direct bearing on the difference in blood sugar concentration is a matter of conjecture. Involution involves many factors. It does not consist simply in a reduction in size of the uterus, but it controls the absorption and elimination of certain products of conception and is accompanied by great vascular and cellular changes in the whole body, together with the establishment of a new function, viz, that of lactation.

CONCLUSIONS. The results of the blood sugar estimations in cancer are inconclusive. It would appear that in certain cases of advanced cancer there is a hyperglycemia. That is that in certain cases, a condition of raised blood sugar percentage is one that does not offer resistance to the growth of the tumour. The effect of pregnancy on cancer is generally considered unfavourable. Apart from the obstruction which tumours may cause to labour there is frequently a rapid extension in the puerperium both locally and by metastases.

Most authors are in favour of the removal of ovarian tumours and of fibroids of the uterus as soon after labour as possible, as there is a tendency for them to become malignant. Could we look upon the hyperglycemia of the puerperium as one of the factors which brings about this change?

The cases of advanced tuberculosis all showed a hyperglycemia and a delayed fall after glucose, of the diabetic type.

Remembering that tuberculosis is a complication of severe cases of diabetes, it would appear that a state of raised blood sugar is one that favours the growth of the tubercle bacillus.

Tubercular toxaemia has a profound influence on sexual organs and their functions. Menstrual disturbances are common in women during the course of the disease and quite often these disturbances are noted before the onset of the evident signs of the disease. In some cases in young girls the appearance of menstruation may stay the progress of the disease.

During the menstrual flow and at times before its appearance there is often an aggravation of the pulmonary condition. Fever may rise, the cough increase, new areas of lung tissue may become invaded and haemoptysis is quite common during this period.

During pregnancy the tubercular process seems to be in abeyance. Perhaps an explanation may be found in the circulatory changes

occurring during pregnancy. The mucous membranes of the respiratory tract become congested during the period of pregnancy, and this may retard the progress of the tuberculous process for the time being. An allied condition is seen in cases of mitral stenosis.

Patients with mild symptoms, which do not progress, suffer no aggravation of the disease as a result of pregnancy, labour or the puerperium.

Patients in whom the disease is active and progressive, that is the emaciated weakly patients and especially those with laryngeal and intestinal complications, frequently succumb after labour. It is an extremely rare thing to see a tubercular woman die with the foctus in utero.

The tubercle bacillus has been found in the placenta in advanced tuberculosis, and it is thought that it gains access to the general circulation through the uterine sinuses, at the separation of the placenta, thus converting a local infection into a systemic one, with fatal results.

Another explanation offered is that with the descent of the disphragm, following labour, the aspiration of tuberculous material from the upper part of the lung to the lower is facilitated. It is doubtful if metastasis takes place in this way. Could an explanation be found in the hyperglycemia which appears to develop with the onset of labour and which lasts through the early days of the puerperium? By furnishing a suitable culture medium for the rapid growth of the tubercle bacillus, the resistance which has been present throughout pregnancy is rapidly lowered. And if this condition of raised blood sugar is beneficial to the growth of the tubercle bacillus, may it not also be for other organisms, e.g., the streptococcus? That is, this hyperglycemia of the puerperium may be a factor in the lowered resistance to infection found during that period, and also a factor in the fatal results so frequently following puerperal fever. No case of puerperal fever occurred while these estimations were being made, so it was not possible to compare the blood sugar percentage with its development.

Lawrence and Hewlett (80) describe unusual and sometimes alarming symptoms which, also described by Sacks (81) followed the injection of 1 cc of pituitrin. In ten to thirty minutes the patients became ghastly pale and some became dizzy and faint. They did not find this followed injection in five diabetics examined.

Pituitrin is used very frequently in obstetrics without the above effect. No case examined by me showed any unpleasant signs or symptoms following the pituitrin injections.

The mechanism which controls the altered metabolism of the puerperium, with its accompanying hyperglycemia, may offer the necessary explanation.

- SUMMARY. (i) Certain of the advanced cases of cancer and particularly those with a superadded infection showed a hyperglycemia and a delayed blood sugar fall of the mild diabetic type following the ingestion of 50 gms. of glucose. In certain cases also, there appeared to be a raised renal threshold for sugar.
- (ii) In advanced tuberculosis the fasting blood sugar is raised, and the sugar tolerance tests show a response similar to that shown by a mild case of diabetes. The renal threshold for sugar is also raised.
- *(iii) The fasting blood sugar tends to rise with advancing age.
- (iv) The fasting blood sugar level in pregnancy is not raised beyond the normal limits. With labour the percentage blood

sugar gradually rises to varying levels up to the end of the second stage. During the early days of the puerperium a hyperglycemia exists. The mechanism controlling this hyperglycemia is not known. It is not due to an excessive secretion of the pituitary gland.

- (v) This hyperglycemia of the puerperium is offered as an explanatory hypothesis of the rapid development of tuberculosis and of the tendency for innocent tumours to become malignant following labour. Also of the lowered resistance to general infections and especially streptococcal infections found during the puerperium.
- (vi) It is also offered as bearing some relationship to the absence of symptoms following repeated injections of pituitrin in pregnant women and women in the puerperium.

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I wish to express my indebtedness to Dr. W.Brander, Medical Superintendent, Hackney Hospital, where this work was carried out, for placing the clinical material in the Hospital at my disposal, and for many helpful suggestions and much interest taken during the course of these investigations.

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