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THE PHYSICAL BASIS OF "BILIOUSNESS" AND "WIND ROUND THE HEART"*

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"BILIOUSNESS" OR A "TOUCH OF LIVER"

Among the commonest conditions of which patients complain is a "touch of liver" or a "bilious attack." As neither is mentioned in most textbooks of medicine, it is natural that a recently qualified doctor should conclude that there is no such thing and should be driven to explain to the sufferer that what he puts down to his liver is really a disorder of his stomach, his bowels, or his nerves. But the patient remains unconvinced, and when next he wakes up with a dull headache, a dirty tongue, no appetite for breakfast, and the conviction that life is not worth living, he will tell his wife that his bad temper is due to his liver, and the doctor be damned. It is a curious fact that there is no equivalent in French or German for the word "liverish" or a "touch of liver," though a bad-tempered Frenchman is said to be "un bilieux." There is also no record of the word "liverish" being used in England before the first quarter of the nineteenth century, and I am inclined to think that it was introduced by soldiers and civilians who came home to nurse their damaged livers in Cheltenham and Bath, as it was in India that the frequency of hepatic abscess first led Army surgeons to recognize the premonitory symptoms of a disordered liver.

I believe that the patient who says he is liverish is often correct, and that functional disorders of the liver are actually far more common than organic diseases. The liver has more ways in which it can be attacked than any other organ. Poisons absorbed from the stomach, intestines, gall-bladder, and spleen reach it in the blood of the portal vein; poisons and organisms in the systemic circulation are conveyed to it by the hepatic artery; infections may ascend the bile ducts from the duodenum, especially in the presence of achlorhydria; and infection may be carried by lymphatics from the wall of the gall-bladder.

Alcohol is the commonest cause of liverishness, but there are many others. The intestinal toxæmia which results from the habitual abuse of purgatives, though never from untreated constipation, and all forms of food poisoning and intestinal infections, such as those with typhoid and various parenteric bacilli and with *Amoeba histolytica*, as well as such general infections as septicaemia and malaria, may injure the liver. With the exception of alcohol and amoebiasis they rarely produce enough damage to give rise to symptoms unless two or more are associated together. But an acute "liver attack" may occur in all these conditions as a result of indulgence in an amount of alcohol which formerly would have had no ill effect, and indiscretions in diet, fatigue, and excitement

are often contributory causes. A patient of mine, a man of 58, found it difficult to decide whether a bad liver attack was too high a price to pay for his sole pleasures in life, betting at race meetings and gambling at Monte Carlo, both of which invariably brought one on even if he drank no more alcohol than usual.

The liver is well provided with means for dealing with toxins and bacteria, but it is not always capable of destroying them when they arrive in excess. The hepatic cells are then damaged and their functional capacity is impaired. The damage in the early stages is not irreparable, and although microscopical examination would doubtless reveal the presence of structural changes, they are at first of a type from which complete recovery can take place. The ordinary clinical methods of physical examination do not give any safe guide to the diagnosis of these early stages of hepatic disorder, but fortunately in the laevulose test we have a means of recognizing them. Our experience of over a thousand cases at New Lodge Clinic in which the possibility of hepatic insufficiency required consideration has led us to regard it as a very reliable test of liver function. We now consider a combined one-hour and two-hour rise in the blood sugar of more than 25 mg. per 100 c.cm. after taking 50 grammes of laevulose as suspicious, and of more than 30 mg. as certain evidence of hepatic insufficiency.

Alcoholic Hepatosis

It is obvious that cirrhosis of the liver is only the last phase of a very long-standing disease, the early stages of which have passed unrecognized. As the condition is one of toxic degeneration rather than inflammation it is more suitably described as hepatosis than hepatitis. Whereas the death rate per million living from cirrhosis of the liver has fallen from 248 in 1902 and 185 in 1912 to 81 in 1922 and 50 in 1932, alcoholic hepatosis is quite common, especially among the well-to-do. The familiar symptoms of "the morning after the night before" are the symptoms of acute alcoholic hepatosis, and the laevulose test shows that definite hepatic insufficiency is present and disappears completely within a few days. Table I shows the results of the laevulose test in five healthy young men on the morning before a "night out" compared with the morning after. In each case there was a greater rise in blood sugar with the second test than with the first, which showed an actual fall in four instances. The rise was greatest in A and B, the only ones who felt any the worse for the experiment.

Habitual over-indulgence leads to a chronic alcoholic hepatosis, which is still capable of complete resolution even if it has been present for many months. It is only when it has continued without intermission for years that irreparable damage is done, but the nodular hyperplasia

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TABLE I.—Blood Sugar in mg. per 100 c.cm. Fasting and One and Two Hours after taking 50 grammes of Laevulose in Five Healthy Young Men, (1) the Morning Before, and (2) the Morning After a "Night Out"

	A	B	C	D	E	Total
(1) Fasting ..	86	80	100	100	94	
1 hour ..	88	71	98	111	111	
2 hours ..	74	64	95	87	105	
Total rise ..	-10	-25	-7	-2	.28	-16
(2) Fasting ..	133	82	69	126	114	
1 hour ..	143	87	63	145	139	
2 hours ..	143	87	71	125	121	
Total rise ..	20	10	-4	18	32	+76

caused by new-formed liver tissue may even then compensate for this more or less completely, although areas of complete necrosis are gradually replaced by fibrous tissue, the first stage of cirrhosis having at last developed.

Over-indulgence in alcohol is a very elastic term, what is excess for any given individual depending upon the vulnerability of his liver cells, which varies greatly in different people. It has nothing to do with his general reaction to the effects of alcohol, as alcoholic hepatitis is not often associated with alcoholic psychoses or peripheral neuritis. The premonitory symptoms of cirrhosis are mainly hepatic in origin, though chronic oesophagitis and, less frequently, chronic gastritis may contribute to them; but the latter is not necessarily present, a normal curve of acidity without any excess of mucus being often obtained with a fractional test meal.

Young men and girls who indulge in cocktails three or four times a week may develop alcoholic hepatitis. Their anxious parents are apt to ascribe their sallow complexions, loss of appetite, mental torpor, and irritability to incipient consumption or other serious disease, but the well-marked hepatic insufficiency disclosed by the laevulose test and the tender and often slightly enlarged liver reveal the true nature of their malady. Complete recovery with disappearance of liver tenderness and return to a normal response to the laevulose test quickly follows a period of rest with a light diet and abstention from alcohol.

Table II gives some examples of the results of the laevulose test in alcoholic hepatitis before and after treatment. Patient No. 6 had drunk a bottle of champagne a day for twenty years, and was so ill that he was thought to be dying from some obscure abdominal complaint. His liver was large, hard, and very tender. After three months on a strict diet his liver was no longer palpable, and he returned home feeling perfectly fit and able to play tennis and golf for the first time for five years. No. 7 had been drinking from one to three bottles of whisky a day for over a year, and also recovered completely.

The tender liver often aches, and a man "with a liver" has generally a fairly accurate knowledge of its surface anatomy. He is never jaundiced, and latent jaundice, as shown by a positive indirect van den Bergh reaction, is uncommon; when present it disappears as rapidly as the abnormal response to the laevulose test.

In early cases, after a short period of strict treatment, it is only necessary to forbid alcohol in any form between meals, when it is rapidly absorbed and reaches the liver in a comparatively concentrated form. But in more advanced and chronic cases it is useless to advise anything short of complete and permanent abstinence. This advice is easier to follow than might be expected, as the patients are never dipsomaniacs and have no uncontrollable urge

TABLE II.—Laevulose Tolerance Test in Alcoholic Hepatitis Before and After Treatment

Case	Sex and Age	Interval between Observations	Rise of Blood Sugar above Fasting Level in mg. per 100 c.cm. after taking 50 grammes Laevulose		
			1 hr. after	2 hrs. after	Combined 1 and 2 hrs.
1	F, 22	22 days	51 23	15 10	66 33
2	M, 32	32 "	45 6	80 30	134 36
3	F, 56	9 "	44 16	49 18	93 34
4	M, 49	9 "	44 15	7 -15	51 0
5	M, 56	20 "	49 13	0 -11	49 2
6	M, 52	3 months	73 0	71 -13	144 -13
7	M, 45	6 weeks	58 10	31 -6	89 4
8	M, 40	24 days	51 12	15 -22	66 -10

to drink. They drink for conviviality and because they like it or find it difficult to complete a business deal without celebrating it with a drink. A badly damaged liver is abnormally vulnerable to such toxins as alcohol, and even a small dose is poisonous. But more important is the psychological fact that with his first drink a man's judgment is impaired, and though he may have intended to take no more he will have a second and a third, and so on *ad infinitum*. He is only safe when teetotal.

Amoebic Hepatitis

In 1923 Lieutenant-Colonel Gordon Covell published in the *Guy's Hospital Reports* a paper in which he showed that amoebic dysentery was always accompanied by hepatic insufficiency as measured by the laevulose test, even in the complete absence of symptoms pointing to disorder of the liver. Since that time we have always performed the laevulose test in the many patients who, on returning home after long residence in the East, complain of general unfitness in the absence of any obvious organic disease. They look pale and sallow, though they are neither anaemic nor jaundiced and van den Bergh's reaction is generally negative. They have frequent liver attacks—headache with a dirty tongue, anorexia, discomfort in the region of the liver, and constipation or alternating constipation and diarrhoea. The liver is often slightly enlarged and tender, and the laevulose test shows that hepatic insufficiency is present. Though alcohol and various infections may have contributed to this result the condition is mainly due to a mild chronic form of amoebic hepatitis. The patient may have had definite attacks of dysentery, but more frequently he has had nothing else than an occasional attack of diarrhoea, and sometimes not even that, yet the caecum and ascending colon are often tender, and the appendix has generally been removed for "chronic appendicitis" without benefit. It is remarkable that this condition, which never leads to abscess formation, can persist for several years after returning to England and yet be amenable to treatment. It often remains unrecognized owing to too much reliance being placed on the presence of cysts of *Entamoeba histolytica* in the stools as essential evidence of the existence of amoebiasis.

Complete recovery follows a dozen injections of 1 grain of emetine. The patient not only loses his symptoms but the liver ceases to be palpable and the laevulose test

shows that the hepatic insufficiency has disappeared (Table III). To avoid the risk of recurrence a second series of six injections of emetine should be given at the end of three months and then every six months for a couple of years.

TABLE III.—*Laevulose Tolerance Test in Amoebic Hepatitis Before and After Treatment with Emetine*

Case	Sex and Age		Rise of Blood Sugar above Fasting Level in mg. per 100 c.cm.		
			1 hr. after	2 hrs. after	Combined 1 and 2 hrs.
1	F, 53	Before treatment ..	71	31	102
		After treatment ..	16	18	34
2	F, 40	Before treatment ..	55	30	85
		After treatment ..	6	0	6
3	F, 33	Before treatment ..	34	14	48
		After treatment ..	18	-2	16

Bilious Attacks and Migraine

What is called a bilious attack in a child is in most cases the equivalent of migraine in an adult. One or other parent is often a sufferer from migraine, and the child is likely to develop it when he grows up. The term "bilious attack" is apparently derived from a misinterpretation of the fact that it often terminates with bilious vomiting. There does, however, appear to be some obscure connexion between the liver and migraine in a proportion of cases in both children and adults (Hunt, 1933). We have never found any sign of hepatic insufficiency as shown by the laevulose test, and van den Bergh's test is negative both during and between the attacks. But when in the course of our investigations we aspirated a specimen of bile through Einhorn's tube after making the gall-bladder and bile ducts evacuate their contents by injecting magnesium sulphate into the duodenum, a number of adult patients asked to have the process repeated, as they felt clearer in their heads and altogether less "bilious" than they had done for months. In these cases the gall-bladder was often found to be tender, especially shortly before and during an attack. It is apparently the mechanical effect of unloading the liver of accumulated bile which has this unexpected result, as in every case the bile was quite normal and there was

diseases of the gall-bladder, and although there does not appear to be any special liability to cholelithiasis among the migrainous, it seems not improbable that a disordered liver may be one factor in the complicated pathogenesis of migraine.

"WIND ROUND THE HEART"

Aerophagy

There is no physical basis for the wind which troubles most people who complain about it; it is on their brains, and neither in their stomachs nor round their hearts. Nearly thirty years ago I described experiments which showed that the only adequate stimulus to the sensory nerves of the alimentary tract is tension on the fibres of its muscular coat (Hurst, 1911). A slight increase gives rise to the sensation of fullness and a greater rise to pain. The tension depends upon the postural tone of the muscle fibres and the volume of the contents of the segment concerned. A sensation of fullness and pain may result from increased tone of the muscles with no change in the contents, or upon increase in the volume of the contents with constant tone. The sensation of fullness or pain can be relieved when some or all of the contents consist of gas, which can be evacuated by belching from the stomach or as flatus from the colon. Everybody has had experience of gaining relief in these ways, and consequently the average person is inclined to ascribe a sensation of fullness in the stomach or colon to wind, although in most cases it is due to other causes. Success confirms his suspicion, but instead of accounting failure to a wrong diagnosis he assumes that wind is present but cannot be expelled. In his futile attempts to eructate he swallows air until enough is present in his stomach to be easily and loudly evacuated (Fig. 1). The relief which follows is partly psychological and partly due to the fall in intragastric tension. As the discomfort which initiated the aerophagy is often due to achalasia or spasm of the pyloric sphincter, the primary discomfort may be overcome, as the further rise in intragastric pressure resulting from the aerophagy may be sufficient to force the pylorus as well as the cardia (Fig. 1d). Sodium bicarbonate gives relief in precisely the same way as aerophagy: carbon dioxide is evolved

FIG. 1.—Drawings to illustrate the relief of intragastric tension by aerophagy.

no evidence of coexisting cholecystitis or gall-stones. Such patients derive benefit from stimulation of biliary drainage by means of Epsom salts and olive oil. The former should be given in concentrated solution fasting every morning, the dose being the largest which can be taken without causing looseness, and a tablespoonful of the latter should be taken three times a day half an hour before meals.

A large proportion of sufferers from migraine know from experience that fatty food induces an attack, and among those who have not discovered this for themselves it is common to find that the exclusion of eggs, cream, fat meat, fried food, and chocolates helps to prevent migraine. It is interesting to observe that these are just the cholesterol-rich foods which frequently upset patients with

by the action of the acid gastric juice, and the increased tension in the stomach forces gas through the cardia and fluid through the pylorus. In both cases the patient brings up gas, and it is difficult to convince him that this is not the product of fermentation in his stomach. But owing to the inhibiting action of free acid on bacterial activity and the continuous passage of food into the duodenum fermentation cannot occur; we have found that even in complete achlorhydria very little gas is produced by fermentation unless pyloric obstruction is also present.

Neurotic patients may get so much satisfaction from belching wind with a resounding noise that they continue to swallow air, and the whole process is repeated again and again. Eventually attacks of aerophagy occur with-

out any preceding epigastric discomfort, the condition then having all the characteristics of a tic. The action, though originally serving a useful purpose, no longer does so; its repetition depends upon the subconscious gratification which it gives to the patient, who is able to restrain it by an effort of will, but after a short time gives way to an overwhelming impulse to continue, though often ashamed of his weakness.

Aerophagy can be cured by explaining the true cause of the "flatulence" in language suited to the patient's intelligence. He is instructed to make no voluntary effort to eructate, however much he may desire to do so. At the same time an attempt must be made to discover and relieve the primary cause of the discomfort which led to the aerophagy, whether this is some form of functional dyspepsia or of organic disease, such as gastritis, ulcer, or cholecystitis.

Intestinal Carbohydrate Dyspepsia

The most common cause of intestinal flatulence is carbohydrate dyspepsia (Hurst and Knott, 1931). The envelopes of root vegetables are softened but unbroken by cooking. Under normal conditions amylase of the pancreatic juice penetrates the envelope in the small intestine and converts the starch into soluble sugars, which diffuse into the surrounding media and are absorbed. When owing to abnormally rapid passage through the small intestine some of the starch reaches the caecum the same thing happens there. But whereas in the relatively sterile small intestine very little undergoes fermentation, in the caecum and ascending colon bacteria are so active that fermentation occurs before the sugar has time to be absorbed. Gases and organic acids are produced, the former causing colonic distension and discomfort, and the latter, if in great excess, irritating the mucous membrane sufficiently to cause diarrhoea. The stools are acid, contain many starch granules, and produce much gas on incubation. During the day the gas collects in the splenic flexure and causes discomfort, which is often mistaken by the patient for gastric flatulence and so gives rise to aerophagy. During the night, when the splenic flexure is no higher than the pelvic colon and rectum, the gas moves onwards, and the discomfort in the lower abdomen is often enough to interfere with sleep until relief is obtained by the passage of odourless flatus. Intestinal carbohydrate dyspepsia can be controlled by giving a diet containing no root vegetables or rice; in severe cases the use of other starchy foods must also be limited. As there is no deficiency of amylase the administration of vegetable diastase is useless. The number of enterococci in the stools is increased owing to the excess of carbohydrate in the colon acting as an excellent culture medium; the intestinal flora return to normal when the condition is relieved by dieting. It is obvious that nothing could be more futile than treating cases of this kind by vaccination with the patient's enterococci or by intestinal lavage, though many patients receive such treatment owing to failure to look for starch in the stools and to see whether fermentation occurs on incubation.

Eventration of the Diaphragm

In certain conditions gas accumulates in the stomach or the colon immediately beneath the diaphragm under excessive tension, with the result that the left dome is displaced upwards into the thorax, so that it is higher than the right dome and may even give rise to dextrocardia. Eventration of the diaphragm produced in this way is very much commoner than that resulting from congenital atrophy of its musculature, for which the name has generally been reserved.

(a) AÉROGASTRIE BLOQUÉE

The gas bubble seen with the x rays under the diaphragm is derived from air swallowed with each mouthful of food and drink. It is permanently absent only in achalasia of the cardia, in which the contents of the dilated oesophagus act as a lock, preventing the passage of swallowed air (Fig. 2). Excess is normally removed

FIG. 2.—Achalasia of the cardia, showing absence of gastric air bubble owing to lock formed by food and saliva permanently filling the lower six inches of the dilated oesophagus.

by unconscious silent eructation in the day and through the pylorus at night, when the horizontal posture makes this possible. In rare cases eructation is prevented by spasm of the lower end of the oesophagus just above the sphincter owing to the presence of a simple oesophageal ulcer (Hurst, 1934a). Enormous quantities of gas collect in the stomach and may cause intense pain, increased each time any food or saliva is swallowed owing to its admixture with air. Failure to recognize the true nature of the condition may have a deplorable effect upon the patient's nervous system. This was the case in a man of 76, who had suffered from "gas pains" since 1926. In 1929 and again in December, 1931, he had a small haematemesis; on both occasions he was x-rayed, but nothing beyond excess of gas in his stomach was discovered. Early in 1932 he noticed that when he swallowed there appeared to be an obstruction at the entrance into his stomach, as the passage seemed to "shut up" in a painful spasm whenever food reached it, this being followed by regurgitation of the food with excess of mucus. An x-ray examination again showed no abnormality, except an enormous gas bubble in the stomach, which caused the left half of the diaphragm to be elevated above the right (Fig. 3). He was regarded as hysterical and was treated by various forms of psychotherapy on the Continent, in America, and in England, but without success. His condition became progressively worse, and when I first saw him in January, 1932, he was intensely depressed and was terrified at the mere idea of eating. When a meal was brought into the room his face became anxious and his hands shook. Several minutes elapsed before he could persuade himself to lift the fork in his trembling hands to his lips, and he masticated much more than was necessary in order to put off the moment of swallowing as long as possible. He had lost much weight and strength. As it seemed impossible that such severe dysphagia could be purely nervous in origin, especially in view of the history of haematemesis, a further radiological examination was made, and Dr. P. J. Briggs succeeded in demonstrating the presence of a deep chronic ulcer just above the cardiac sphincter (Fig. 4). The enormous gas bubble in the stomach was clearly a result of the oesophageal spasm caused by the ulcer interfering with the escape of swallowed air upwards, just as it interfered with the passage of food downwards. He was treated with a diet of citrated milk and with atropine, and rapidly lost his pain and dysphagia; he became comparatively happy, but the physical signs of fear which

occurred when food was brought into his room persisted in a lesser degree after the disappearance of the associated emotion, presumably as a result of a conditioned reflex. The ulcer became much smaller, but after many

FIG. 3.—Man aged 76 with eventration of diaphragm caused by aërogastric bloqué secondary to oesophageal ulcer.

FIG. 4.—Same case as Fig. 3 after taking opaque fluid whilst in horizontal position to show ulcer.

weeks it had not healed owing to the development of cicatricial narrowing, and eventually a gastrostomy was performed. This resulted in complete healing with disappearance of the occult blood from the stools. The cicatrization of the ulcer led to almost complete obstruc-

tion; this would probably have been overcome by gradual dilatation had he not developed a rapidly fatal attack of acute mania.

A similar condition of aërogastric bloqué may result from dislocation of the cardia, which is generally caused by excess of gas in the neighbouring splenic flexure. The excess of gas escapes from the stomach when it can reach the pylorus on assuming the horizontal position. In the morning no excess is present, but with each meal the quantity increases until the afternoon, when the accumulation produces a rise of pressure sufficient to cause pain, the diaphragm at the same time being displaced into the thorax. Immediate relief follows the passage of a stomach tube. One patient with this condition had learnt to lie down at 3 p.m. every day when the pain was at its height (Figs. 5 and 6). In half an hour he was com-

FIG. 5.—Man aged 48 with eventration of diaphragm caused by aërogastric bloqué. Erect position.

fortable, as the gas had passed into his small intestine, and after another hour he evacuated some of it per anum, but enough remained in his splenic flexure to maintain the dislocation of his cardia. Permanent relief occurred only after he had evacuated the gas from his stomach by a tube at 3 p.m. every day for a week, so that no excess passed through his pylorus to collect in the colon.

FIG. 6.—Same case as Fig. 5 in horizontal position, with gas escaping into duodenum and disappearance of eventration.

(b) MEGACOLON AND AÉROCOLIE BLOQUÉE

Megacolon is the result of interference with the normal neuromuscular mechanism controlling the last stage of the act of defaecation, in which the passage of faeces from the pelvic colon into the rectum causes the latter to contract and the sphincter ani to relax. When owing to degeneration of Auerbach's plexus or other causes the sphincter does not relax (achalasia), faeces and gas are retained, and the rectum and especially the more thin-walled pelvic colon become progressively dilated (Hurst, 1934b). The pelvic colon finally forms a huge loop, which reaches the left and occasionally the right dome of the diaphragm. Megacolon is the commonest cause of eventration of the diaphragm. I have seen thirty-five cases in private practice—twenty-four in males and eleven in females, including four boys and one girl (so-called Hirschsprung's disease)—compared with two cases caused

by congenital atrophy of the diaphragm and four cases of *aérogastrie bloquée*. It is remarkable how trivial the symptoms of megacolon may be, the condition often being recognized by the discovery of an enormous gas-containing loop of pelvic colon under the diaphragm in the course of a radiological examination of a patient suffering from nothing more serious than chronic constipation. In a minority of cases recurrent attacks of severe pain from partial volvulus of the dilated pelvic colon occur. Gradual dilatation of the anal sphincter and complete evacuation

FIG. 7.—Woman aged 43. Megacolon showing collection of gas in greatly dilated loop of pelvic colon reaching both domes of the diaphragm.

FIG. 8.—Same case as Fig. 7, after escape of gas under high pressure through tube passed per anum, showing descent of diaphragm from the level of the ninth to that of the eleventh vertebra.

of the colon generally result in complete and permanent relief, although the pelvic colon remains abnormally distensible. In exceptional cases a partial twist of the uppermost part of the pelvic colon prevents the escape of the accumulated gas and painful attacks of partial volvulus may continue. It is sometimes possible to evacuate the air-lock by means of a tube (Figs. 7 and 8). In other cases it may be necessary to excise the volvulus during a quiescent period. I have never found it necessary to advise sympathectomy.

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OUTPUT OF PROLAN A IN URINE IN CERTAIN EXTRAGENITAL CONDITIONS

REPORT OF AN INVESTIGATION

BY

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It is now a well-established fact that in certain tumour conditions of the male and female genital organs the excretion of prolan A in urine is in excess. In the literature the reports in connexion with the relation of prolan excretion to hydatidiform mole and chorionic epithelioma of the uterus on the one hand, and to teratoma and chorionic epithelioma of the testis on the other, are so extensive, and have been so well summarized by Hamburger (1933), that only a few references which bear directly on this investigation will be mentioned. Since Hamburger's publication many workers have found increased prolan A output in the above conditions—for example, Ferguson (1933), Cutler and Owen (1935), and others.

Earlier Investigations

Ferguson carried out numerous quantitative investigations on urinary prolan A excretion in cases of teratomatous testicular tumours, and it is his technique which has been employed in this investigation. He found that 50 to 50,000 mouse units of prolan A per litre of urine were excreted, the amount varying with the embryonal character of the tumour, the extent of the disease, and the status as regards treatment. His work appears to show that the prolan A estimation has a definite clinical value in the diagnosis and prognosis of these cases.

The work recorded in connexion with secondary sex organs and pituitary adenomas is not so extensive as that which has been carried out on the primary sex organs, and the results are not conclusive. In connexion with breast tumours, Engel (1930) and Saphir (1934) investigated a few cases of breast cancer and obtained no positive results. Zondek (1932) and Baudler (1935), however, obtained varying results in patients with similar lesions, some giving a positive and others a negative prolan A reaction. More recently Taylor (1936), dealing with fourteen cases of non-malignant lesions of the breast, found that in three cases of nipple secretion there was a slight increase in the amount of prolan A excreted in the urine. With regard to pituitary tumours Love (1932) reports a case of an adenoma of the pituitary gland in a male which gave a positive Aschheim-Zondek reaction three times as strong as that normally expected in the urine of a pregnant woman. On the other hand, Watts (1932) found no gonadotropic hormone in blood or urine in fourteen cases of pituitary chromophobe and eosinophil adenomas.

I have been unable to discover any record of work on the urinary prolan A content in cases of ordinary prostatic enlargement. The investigations of Burrows (1935), however, appear to have an indirect relation to this subject. He has shown that the effect on the prostate of the mouse of treatment with oestrogenic compounds, which normally are liberated as the result of the action of prolan A, is to produce histological changes resembling in many ways those of benign enlargement in man.

The Present Investigation

The Aschheim-Zondek test is of such generally recognized value in pregnancy and in the somewhat related conditions of chorionic epithelioma and teratoma testis that the paucity of information in this connexion in