success to exterminate the mosquitos in some malarial regions.

I would urge, then, that at the present time, when after all these years of labour no causative agent of malignant growth in general has with certainty been determined, that line of research which promises surer results and greater profit on the part of clinicians as well as of laboratory investigators, lies in the direction of testing various methods of arresting the growth of the tumour cells without injury to the organism in general. Herein it seems to me that Coley has chosen the better part. But over and above all I cannot but feel that the greatest benefit to the patient, the greatest triumph and satisfaction to the practitioner, will for yet some years to come be the recognition and successful removal of malignant tumours at the earliest possible date. Aye, and what is more, the removal of benign tumours in general before they have taken on possible malignant characters.

I wish I could be more optimistic, for optimism is good and healthy, but the above deductions are the necessary outcome of the considerations put before you this evening. As to the theory here put forward, I am quite prepared to find that many will find at first difficulty in grasping it, but when grasped, I cannot but believe most firmly, it will be found to include and to explain the largest number of individual cases—that it will be found to satisfy the conditions of sound theory.

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ON THE OCCURRENCE OF PYREXIA IN CANCER AND OTHER DISEASES OF THE LIVER, AND IN CASES OF GALL STONE.

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THE general attitude to the question of the state of the temperature in cancer of the liver has probably to a large extent been determined, either directly or indirectly, by the statements in Murchison's well-known book on *Diseases of the Liver* and by the parallel passage in Wunderlich's elaborate work on *Medical Thermometry*. According to Murchison "in cancer, unless there be some inflammatory complication, the bodily temperature is at or about the normal standard, and accordingly in the case of an obscure internal disease a continuous elevation of the temperature would in itself be opposed to the diagnosis of cancer." He mentions as quite exceptional events two cases which departed from this rule. In one, the average morning record for the six days before death was 99.3° (maximum 101.1°) and the average evening record 101.6° (maximum 103°), this condition of the temperature, together with other circumstances, inclining the diagnosis in the direction of pyæmic inflammation. The second case is simply noted as one of "primary uncomplicated cancer of the liver with a temperature of 102°." Wunderlich's opinion is that "it is a peculiarity of cancer cases that elevated temperatures are comparatively rare and that the temperature generally maintains itself on a normal or subnormal plane, which, however, by no means precludes

the occurrence of high temperatures through intercurrent complications or at the close of the disease; but fever temperatures of long duration are at least rare in cancer patients."

Some other authorities may also be quoted on this point. Harley says: "All signs and symptoms of pyrexia are in cases of non-complicated cancer of the liver totally absent."

Hilton Fagge: "There is sometimes slight pyrexia (100° or 101° and in one case [Pye-Smith] 104.6°) for which no other cause can be found after death."

Budd: "When the tumours grow rapidly some degree of fever is set up."

Ferichs: "Progress however is never completely uniform.....periods during which the tumours grow rapidly, the pains increase and fever shows itself, are followed by others in which the morbid growth is quiescent or retrogrades"; and

Oslor: "In all rapidly-growing large neoplasms of the liver there is more or less fever, usually continuous and not reaching a high grade."

With one exception these authorities may be quoted to show that, whatever be the explanation, pyrexia more or less extreme is an event which may undoubtedly appear in the course of a case of hepatic cancer. In reference to the phrase cases of "non-complicated cancer of the liver," which is used by several authorities, it may be remarked that whilst the suggested limitation may be of importance to the issue in an academic discussion, it is of little value from the practical and clinical point of view unless the existence of "complications" can be definitely and confidently determined. And it is notorious that as a matter of fact this is not the case. Not only, as stated above and as will also appear in the sequel, are there cases of cancer with accompanying pyrexia in which no complication can be discovered after death, but it is common to find in the neighbourhood of a cancerous liver inflammatory changes of the existence of which during life there was an entire absence of specific evidence. Further, there is the fact that the occurrence of such inflammatory changes in conditions other than cancer—as, for example, from the irritation due to a long-impacted gall stone—produces in the examination of the patient facts which are the very crux of the physical diagnosis. The problem at the bedside is not, Does cancer pure and simple cause pyrexia? but rather, What is the interpretation of the physical facts in this case, and what bearing has the state of the temperature on the diagnosis? If the physician is able to say the case is one of cancer, it is of little practical moment whether he believes any existent pyrexia to be due to "complications," or to be a direct result of the malignant process. There is not in the circumstances just suggested any diagnostic difficulty. Such difficulty arises when—and it is not an exceptional experience—the physical facts are of doubtful interpretation, and the weight and bearing of the other features of the case, including the state of the temperature, have to be carefully reviewed and estimated.

The clinical question in short is not, Is the case one of cancer with or without complications? but, Is the case one of cancer at all? And it is the not infrequent ambiguity of the physical facts in cases of hepatic disease which raises to a level of high importance the study of the value and significance of the symptomatic and general evidence in these cases. Of course if it is true, as it undoubtedly is, that a considerable degree of pyrexia may attend cancer of the liver, the clinical distinction of that disease from impacted gall stone, abscess, and other hepatic conditions in which febrile disturbances more or less frequently occur, is not facilitated. But the recognition of this clinical truth may at least save the physician from an inclination to place undue stress upon the existence of pyrexia as a reason for excluding cancer from the diagnosis.

The facts as to temperature in some cases of cancer of the liver are displayed in the following charts. In Case III there was no necropsy, but in the other instances the diagnosis was confirmed by *post-mortem* examination.

CASE I.—The patient was a man, aged 48. His illness commenced two months before the date of the chart with "attacks of cold and shivering," after which he became jaundiced; there were no rigors under observation. The physical facts were highly suggestive. Towards the end fluid accumulated in the cavity of the peritoneum and there was œdema of the lower limbs. The necropsy showed numerous carcinomatous tumours in the liver. On the surface of one of these was a red hæmorrhagic area with a brown coagulum in the neighbourhood, and the peritoneal cavity contained a large quantity of blood, some manifestly recent, some old, which weighed several pounds. The occurrence of hæmorrhage within the cavity of the peritoneum is of interest.

Chart 1.

Murchison speaks of this as "a rare mode of fatal termination of cancer of the liver" and records one case. Frerichs also records a case in which the abdomen contained about 12 lbs. of blood, and figures the liver with two cancerous nodules which had perforated the peritoneum in the form of soft cauliflower excrescences, which were covered with recent blood coagula. In Murchison's patient death occurred somewhat suddenly; in Frerichs's case the hæmorrhage probably commenced about three days before death; whilst in the instance above recorded the condition of the clots showed that the hæmorrhage had been a much more chronic process. It may well have extended over the last fortnight when, it will be observed, the temperatures were for the most part subnormal.

Chart 2.

CASE II.—The diagnosis in this case was very obscure, and subphrenic abscess, abscess of the liver, and cancer of the liver, were all discussed. In consequence of the physical facts existing in the right chest, para-

Chart 3.

Chart 4.

centesis was performed, on the first occasion with negative results, and on the second with the withdrawal of a large quantity of a creamy fluid. This was proved after death to have come from a large cancerous cyst, which, growing from the upper surface of the right lobe of the liver, had pushed up the diaphragm and compressed the lung. Though the patient had not complained of gastric symptoms, there was a malignant ulcer in the wall of the stomach. The temperature was a confusing element in the diagnosis.

CASE III.—In this case there was little or no doubt about the diagnosis, and the patient died some six weeks after leaving the hospital. The degree of fever is but slight, yet the chart is not without interest on account of the tendency, more marked in the earlier records, to a decided rise of the temperature in the evening.

CASE IV.—The patient was a man of 56 years. He had been gradually losing strength and flesh for six months, and had occasionally vomited. Jaundice had been present for four months, and was very pronounced. At no time had pain been a feature of the case. The liver was moderately enlarged, and there was evidence of distension of the gall bladder. As the chart shows, the patient suffered from a series of brief intermittent pyrexial attacks, each of the most severe being preceded by a rigor. The jaundice was extreme, the skin being of a deep olive tint. At the post-mortem examination a malignant ulcer, about 1½ inch in diameter, was found in the duodenum. About the centre of the ulcer was the opening of the common bile duct, which was greatly dilated. The cystic duct was blocked by a mass of tumour tissue, and the gall bladder was distended with a quantity of milky-looking fluid, which under the microscope showed numerous fat globules and leucocytes. Scattered throughout the liver were numerous small, softening, cancerous nodules, and a mass of enlarged and indurated glands was adherent to the duodenum.

In this case it is not the mere occurrence of pyrexia which is of chief interest, but rather the course and character of the pyrexia, and the fact that on many occasions each of the sharp, short-lived outbreaks of fever was preceded by a severe rigor. And the interest has a marked practical aspect when it is recollected that pyrexial disturbances of exactly this character, and with identical attendants, are often to be recognised in cases of impacted gall stone (see Chart 5); that cancer and gall stone each frequently causes jaundice and pain; that, as already suggested, the physical evidences in cancer are frequently non-characteristic; and that an impacted gall stone, by producing hepatic congestion with peritoneal thickening and matting together of neighbouring tissues, may be attended by physical signs which are ambiguous or misleading (see Case v). In this connection it is of importance to observe the complete absence of pain from the above case, and the value of this fact in the exclusion of gall stone from the diagnosis. The fact that the gall bladder was distended also pointed to malignant disease, the association of jaundice with such distension being in Mayo Robson's very special experience significant of the more serious malady.

The same author also lays down the rule that the "absence of ague-like attacks" favours a diagnosis of malignant disease. It is well to note that this statement does not imply that the presence of such attacks is conclusively in favour of gall stone. The above case shows that such a proposition could not be sustained, and among Mayo Robson's records there are several instances in which jaundice due to malignant disease was associated with rigors, intermittent fever, and ague-like seizures.

In Murchison's list there is a case (CXLII) almost identical with the one just recorded, and here also in the later stages there were rigors, pyrexia, and sweatings. Rather curiously, too, in view of what is stated above, there were physical signs which were regarded as due to a dilated gall bladder, but which were found after death to be caused by a malignant tumour that "occupied the situation of the gall bladder, but was unconnected with it, having originated in the coats of the duodenum." Though not strictly to the present purpose, it is difficult to avoid remarking that in this case jaundice, which had existed for nine months, almost entirely disappeared two months before death. This very unusual occurrence in jaundice from malignant disease appears to have been due to sloughing of the tumour which had previously blocked the orifice of the common duct. On this point a very important remark is made by Mayo Robson—namely, that jaundice in cancer may be due to catarrh of the biliary passages, and so may be relieved by treatment, without, of course, any benefit to the original disease. Considering that in a balanced diagnosis between gall stone and cancer, disappearance of the jaundice would be strongly in favour of the former, the qualification of this conclusion implied in Mayo Robson's observation is of some moment.

But it may be said that cases such as Murchison's, and the one described above, cannot be quoted in support of the statement that a considerable degree of pyrexia may accompany cancer of the liver, for in each there was an ulcerated surface in the intestine through which septic poisoning may easily have occurred. It may readily be allowed that the febrile disturbances possibly originated in the way just suggested, and even, for the matter of that, it may be conceded that the actual cancerous changes in the liver had no part in the production of the pyrexia. Yet the fact remains that in consequence of the latency of the duodenal ulcer, of the existence of jaundice, and of the discovery of certain physical facts in the examination of the hepatic region, the cases as clinical problems were cases of hepatic disease with jaundice. And it thus was necessary in each instance to contrast the facts, including the existence of pyrexia, with the various diseased conditions of the liver possibly competent to produce them. A failure to recognise that the pyrexial phenomena, whatever be the theory of their production, were quite consistent in such cases with the existence of cancer of the liver, would have led to an error of diagnosis. If it is known that there is a primary malignant tumour in the uterus, breast, alimentary canal, or elsewhere, the development of jaundice and of enlargement of the liver, whether accompanied by fever or not, have an interpretation only too manifest. But when no such knowledge exists, and, as at least three of the present cases show, this is a frequent position, such facts as jaundice and enlargement of the liver are open to various explanations. Hence the necessity for recognising that neither a distinct degree of pyrexia, nor the occurrence of rigors and intermittent febrile attacks, is by any means conclusive against one of these possible explanations, namely, malignant disease.

The two statements, that a malignant process which commences in the gastro-intestinal tract frequently comes into practical view only when secondary tumours have formed in the liver, and that hepatic cancer may be associated with considerable febrile disturbances, are well illustrated in Cases II and IV above reported, and also in two cases recorded by Finlayson. The first of the last mentioned was one in which with feverish symptoms there was such a degree of bulging or swelling of the liver that an operation was undertaken in the expectation of finding pus. The *post-mortem* examination revealed malignant growths in the liver and a large sloughing ulcer of the stomach. In the second case the patient had jaundice, and for ten weeks there was remittent fever; after death a cancerous ulcer was found in the

duodenum and numerous malignant tumours in the liver. As showing the occurrence of pyrexia in malignant disease, the same author reports a case of epithelioma of the colon, of which the early symptoms closely resembled the onset of enteric fever; later, there were definite rigors for the occurrence of which the *post-mortem* examination gave no explanation other than the malignant tumour. From these and other cases Finlayson concludes that rapidly-growing or rapidly-diffused cancers are often associated with a distinct but moderate pyrexia.

Hale White has suggested that pyrexia is more common in primary than in secondary cancer of the liver, but the extensive series of observations necessary to raise this suggestion to the level of established doctrine has yet to be made, and considering the frequency with which secondary cancer is associated with the existence of an ulcerated surface in the gastro-intestinal tract, one would expect pyrexial manifestations here rather than in primary cancer, where no such opportunity for septic absorption exists. In Murchison's case (CXLII), and in several of Finlayson's cases, as well as in Cases II and IV of the present paper, the facts, so far as they go, are in harmony with this expectation.

The occurrence of intermittent febrile attacks in cases of hepatic disease was noted by Charcot, and in his *Maladies du Foie* he devotes a special chapter to what he calls "*fièvre intermittente hépatique*." The circumstances which favour the production of this condition he considers to be the presence in the dilated biliary passages of pus or muco-pus mixed with the bile in a state of stagnation. Nevertheless the intermittent fever may exist, he says, when there is no suppuration, and he attributes it to the presence in the inflamed and dilated biliary passages of a morbid poison resulting from an alteration in the bile. It is particularly to be observed that Charcot does not confine the occurrence of the intermittent fever to cases of gall stone. He says distinctly that it may be found in any case where there is a prolonged or permanent obstruction in the bile duct, as fibrous stricture, cancer of the head of the pancreas, etc.

Similarly, Murchison writes: "The paroxysms of fever are comparatively rare in obstruction of the bile duct other than from gall stones. Still I have observed them in two or three instances of catarrhal jaundice and also in cancerous stricture."

Chart 5.

CASE V.—The patient was a man of 32 years. When first seen he had been jaundiced for fifteen months, during which time he had had a number of attacks of severe paroxysmal pain. There was considerable enlargement of the liver, which was tender to palpation but without any appreciable nodulation; little or no evidence of distension of the gall bladder. The spleen was definitely enlarged. Under observation the temperature pursued the above course (see Chart 5), some of the febrile attacks being preceded by rigors and accompanied by epigastric pain, others occurring without either rigors or pain. There were some attacks of pain without accompanying rise of temperature. After each febrile outbreak there was sensible deepening of the jaundice. The case was regarded as one of impacted gall stone, and an operation was performed, but no gall stone was discovered. Nine months later the patient was seen with evidences of pleural effusion and pulmonary condensation at the base on the right side. The jaundice remained unchanged, and there was considerable enlargement of the liver and spleen, with a widely-diffused sense of irregular thickening and resistance in the upper abdomen. The patient died in the course of a few days, and a large gall stone was found impacted in the orifice of the bile duct, part of the calculus protruding into the duodenum. There was considerable dilatation of the biliary passages, and the liver was highly congested but otherwise normal. In the neighbourhood of the liver, spleen, stomach, and transverse colon there was extensive peritoneal thickening, and numerous fibrous adhesions existed between neighbouring organs.

The age of this patient, the history of the illness, the physical facts, and the irregularly intermittent temperature combined to urge a diagnosis of gall stone. Unfortunately at the operation the calculus was not detected, and this failure, together with the discovery by the surgeon of some "nodules" in the neighbourhood of the cystic duct, rendered a suspicion of cancer inevitable. When the patient was seen a short time before his death this suspicion appeared to receive strong confirmation from the facts discovered on palpation of the upper abdomen. Yet these facts, equally with the jaundice, were the consequence of gall stone, though, as just pointed out, they seemed to support a diagnosis of cancer. That—at least under the circumstances just described—the physical examination in a case of impacted gall stone is capable of affording such support is not the least instructive feature of the case.

Many observers have written upon the occurrence of paroxysmal febrile attacks in cases of gall stone. A quite characteristic case is quoted by Hutchinson from Richter's *Medical and Surgical Observations*. The patient, a man of 40, died in the Hospital at Goettingen in 1792, and a gall stone weighing 3 ounces and 5 drachms was found in the common duct. For four years the patient had had jaundice with attacks of colic, rigors, and fever. Before death bile returned to the stools, and at the *post-mortem* examination fluid bile was found all round the calculus, so that the case partially illustrates what has been described as the "ball-valve" action of a gall stone by which the passage of bile into the duodenum is permitted in spite of the presence of a stone in the common bile duct. The explanation which Charcot offered of the paroxysmal fever in these cases has already been quoted. Murchison allowed that in some cases the fever might result from ulceration of the duct leading to pyæmic inflammation of the liver, but contended that as in some instances "the fever ceases and the patient gets perfectly well," this was not the invariable explanation. "It may," he writes, "be due to a movement of the stone in the narrow duct just as . . . a paroxysm of fever may follow the introduction of a catheter into the urethra." Budd, Thudichum, Lionel Beale and Ord, all incline to the view that the rigors and fever are results of nervous disturbance produced by the calculus irritating the mucous membrane and stretching the walls of the ducts. That considerable central and reflex nervous disturbance may be produced by the irritation of a calculus is evident from the occasional occurrence of muscular cramps and convulsions in association with hepatic colic. Mayo Robson, on the basis of his own experience, believes that the fever may be an expression both of a septic element and of nervous irritation. Osler records two cases of stenosis of the common duct without fever or rigors as sufficient to show that mere obstruction will not cause these events. He allows that the condition of the bile passages in cases of impacted gall stone is usually one of catarrhal, not of suppurative, cholangitis, but points out that the discovery of micro-organisms in both these conditions renders it probable that the fever now in question is due to absorption of a ferment.

From the occurrence of intermittent febrile attacks and jaundice, with physical signs of enlarged liver, both in malignant disease and impacted gall stone, the differential diagnosis of these two conditions becomes an important practical question, all the more so that modern surgery has rendered the relief of one of them a comparatively secure undertaking. Attention has already been drawn to the fact that, as in Case iv, evidence of distended gall bladder favours the diagnosis of malignant disease. Murchison laid considerable stress upon the statement that when the jaundice becomes more intense after each febrile paroxysm it depends upon gall stone. Osler confirms Murchison's observation, and believes that intermittent fever, jaundice deepening after the attack, more or less pain, and gastric disturbance, combine to indicate quite clearly obstruction of the common duct by a calculus. Increase in the intensity of the jaundice after each febrile explosion was quite appreciable in Case v (gall stone), and there was considerable pain; in Case iv (cancer) the jaundice was so deep that it was impossible to imagine further exaggeration, and there was practically no pain. But it is to be noted that in this case the paroxysms occurred almost daily, and it is certain that they may be equally frequent in gall stone, a circumstance which would

allow but little opportunity for appreciating variations in the depth of the jaundice supposing this to be aggravated by each repetition of the event which determines the fever. Further, it is of course not unusual to have pain with malignant disease, and in gall stone the pain is not always characteristic or even suggestive, as is well seen in a case described by Gairdner. It may even be entirely absent, as in a man aged 69, who, after jaundice of six months' duration without pain, tumour, or vomiting, was entirely relieved by cholecystotomy and the extraction of 43 stones (Henry Morris). In a case reported by Chadwick there was only a solitary attack of biliary colic followed by jaundice, which persisted until death six years later.

From these facts it is evident that a combination of jaundice, intermittent fever, and hepatic enlargement may demand very careful consideration before deciding to cast the verdict for gall stone on the one hand or malignant disease on the other. Of course there will be cases in which the patient's age, history, general condition, etc., or some conspicuous physical fact, will make the diagnosis distinct, but in other cases the problem must be an anxious and difficult one. The knowledge, too, that cancer and gall stone may well exist together, with a correspondingly complex symptomatology, necessarily adds to the difficulties of the situation.

The development of rigors and intermittent fever as a result of gall stone is not limited to cases accompanied by jaundice. Hepatic colic may of course occur without jaundice as the result of the successful passage of small stones, or in consequence of the impaction of a calculus in the cystic duct. Under similar circumstances there may be intermittent fever, and in some of these cases pain is not a uniform feature. Murchison's statement is that "now and then a gall stone in one of the biliary ducts excites paroxysms of intermittent fever with little or no pain. These paroxysms may be more or less periodic, and may extend over several months without necessarily indicating pyæmic hepatitis, and the patient may ultimately recover." He draws attention to a case of Howship's in which, while spasmodic pains with ague-like attacks had been present for six months, the patient had been jaundiced—as a result doubtless of the onward movement of the calculus into the common duct—only during the last month of life. The preparation, showing a large calculus fitted tightly into the end of the duct, is in the Museum of the Royal College of Surgeons. In Murchison's own series, too, there is an analogous case (cxxxix). Waring also describes the occurrence of rigors from gall stone without the development of jaundice, and from these cases, and especially from the fact that the patients may recover after the febrile paroxysms have been present over a prolonged term, some support may be derived for the "nervous" as opposed to the "septic" theory of the fever. Thudichum's view was that intermittent febrile attacks were the peculiar feature of calculi in the hepatic duct or ducts. "When so situated," he says, "calculi produce symptoms of a peculiar kind, differing from the symptoms of gall stones in the gall bladder and common duct by the absence of pain, and having the greatest resemblance to chronic intermittent fever." And again, "as these calculi are rarely moved from the place in which they are formed, and as their formation is so gradual as to effect a corresponding expansion of the canal, they rarely produce symptoms of the passage of calculi and do not easily give rise to jaundice."

It will scarcely be allowed that the formation of calculi on the proximal side of the gall bladder is anything but a most unusual occurrence, and certainly the occurrence of rigors is not restricted to calculi so situated, as Case v and other instances definitely show.

One other remark falls to be made about the temperature in gall stone—namely, that the fever, instead of being intermittent, may be of a more sustained character, and may continue for some time after the pain has ceased. This condition appears to be associated with wounding or ulceration of the mucous membrane produced by the passage of the calculus (Murchison, Kraus). Trousseau considered that when hepatic colic had been of long duration or had recurred at short intervals, the feverish condition of the patient was due to inflammation of the liver.

In the various forms of abscess of the liver, rigors and elevation of the temperature, remittent or intermittent in

character are to be expected. But this expectation is not always realised, as the following case shows.

Chart 6.

CASE VI.—The patient, a Lascar, had suffered from abdominal pain and diarrhoea for three weeks. The pain was referred to the left iliac and hepatic regions, and there was some tenderness in the latter situation, but without much evidence of enlargement of the liver. The stools were frequent, fluid in character, and contained small shreddy masses like blood clot. Temperature as above; no rigors. At the *post-mortem* examination there was found extensive destruction of the mucous membrane of the colon, with firm adhesions between the bowel and neighbouring parts. The liver contained four abscesses, three each about the size of a walnut, and a smaller one.

Murchison records a case (LXXIV) of gall stones with ulceration and perforation of the cystic duct and numerous abscesses in the liver in which there were no rigors, and the temperature never exceeded 98°, the patient being under observation for five days before death. He adds: "I was scarcely prepared to meet with pyæmic inflammation of the liver with no elevation of temperature during at least five successive days." Murchison also reports the occurrence (LXXXVI) of an enormous tropical abscess of the liver without any elevation of temperature, and says, whilst the case is exceptional: "I am inclined to think it is far from unique."

Intermittent febrile attacks with jaundice and pain have been observed in hepatic diseases other than cancer, gall stone, and abscess. Identical symptoms have followed the bursting of a hydatid cyst with the passage of secondary cysts into the bile duct (Frerichs, Trousseau, Murchison, Mayo Robson). The same association of events has followed the entrance of lumbricoid worms into the biliary passages (Frerichs, Trousseau, Murchison).

Chart 7.

CASE VII.—The patient was a man, aged 34, and was believed to be the subject of cirrhosis of the liver. The history was of long-continued spirit drinking with recent failure of general health, two or three attacks of vomiting of blood, and more frequent passage of blood *per rectum*. Patient's face was sallow but not jaundiced. The urine yielded a copious deposit of pink urates but was free from bile pigment. The spleen was considerably enlarged, and the area of hepatic percussion, if anything, below normal; no hepatic pain or tenderness. There was some dilatation of the superficial veins over the right half of the abdomen but no ascites. The bowels were loose, and the stools contained a considerable quantity of blood so intimately mixed as to give a uniform darkish-red colour to the motions: no hæmorrhoids could be detected. The high temperature, the diarrhoea, and the presence of blood in the stools gave rise for a time to a suspicion of the possibility of enteric fever, but there was no further evidence to sustain this. The patient was seen again for two or three days a year after he had left the hospital. His general condition was much the same and the physical facts substantially unchanged. The temperature showed a decided pyrexia. He had had only one further attack of hæmatemesis. There was no suspicion of malarial infection.

Pyrexia is not usually recognised as one of the results of

hepatic cirrhosis. Yet its occasional existence has been noticed by various authors. Murchison, in his account of the symptoms, only mentions the existence of fever as attending an occasionally more acute onset of the disease, or as accompanying vomiting and diarrhoea from catarrh of the stomach and bowels. In one (CXVI) of his cases, however, there is a note of a temperature of 101.2°, and in another (CXXII)—a boy of 9 years—the temperature was at times as high as 100.6°, and among the evening records was one of 102.8° and one of 103.4°.

Frerichs also speaks of an occasional febrile onset of the disease, and mentions "slight febrile excitement" as one of the possibilities of the latter stages of its progress. In reviewing the etiology of the 36 cases which he had observed, he says: "In 5 patients the cirrhosis was preceded by persistent intermittent fever—a coincidence which has been repeatedly mentioned by other observers."

Carrington reports from the clinical records of Guy's Hospital the occurrence of irregularly febrile temperatures in 18 out of 44 cases of cirrhosis of the liver. He also describes a case of hypertrophic cirrhosis in which the symptoms for four weeks before death "completely simulated" those of multiple hepatic abscess.

According to Webber, in a series of 50 cases of cirrhosis of the liver, pyrexia was present in 9; in 3 the temperature rose to 103°, and in one of these the pyrexia was of an intermittent type.

Hawkins, in a recent article, recognises the separation of alcoholic cirrhosis into two classes, namely, multilobular and unilobular. The latter and less common variety is marked by considerable and even extreme enlargement of the liver, a great tendency to jaundice, and little or no evidence of portal obstruction. "There is often an evening rise of temperature the fever may range from 102° to 104° and it may assume a hectic course suggestive of hepatic abscess or pyelophlebitis." In the multilobular or atrophic form, on the other hand, there is, as a rule, no fever, though "if a patient be under observation for a long time, we may often observe an occasional rise of two or three degrees for a few successive evenings."

Sharkey has recorded a case of unilobular cirrhosis in which there was much and irregular fever, and which exactly corresponds to the above quoted description, except that jaundice was slight, and disappeared entirely before death. No explanation of the pyrexia was found at the *post-mortem* examination. Charcot also describes the development of jaundice, often accompanied by fever, in hypertrophic cirrhosis. Writing on this subject Osler says: "I have a distinct recollection of one or two instances, particularly in the hypertrophic form, of marked increase in the temperature, but I should say that in the majority of instances of cirrhosis pyrexia was not a special symptom." The verdict of the authorities who recognise the existence of two varieties of cirrhosis is in favour of the occurrence of pyrexia in the hypertrophic rather than in the atrophic form. The case above recorded (Case VII) has the peculiarity that whilst it follows the multilobar or atrophic type—the liver not enlarged, distinct evidence of portal obstruction, no jaundice—it is associated with considerable pyrexia, irregular in its course no doubt, but having generally the hectic character. There is also this noteworthy feature, that the man seen after an interval of a year had not to any great extent declined in health, and that he again showed quite decided pyrexia. The lapse of time in itself seems more than sufficient to exclude any suppurative process; the absence of tenderness negatives the suggestion of perihepatitis, even if the element of time is neglected; and similarly the absence of jaundice excludes, or at least renders highly unlikely, the possibility of those conditions, whatever they be, which are associated with obstruction of the biliary passages, and which produce "intermittent hepatic fever." It seems, therefore, that cirrhosis of the liver, even when of the atrophic or multilobular type, must be added to the numerous clinical events capable of producing considerable and indefinitely prolonged pyrexia by a method or agency of unknown nature.

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DIGESTION LEUCOCYTOSIS IN CANCER OF THE STOMACH.*

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An increase in the number of leucocytes in the blood after the ingestion of food is a well-known physiological phenomenon, and one which we may say is always present in health. The increase is notably among the lymphocytes, and its intensity varies with the age of the individual, his state of health, and the nature of the food.

This digestion leucocytosis, as it is called, is always well marked in infants. Schiff,¹ for example, found about 19,000 white cells per c.mm. in the blood of a newly-born infant, the count being made at 5 P.M. At 7 P.M. 15 grams of milk were given, and at 8 P.M. the number was found to have risen to 27,600. Next morning, at 6 A.M., after four more drinks, the leucocyte count had reached 36,000 per c.mm.

The nature of the food plays an important part, for it is always found that a meal rich in proteids is most effective in increasing the number of the white cells, and some observers even affirm that it is only when nitrogenous food is digested and absorbed that digestion leucocytosis occurs. This is probably not quite correct, for I have found, from observations made on myself, that a distinct leucocytosis can follow a meal consisting solely of potatoes and a little butter, a diet in which proteids are very scanty. In Fig. 1 is shown the effect produced by a single abundant mixed meal containing an average amount of proteid food. The observations were made on myself after a fast of twelve hours, the following being the counts obtained:

Fig. 1.

Count at 8 A.M., after twelve hours fast ... 5,100 per c.mm.
Mixed meal at 8.15 A.M.

Count at 9 A.M.	...	...	...	...	5,100	"
" 10 A.M.	...	...	...	...	7,810	"
" 11 A.M.	...	...	...	...	8,130	"
" 12 A.M.	...	...	...	...	9,800	"
" 1 P.M.	...	...	...	...	6,000	"

* Read before the Glasgow Medico-Chirurgical Society on March 1st, 1901.

In this as in all the observations made the Thoma-Zeiss hæmocytometer and special leucocyte pipette were employed, a 0.3 per cent. solution of acetic acid, tinted with methyl green, being used as the diluent.

It will be noted that the maximum increase occurred four hours after the meal was taken (a little later than is usually the case), and that the count then was about 95 per cent. higher than in the fasting state.

In our usual mode of life, however, where meals succeed one another in the regular course of the day, the leucocytosis produced by one has not time to pass off before another becomes due, and the results obtained are accordingly somewhat modified, and the curve is more complex than that depicted in Fig. 1. In Fig. 2 the digestion-leucocytosis curve is marked out from observations made on myself throughout a whole day in which ordinary meals were taken, a substantial dinner, however, being substituted for the usual lighter lunch in the middle of the day in order that the effect of food might be more marked.

A = Breakfast, 9.30 A.M.	C = Tea, 5.15 P.M.
B = Early dinner, 1.45 P.M.	D = Supper, 8.30 P.M.
Leucocytes at 9.15 A.M. after thirteen hours fast =	7,500 per c.mm.
" 10.30 A.M.	11,750 "
" 12.30 P.M.	8,300 "
" 2.45 P.M.	9,250 "
" 4.45 P.M.	14,000 "
" 6.45 P.M.	7,500 "
" 9.30 P.M.	9,500 "

Fig. 2.

As regards the cause of this leucocytosis, we must ascribe it to some effect produced by the absorption of food (especially of proteid food) on the white cells, either by a direct stimulation of the lymphatic glands and bone marrow where these cells are formed, or by an influence exerted on the lymphatic circulation of the abdomen leading either to an increase in the lymphocytes in the blood, or simply to an alteration in the distribution of the white corpuscles in consequence of the quickened flow of lymph through the abdomen. Hofmeister² held the view that the lymph cells of the alimentary canal were specially concerned with the absorption of peptones from the stomach and bowels, and with the change they underwent during the passage through the walls of these organs. He held that peptones exerted a formative influence on the lymph tissue, and that it was notably the digestive products of proteid food that augmented the cell substance of that tissue. Pohl³ held a similar view, namely, that along with increased formation of lymph cells there occurs during the absorption of peptones an increased passage of these cells into the blood. According to him, it is only the digestion of nitrogenous food that calls forth this leucocytosis. Hofmeister believed that one of the functions of these increased leucocytes was the conversion of albumoses and peptones back again into proteids in the adenoid tissue in the wall of the bowel and the lymphatics of the mesentery. Against this theory, with which we have nothing further to do here, various objections⁴ of considerable weight have been adduced. Whatever explanation of this phenomenon we accept, the fact remains that it exists as an almost constant factor in health. This having been established, it was natural that attention should next be directed to its occurrence in disease of the stomach, and observations have been made from time to time