THE EPIDEMIC JAUNDICE OF CAMPAIGNS.

BY WILLIAM HENRY WILLCOX, M.D.,
F.R.C.P.LOND.,

LIEUTENANT-COLONEL, R.A.M.C.; CONSULTING PHYSICIAN TO THE
MEDITERRANEAN EXPEDITIONARY FORCE; PHYSICIAN TO
OUT-PATIENTS, ST. MARY'S HOSPITAL, LONDON.

THE following paper is based upon the study of a considerable number of cases of jaundice in the Mediterranean area during the past six months, and also on the study of a number of cases of jaundice from the Expeditionary Force in France during the earlier part of the war.

Jaundice is of common occurrence amongst troops on campaign. In the South African war a considerable number of cases were reported. In the present war jaundice has occurred amongst our troops in almost all parts of the sphere of operations.

The cases of jaundice of the epidemic type have fortunately been of a mild nature generally, and very few deaths have been reported. A considerable amount of incapacity for duty has, however, resulted, so that epidemic jaundice is a disease of importance from the military point of view.

The epidemic jaundice of campaigns is of great pathological interest, since it throws considerable light on the pathology of jaundice generally.

It will be convenient to consider, first, the symptoms of the common type of epidemic jaundice as seen in the Mediterranean area during the later half of the past year. Other varieties of jaundice which were also observed will then be considered, and the relation between them will be discussed.

SYMPTOMS OF EPIDEMIC JAUNDICE (THE COMMON TYPE).

The patient had usually some abdominal discomfort for a few days, associated with anorexia, nausea, and either diarrhoea or constipation.

Pyrexia, generally of a mild type, would then set in, and this was associated with some chilliness, and in some cases by an actual rigor. Vomiting occurred sometimes at this stage, and also headache. Sometimes there were "pains all over." Abdominal discomfort in the hepatic and epigastric regions usually occurred. The pyrexial period in some cases lasted only one or two days. Generally it was from two to four days, but cases have been observed in which it lasted as long as eight days.

Liver: Gall Bladder.

Jaundice now occurred, at first slight, but it gradually increased in intensity and became of the ordinary type of obstructive jaundice. The stools were pale and the urine bile-coloured when the jaundice became marked. With the onset of jaundice the temperature usually fell to normal and remained so.

At this stage definite enlargement of the liver could be made out. It was felt usually extending to one or two inches, or even more, below the subcostal border in the right nipple line.

The surface was smooth and the enlargement uniform. There was slight tenderness on palpation over the liver. It moved freely with respiration. In some cases there was definite enlargement over the gall bladder region, and on palpation the gall bladder could be felt. This enlargement of the gall bladder occurred in about 10 per cent. of the cases, and it no doubt indicated an obstruction due to the catarrhal inflammation of the duodenum, involving the common bile duct and its ampullary orifice into the duodenum.

The stools were pale when the jaundice was marked, and unless aperients were given they were constipated.

Spleen.

At this stage the spleen could usually be felt, extending for half an inch, or considerably more, below the left subcostal border on inspiration. In some cases there was definite tenderness on palpation over the spleen. Percussion over the splenic area showed an increase of dullness upwards. The tongue was often moist and clean, but in some cases it was moist and somewhat furred.

Circulation.

The pulse was quickened during the pyrexial period to, for example, 80 to 90 per minute, but with the onset of jaundice it became slow, in some cases being only about 50 per minute.

The heart condition was very interesting. A definite increase of the deep cardiac dullness occurred. This was most marked on the right side. On percussion in the fourth space to the right of the sternum the cardiac dullness extended often to two inches beyond the right sternal margin. The cardiac dullness showed only slight increase to the left, reaching to the left nipple line or half an inch or so beyond.

The dilatation of the right side of the heart in epidemic jaundice is very characteristic, and, apart from pulmonary conditions, the only other acute disease showing commonly a specific dilatation of the right side of the heart is acute rheumatism. Usually no cardiac murmurs were present on auscultation, though occasionally a systolic murmur would be heard with the first sound. The dilatation of the right side of the heart subsided with rest, but it usually persisted for several days.

Urine.

The urine showed the usual signs of a specimen from a case of obstructive jaundice. It was acid and contained bile pigments. Acetone and diacetic acid were not present in the cases examined. Albumin was absent, except in the exceptional severe cases. Casts were usually absent, except in very severe cases.

General Symptoms.

No anaemia was noticed in the cases observed, showing that this type of epidemic jaundice was not associated with haemolysis.

Pruritus was not a marked symptom in the cases of epidemic jaundice, though the jaundice was often quite deep for two or three weeks or more. Purpura occurred in a few of the cases. The cutaneous manifestations, such as lichen, urticaria, boils, xanthoma, telangiectasis, etc., which are common in cases of protracted obstructive jaundice due to other causes, were not observed here.

It is remarkable in cases of jaundice due to mechanical obstruction of the duct, without liver involvement, for what a long time the deep jaundice will persist without toxic symptoms due to bile absorption (cholaemia) developing.

In the cases of epidemic jaundice the toxic symptoms which occurred must be regarded as due either to the toxæmia of the infection, or to autointoxication from resulting degenerative changes in the liver, and not to the toxic effect *per se* of the bile in the blood.

Nervous System.

Asthenia was a marked symptom in all but the very mild cases of epidemic jaundice, and depression was a characteristic symptom in most of the cases while the jaundice persisted. It must be mentioned, however, that several officers remained on active duty throughout the whole period of their attack, and it was remarkable to see them doing responsible and important work while deeply jaundiced.

The reflexes (knee-jerks, plantar, and abdominal) showed usually no change, and signs of organic disease of the nervous system were usually absent.

In another paper I have called attention¹ to the frequency of the occurrence of epidemic jaundice amongst the few beri-beri cases occurring amongst the troops in the Dardanelles area. The beri-beri cases all showed marked signs of multiple neuritis, and it is possible that in some of the cases the toxæmia associated with a previous attack of jaundice may have been a factor in the development of beri-beri.

Epidemic jaundice was, however, not the sole etiological factor in these cases; there was a more important dietetic factor, to which was added a toxic factor associated with jaundice.

The marked general weakness which usually occurred in the cases of epidemic jaundice rendered convalescence slow. This was especially evident in the cases showing cardiac dilatation and marked hepatic and splenic enlargement. In these cases weakness and dyspnoea on exertion

occurred for some weeks, and the diminution in the size of the liver and spleen was slow.

Usually in the moderately severe cases of epidemic jaundice two months, or even more, would elapse before the patient was fit to return to active duty. In the milder cases the period of inability for duty might be less, but it was usually about two months.

Secondary Pyrexia.

Some of the moderately severe cases of epidemic jaundice showed a second period of pyrexia occurring after the temperature had become normal. This was exceptional unless the patient had contracted some other infection—for example, paratyphoid fever—in addition to the epidemic jaundice.

Toxaemia.

In very rare instances cases of epidemic jaundice showed symptoms of marked toxaemia after the development of the jaundice. Stupor and a low delirium and vomiting, sometimes associated with hiccup, occurred. The pulse became feeble and usually quickened in rate. Some collapse occurred, the temperature being usually subnormal. Coma supervened and death occurred.

The above symptoms of the gravest cases were similar to those associated with acute yellow atrophy of the liver. They resulted, no doubt, from the degenerative changes in the liver cells, caused by the toxins of the infective agent, and the final symptoms were mainly due to an autointoxication from defective liver function. Fortunately only two out of a large number of cases examined were of this grave type, terminating fatally.

OTHER TYPES OF JAUNDICE.

Other types of jaundice commonly met with were:

1. *Catarrhal Jaundice.*

In this type of case the patient had for a few days symptoms of anorexia, nausea, sometimes vomiting, epigastric discomfort, and general malaise. Pyrexia was generally absent. Jaundice occurred of the obstructive type, associated with pale stools, and bile in the urine. The liver was slightly enlarged, but the spleen could not usually be felt.

In these cases the general symptoms were slight, except that depression and general weakness were marked, and it was usually several weeks before the patient was fit for duty.

2. *Jaundice associated with Specific Infections.*

Patients suffering from such diseases as typhoid fever, paratyphoid fever, relapsing fever, dysentery, malaria, etc., sometimes developed jaundice in the course of them.

With typhoid and paratyphoid fever the occurrence of jaundice of a catarrhal type was not uncommon. The jaundice generally occurred about the second or third week of the disease, and it was not a grave complication, unless associated with acute cholecystitis, when in a few cases operative treatment was necessitated.

Dysentery, both amoebic and bacillary, was sometimes associated with jaundice of a catarrhal type in the course of the attack. This was no doubt due to secondary infection of the bile duct and bile capillaries. The dysentery cases showed a great susceptibility to secondary infections of various kinds. Thus in amoebic dysentery secondary paratyphoid infections were not at all uncommon.

In *relapsing fever* jaundice was observed in a number of cases. The jaundice was not of the type of the epidemic jaundice described above, but was usually of a slight intensity, occurring after the second or third day of pyrexia, and it was of the haemolytic and not of the obstructive type. Pale stools did not occur, and bile in the urine was not constant. This jaundice rapidly cleared up when the fever subsided, and it was often so slight as to escape notice unless specially looked for.

In *malaria* slight jaundice of the haemolytic type and accompanied by definite anaemia was seen in chronic cases. Occasionally jaundice of the catarrhal type occurred in association with a malarial attack.

Mediterranean Yellow Fever.

Fortunately no cases of this type have occurred in the Mediterranean Expeditionary Forces, as far as I am aware.

Mediterranean yellow fever sometimes occurs in the Mediterranean area; it has been carefully studied by Dr. Ruffer, who has seen many cases and to whom I am indebted for a description of the disease.

It is a disease of high mortality. It begins with an acute onset, chilliness or rigor, headache, severe pains in the back and limbs, and high temperature being marked. Vomiting is common. The face is flushed and the eyelids are injected. Slight jaundice may occur during the first two or three days. Albuminuria is common and sometimes casts are present. In severe cases suppression of urine and fatal uraemia may supervene.

The temperature in a case of moderate severity will remain up for three or four days and then subside for a day or so, after which it rises again. In this secondary pyrexial period the jaundice becomes marked, haemorrhages such as haematemesis or melaena may occur, and frequently a profound toxaemia, like that of acute yellow atrophy, results, and death occurs. Mediterranean yellow fever resembles closely ordinary yellow fever, and it is probable that the infection is conveyed by the mosquito *Stegomyia fasciata*.

PATHOLOGY AND DIAGNOSIS.

Every case of jaundice seen on campaign should be examined with an open mind, and one should aim at making a true pathological diagnosis of the type of jaundice present. It is only by this means that prophylaxis and treatment can be carried out on correct lines.

It will be convenient briefly to review the causes of jaundice, and to consider the relationship of the "epidemic jaundice of campaigns" to other types of jaundice.

CLASSIFICATION OF JAUNDICE CASES.

These can be conveniently divided into two main groups:

1. *Obstructive jaundice*, where there is a mechanical obstruction in the common bile duct, preventing the flow of bile into the intestine. Types of this are:

1. Congenital absence of the bile duct.
2. Stricture of duct.
3. Obstruction in the duct itself:
 - (a) From foreign bodies—for example, gall stones, bile sand, or parasites;
 - (b) From growth in the wall of the duct;
 - (c) From swelling of the mucous membrane of the duct or its ampullary opening—for example, catarrhal jaundice.
4. Pressure on the duct from without—for example, tumours of pancreas, liver, stomach, etc., enlarged glands in portal fissure, aneurysm, etc., or kinking of the duct from dragging on it, as may occur in movable kidney.

2. *Non-obstructive Jaundice*.—This type has been called haematogenous jaundice, owing to the idea that the symptoms were the result of excessive bile formation consequent on increased blood destruction.

Modern research has shown that the distinction between the two types of jaundice is to some extent an artificial one. In most cases of non-obstructive jaundice, although no gross obstruction exists in the common bile duct or main hepatic ducts, yet there is an obstruction in the smaller bile ducts due to catarrh (choolangitis). Also in these cases the bile is altered in character, and often the viscosity is much increased. In many varieties of this type of jaundice there is increased destruction of red blood corpuscles and increased bile formation.

Hepatogenous Jaundice.

The terms "hepatogenous," "haemohepatogenous," and "intrahepatic" have been suggested for this type of jaundice—that is, for the non-obstructive type.

The following are its chief varieties:

1. *Toxic*, caused by chemical poisons. These may act by causing a cholangitis, and degenerative changes in the liver cells—for example, tetrachlorethane, chloroform, etc.—or by causing in addition marked haemolysis—for example, phosphorus, arseniuretted hydrogen, toluylendiamine, snake venom, etc.

2. *Toxaemic*, caused by the toxins set free by specific pathogenic organisms—for example, typhoid fever, paratyphoid fever, malaria, yellow fever, relapsing fever, typhus fever, septicaemia, pyaemia, etc. In the first two of these diseases the jaundice is due to an infective cholangitis.

that is, it is hepatogenous in type, while in the remaining diseases there is in addition increased haemolysis, so that the term "haemohepatogenous" applies to the type of jaundice.

3. *The Epidemic or Infective Jaundice of Campaigns and Weil's Disease.*—Both of these diseases are types of toxæmic jaundice and should really be classed with the preceding group. Weil's disease is a special type of infectious jaundice, due to infection with the *Bacillus proteus*. Its symptoms are very similar to those of the epidemic jaundice of campaigns, but are of a more acute and severe type.

4. *Icterus Gravis, or Acute Yellow Atrophy of the Liver.*—This condition is really a "symptom complex," the result of cessation of liver function consequent on extreme degenerative changes in the liver cells. The symptoms of acute yellow atrophy of the liver are identical with those of the grave cases of either the toxic or toxæmic types of non-obstructive jaundice—for example, tetrachlorethane jaundice.

5. *Other Special Types of Jaundice:*

I. Hereditary icterus.

II. *Icterus neonatorum* due to:

- (1) The physiological haemolysis occurring with the circulatory changes at birth;
- (2) Congenital absence of the bile or hepatic ducts;
- (3) Congenital syphilis;
- (4) Septic pyelophlebitis due to septic inflammation spreading from the umbilical cord.

PATHOLOGY OF "EPIDEMIC JAUNDICE OF CAMPAIGNS."

Post-mortem examinations were made on two fatal cases in this series of cases.

Post-mortem Appearances.

There was the usual bile staining of the skin and tissues associated with a case of deep jaundice.

Small Intestines.—The duodenum showed a marked red velvety appearance of the mucous membrane, which was swollen. There was congestion of the ileum in one case; this was most marked in the lower half. It was much less intense than that of the duodenum.

The common bile duct showed redness and swelling of the mucous membrane. This catarrhal condition had spread up the cystic duct and into the hepatic ducts.

The gall bladder was distended in one case with a thin semi-purulent greenish fluid, from which paratyphoid B organisms were obtained.

The liver showed a pale yellowish appearance and some bile staining. The fatty degeneration was more marked in patches.

The heart showed dilatation, which was especially marked in the right auricle and ventricle.

The heart muscle was somewhat pale and showed some degenerative changes. In one case an *ante-mortem* thrombus was present in the right auricle and ventricle. A portion of this had become dislodged and caused an infarct in the lower lobe of the right lung.

The kidneys showed some degenerative changes of the epithelium.

In neither of the above cases was there any complete mechanical obstruction of the larger bile ducts.

Duodenitis.

In the above cases a marked duodenitis had occurred. In one case this was primary, in the other it had probably spread from a paratyphoid infection of the lower intestine.

The common bile duct and larger bile ducts showed marked catarrh spreading along their course and causing a definite cholangitis.

There were fatty changes present in the liver, and also in the kidneys and heart muscle.

The duodenitis had given rise to a cholangitis, which caused obstruction not in the large bile ducts but in the smaller ducts in the liver itself.

As a consequence of the toxæmia associated with the disease, fatty degeneration had occurred in the liver cells, and to a less extent in the kidney, epithelium and heart muscle. These degenerative changes caused impairment of function of the liver, and autointoxication, so that the terminal symptoms of both the fatal cases of jaundice were those of a toxæmia such as is observed in acute yellow atrophy.

The pathological condition found in the two fatal cases of epidemic jaundice described, was almost identical with that observed in cases of tetrachlorethane poisoning which I have described elsewhere.² In each condition the jaundice is deep and due to a cholangitis, causing block-

ing of the finer bile ducts in the liver itself. In each duodenitis is marked.

In tetrachlorethane poisoning the poison is of a deadly nature, producing marked fatty degeneration of the liver cells, and so much consequent autointoxication that a fatal result is common, and the prognosis always grave when the jaundice is deep. The terminal symptoms are exactly similar to those of acute yellow atrophy.

In epidemic jaundice, fortunately, the toxin from the bacterial infection is less deadly in nature, so that fatty degeneration of the liver cells or those of the kidney or heart is very rare, consequently symptoms of autointoxication such as occur in the late stages of tetrachlorethane poisoning or in acute yellow atrophy are very rare.

THE BACTERIOLOGY OF EPIDEMIC JAUNDICE.

In a few of the cases examined a paratyphoid organism, usually of the "B" type, was found, but in the great majority of the cases of epidemic jaundice special tests for paratyphoid "A" and "B" were negative.

Captain Archibald, R.A.M.C., made blood cultures from several cases while in the pyrexial stage, before the development of jaundice, but the results were negative. Blood culture tests, after the development of jaundice, likewise proved negative.

The specific organism which is the cause of epidemic jaundice of campaigns has yet to be isolated.

It is interesting to note that in a small outbreak of infectious jaundice investigated at Bruyères, France, by Dr. Carnot and Dr. Weill-Halle,³ an organism of the paratyphoid group was isolated from the stools. The organism did not correspond to either the "A" or "B" varieties of paratyphoid. The cases occurred in the civil population.

SUMMARY.

The epidemic jaundice of campaigns thus appears to start as a gastro-intestinal infection, the inflammatory catarrh being most marked in the duodenum.

At this stage pyrexia and a certain amount of toxæmia occurs, but there does not appear to be a general blood infection usually, since blood cultures have generally been negative. A catarrhal cholangitis follows from spread from the duodenum, and marked jaundice now sets in, due to obstruction in the finer bile ducts.

The jaundice is hepatogenous in type and does not appear to be associated with increased haemolysis of red blood corpuscles, anaemia being absent.

Fortunately, most cases do not progress beyond this stage, and the catarrhal condition subsides with clearing up of the jaundice. In very exceptional cases the infective condition may give rise to degenerative changes in the liver, and symptoms of icterus gravis will then supervene.

It is interesting to note that sometimes mild gastro-enteritis occurs in cases exposed to similar conditions, and that in many of them jaundice will develop, while in a few it will not. It has been thought that as regards the infection and toxæmia associated with it the two groups of cases were similar.

Catarrhal Jaundice of Campaigns.

This is very common, and it must be classed etiologically with epidemic jaundice. When on campaign numerous cases of epidemic jaundice of the type described above are occurring there will also occur with them many cases in which there is no pyrexia or splenic enlargement.

These cases are undoubtedly due to an infection of a mild type, similar to that of the epidemic cases, and the asthenia and nervous weakness of the two conditions are very similar.

The French school have long regarded catarrhal jaundice as a benign form of infective jaundice, and this view appears to be correct as regards the catarrhal jaundice of campaigns.

Toxæmic Jaundice.

In cases of jaundice symptoms of any specific infection which may be the primary cause of the jaundice should always be looked for.

The clinical symptoms will usually indicate this type of jaundice—for example, the prolonged pyrexia of typhoid and paratyphoid is unlike that of epidemic jaundice, the rigor and very high temperature of malaria; the early delirium and profound toxæmia of relapsing fever

are quite distinctive. In every case of jaundice any accompanying specific infection should be elucidated without delay by means of appropriate pathological investigations.

ETIOLOGY.

Since the causal agent of "epidemic jaundice of campaigns" is not known with certainty, the etiological factors cannot be stated with precision. It is certain that the insanitary conditions inevitably associated with military campaigns play a most important part.

Food.—The infection is almost certainly conveyed by the alimentary tract, and contamination of food with infected dust probably plays a most important part in the causation. Flies, also, as in paratyphoid and typhoid fever, may convey infection to food; but they are probably not the main cause of the spread of the disease, since, in the Dardanelles area epidemic, jaundice occurred after the flies had largely disappeared.

Water.—The infection may be conveyed by water, but cases occurred where this channel of infection could be excluded.

Carriers of the disease very probably, as in paratyphoid and typhoid fevers, are responsible for the spread of infection.

Air.—In civil practice outbreaks of epidemic jaundice have been described⁴ in which the evidence pointed to the disease being air-borne and conveyed by the respiratory tract. Thus infection was spread in day schools amongst children sitting at the same desk.

Probably in the "epidemic jaundice of campaigns" the infection is almost entirely gastro-intestinal in its mode of spread, since air-borne infection was not observed—for example, epidemic jaundice was not observed to be conveyed in hospitals from one patient to another, when isolation of the jaundice cases was not carried out.

PROPHYLAXIS.

As regards prophylaxis, careful attention to latrines, to prevent spread of infection by dust and flies, is most important. Fly and dust proof latrines are very valuable as regards prevention. Refuse destruction by means of incinerators is most important.

The greatest care possible should be paid to prevent contamination of food and water.

Patients suffering from epidemic jaundice should receive hospital treatment in order that spread of infection may be guarded against.

Notification of jaundice cases is a most important prophylactic measure in order that immediate preventive measures may be instituted.

TREATMENT.

Rest in bed in the early part of the disease should be insisted upon. Careful dieting, which will be mainly liquid, is important.

It must be remembered that on campaign the milk will, owing to its sterilization, be devoid of anti-scorbutic and anti-beri-beri vitamins, so that some articles of diet should be given to counteract that deficiency. Thus fresh lemon juice in lemon drink is important. Porridge, pea-flour in soups, mashed potato, yeast in some form—for example, dried yeast added to hot milk, or yeast cakes made into a paste with milk—are important additions to the dietary. Soups to which fresh vegetables are added are valuable.

Owing to the anorexia present, the diet must necessarily be quite light. Excess of protein should be avoided, and meat is best not given until the jaundice is clearing up.

As regards medicines the following mixture may be given with advantage:

Sod. bicarb.	...	...	...	gr. xx
Potass. citrate	...	...	...	gr. xxx
Sod. sulph.	...	...	...	gr. xxx
Syrup. aurantii	...	...	...	ʒj
Aqua	...	...	ad	ʒj
t.i.d.s.				

Urotropin gr. x t.d.s. in water, as a gastro-intestinal anti-septic seemed to do good in many cases. Calomel should not be given in repeated doses, since it appeared that patients suffering from epidemic jaundice were very susceptible to the effect of calomel thus given. In some

cases mercurial stomatitis occurred. There is, however, no objection to giving a single dose of calomel in the early stages.

The cases almost without exception progressed favourably under treatment, though, as described above, convalescence was often somewhat slow.

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THE TREATMENT OF TOXIC JAUNDICE DUE TO TETRACHLORETHANE POISONING.

BY

WILLIAM HENRY WILLCOX, M.D., F.R.C.P. LOND.,

LIEUTENANT-COLONEL R.A.M.C.,

PHYSICIAN TO OUT-PATIENTS, ST. MARY'S HOSPITAL, LONDON, W.

THE subject of toxic jaundice from tetrachlorethane poisoning was fully dealt with in a paper read before the Medical Society of London, March 1st, 1915.¹

It was pointed out that this type of toxic jaundice was of frequent occurrence amongst the workers in aeroplane factories, who were exposed to the vapour of the "dope" or cellulose varnish used for the wings of aeroplanes. One of the constituents of the dope or cellulose solution is tetrachlorethane. It was shown that the vapour of the tetrachlorethane in the dope, if inhaled for long periods, as occurred in the case of aeroplane workers, was likely to give rise to malaise and jaundice, and that this jaundice was of a serious type, and in severe cases often terminated fatally. The pathology of the condition showed that the jaundice was due to a cholangitis set up in the smaller bile ducts, causing an obstruction to the flow of bile from the liver, and also there was present marked fatty degeneration of the liver cells.

In severe cases this fatty degeneration was followed by necrosis of the liver cells and symptoms of autointoxication identical with those of acute yellow atrophy of the liver.

Did the patient survive the effect of necrosis of some portion of the liver, then the affected area became replaced by fibrous tissue; that is, a replacement fibrosis occurred and symptoms of portal obstruction—for example, ascites, etc.—resulted.

The jaundice of tetrachlorethane poisoning was found to be "hepatogenous" in type. It was not associated with haemolysis or anaemia, and no changes in the red blood corpuscles were observed.

The kidneys in severe cases showed degenerative changes—for example, fatty degeneration.

Pathology.

It is important that the pathology of this type of jaundice be thoroughly understood in order that the treatment of cases can be carried out on right lines.

Early Symptoms.

Obviously the first indication of the treatment of an early case is the removal of the patient from all influence of the poison. The presence of anorexia, drowsiness, general malaise, constipation, headache, and occasional vomiting, are quite sufficient indications for this step to be at once taken in the case of aeroplane workers.

The above early symptoms are the first indications of the poisoning, and treatment should be at once commenced. Unless at this stage the patient is removed entirely from the toxic action of tetrachlorethane, jaundice is almost certain to supervene and render the prognosis much more serious.

It is thus seen how important is the periodical medical inspection of factories where tetrachlorethane is used.