Treatment consists in the avoidance of undue exertion, and in the management of the associated respiratory infections.

Biopsy report.—In one patient with a large swelling of his second left costal cartilage, of two weeks' duration, a portion of the cartilage including its costal end was removed by Lieut.-Col. J. G. Shannon. He reported the cartilage and perichondrium swollen, but felt no swelling of other contiguous structures.

Lieut.-Col. R. A. H. MacKeen studied sections at three different levels from this specimen and reported, "The appearances here do not suggest a true neoplasm. There is a hyperplasia of the cartilage, some of which is fibrocartilage, particularly on the external aspect. In a few areas there is metaplasia of cartilage with early bone formation; in these areas there is an increase in vascularity. In other areas there is some calcification. In the bony portion, sectioned, there is fibrosis of the marrow. The perichondrium is thickened due to an increase in fibrous tissue. It is difficult to evaluate the varied picture seen but some areas suggest atypical callus formation. It does not appear to me to be a simple chrondroma."

SUMMARY

Twenty-two cases are reported (of a total of 30) of non-suppurative, non-specific, painful swellings of the costal cartilage, of unknown etiology, of variable and often prolonged and fluctuating course.

The disability produced is minor, not necessitating hospitalization, but may be very annoying, and in most cases necessitates light duty for weeks.

The cause is unknown. There is no reason to suspect dietary deficiency in any of these cases. The association with respiratory disease, which appears before, coincidentally with, or after the chest pain, in invariable. Exacerbations frequently occur with each bout of minor respiratory infection.

Four cases are reported from one unit.

Trauma appears not to be a factor of any importance. Tuberculosis and syphilis are ruled out.

This syndrome of non-suppurative, non-specific painful tender swellings of one or several costal cartilages, with little or no constitutional disturbance, associated with infection, usually upper respiratory infection, possibly always respiratory infection, appears to be a not uncommon cause of "chest" pain.

When men present themselves with thoracic pain—admittedly a difficult diagnostic field at times—the possibility of Tietze's syndrome should be borne in mind.

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RÉSUMÉ

Le syndrôme de Tietze consiste dans le gonflement de plusieurs cartilages costaux; ce gonflement n'est pas spécifique et ne suppure pas. Il ne s'accompagne pas de malaises généraux. Il détermine simplement un syndrôme thoracique douloureux dont l'élément essentiel est la douleur localisée. Ce syndrome est le plus souvent associé à une infection des voies respiratoires. La cause en est inconnue et l'évolution est variable. Le régime alimentaire n'a rien à voir avec son apparition. Les traumatismes, la syphilis et la tuberculose ne sont pas en cause. 22 cas ont été observés qui coincident avec la description de ce syndrôme, plus fréquent que l'on ne croit s'il est bien recherché. JEAN SAUCIER

INFECTIVE HEPATITIS*

By C. H. A. Walton,† M.Sc., M.D., F.A.C.P.

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INFECTIVE hepatitis has proved to be one of the most important diseases, at least numerically, affecting our armies, those of our allies and probably those of the enemy. The notable advances made in the study of its pathology during the last few years make it a timely subject for discussion. As I shall show later, this disease is probably synonymous with what we know as catarrhal jaundice. Although British troops suffered to a fairly large extent from this disease in the Middle East in the last war, it was uncommon in France. Accordingly, the Canadian Army suffered little.

In peace time and in civil life we are all familiar with a mild form of this disease and we all see occasional cases. My interest in it was not really aroused until I met it in my wards in England. In the three years that I served in that country some 130 cases went through the medical division. While this number was not large, representing only about 1% of our medical admissions, the disease was exceedingly interesting to us because of its severity.

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There were two deaths from acute yellow atrophy and in a few other cases the severity of the illness and course suggested that they had at least a subacute yellow atrophy. One case developed frank cirrhosis and ascites within three months of the onset of his jaundice, and others gave us reason for some anxiety that a similar process was developing. When we reached the Mediterranean theatre we found in the first six weeks, *i.e.*, to the end of August, 1943, that we had the usual small but steady flow of cases, some twenty in all. However, in September, the number suddenly rose to 278 and in the ensuing eight-month period we admitted 1,900 cases of this disease. Since I have returned I have been informed that the admission rate continues at the same level. This large epidemic rate was experienced by all military hospitals in the theatre, British and American.

The disease was endemic in England and epidemic in the Central Mediterranean area. There were many reports of small epidemics among both soldiers and civilians in England but such epidemics never became widespread. Reinforcements coming from England rarely developed jaundice until six weeks after arrival, indicating the epidemic nature of the disease in Sicily and Italy. I do not know if it was widespread among the civilian population of Italy or Sicily but it undoubtedly existed. It appeared to be as common among prisoners of war both German and Italian. Although there were few women with us, many of them acquired the infection. Deaths were uncommon in the Central Mediterranean Forces and probably were less than 0.5%. However, the disease was of such severity that soldiers frequently lost three or more months from duty, so that the loss to the army was very great. Some cases even required evacuation to the United Kingdom. Line of communication and base hospitals and convalescent depots were heavily taxed to care for them and often as many as 50% of the available beds were occupied with this disease alone.

Sir Arthur Hurst,[1] in a review of his experience in the last war in the Middle East and of the literature, attempts to distinguish catarrhal jaundice and infective hepatic jaundice and suggests that the former is much commoner and accounts for the epidemic cases. He advances the theory first elaborated by Virchow in 1865 and developed by Rolleston, Wilcox, Eppinger and others that it is due to obstruction of the common bile duct at the ampulla of Vater, due to a mucus plug resulting from a duodenal catarrh, and that the liver is unaffected except perhaps for an ascending cholangitis of mild degree. I am sure that this is the conception which we were all taught and which is still widely held. The pathology of a disease which is rarely fatal is, of course, hard to establish. However, much light has been thrown on the problem in the last few years by means of biopsy studies and the evidence now clearly indicates that epidemic jaundice is a true hepatitis and not a duodenitis with obstruction of the common bile duct, and it is interesting to note that Hurst[2] writing just before he died, says that catarrhal jaundice, as he knew it, was now a rare disease and that most, if not all, cases of epidemic jaundice are a true hepatitis.

PATHOLOGY

In Denmark, Iverson and Roholm,[3] published a report of 160 liver aspiration biopsies without mortality. Because of the importance of the disease in wartime, Dible, McMichael and Sherlock,[4] at the British Post-Graduate Medical School, Hammersmith, undertook a study of jaundice using this method. A small cylinder of liver tissue is aspirated into a 2 mm. bore cannula passed transpleurally into the right lobe of the liver, under local anæsthesia. The specimen is fixed in absolute alcohol, sectioned and stained. I have watched this procedure carried out. It did not bother the patients and seemed to be quite safe. In fact, we were so impressed by its simplicity that we carried out a few such examinations ourselves.

However, these authors did have signs of hæmorrhage in 3 out of 126 biopsies with one death (in a patient who was almost moribund). Very properly, they emphasize this danger and after their report we desisted from further studies of this kind. Their report is full and very striking but space does not permit a description here other than along general lines. The picture is one of hepatic cell necrosis and autolysis, most marked about the hepatic vein, and leucocytic and histiocytic reaction in the portal tracts. The latter is more prominent in the mild cases and the former in severe cases. The appearance is remarkably uniform, and in many there is remarkable destruction of the liver lobule. In fact, when one studies these sections one is impressed by the widespread liver damage and one wonders how recovery can

possibly take place. However, the reticular framework of the lobules is not lost and the amazing property of liver cells to regenerate permits the rapid recovery and return to normal on this scaffold, which is usual. Serial sections throughout the course of the disease show this process clearly. Further, biopsies done on the first day of detectable jaundice show advanced hepatitis indicating that liver damage probably begins with the prodromal symptoms which are so often regarded as gastro-intestinal in origin. Intubation studies by Van Rooyen and Gordon[5] in 1942 showed that there was no evidence of duodeno-biliary catarrh. In the sections studied by Dible and McMichael there was no evidence of biliary stasis such as would occur with common bile duct obstruction. These observations are in accord with a mass of evidence by other workers that epidemic jaundice is indeed a hepatitis and the old view of Virchow and Hurst need hardly be entertained now.

The evolution of this widespread diffuse hepatitis appears to present four distinct possibilities:

1. *Complete recovery with complete restitution of the liver.*—This occurs in the great majority of cases and is shown in serial biopsies and also in post-mortem examinations on recovered cases dying from some other cause.

2. *Continuous progress of the lesion leading to death* with the pathological picture of acute or subacute liver necrosis. We demonstrated this in our fatal cases. Such cases are usually fulminating and death occurs in a very few days.

3. *Development of liver cirrhosis.*—When the disease is greatly prolonged and fibrotic changes become predominant classical cirrhosis is produced. This occurred in at least one of our cases and was suspected in several others. Several such cases were followed by serial biopsies by Dible *et al.*

4. *Residual fibrosis.*—Some cases were observed with complete clinical recovery with some residual portal scarring, and this probably undergoes complete resolution. Reversible fibrosis has been demonstrated in animals and is a similar phenomenon.

ARSENICAL JAUNDICE

The occurrence of jaundice in syphilitics undergoing treatment with arsenicals is a well known phenomenon. It has always been thought to be a toxic arsenical hepatitis. We saw many patients who were receiving arsenical treatment develop jaundice. Apart from this fact in their histories, they were indistinguishable from epidemic jaundice on clinical grounds. Aspiration biopsies showed that they were indistinguishable pathologically. However, soldiers undergoing anti-syphilitic treatment had an incidence of jaundice about ten times that of other soldiers. That the toxic action of arsenicals made them more liable to the infecting agent is a plausible and even probable explanation but it has been suggested that the infecting agent is a virus which is resistant to the usual disinfecting methods used for syringes and needles in V.D. clinics and that this might be the explanation. Non-syphilitics treated with intravenous arsenicals also had a high jaundice rate (*e.g.* Vincent's cases).

SERUM JAUNDICE

Further, there were a large number of cases of clinically indistinguishable hepatitis occurring in soldiers given yellow fever vaccine prepared with human serum, and in others given convalescent serum for the prevention of measles and mumps. Pathologically and clinically, these cases were identical with the epidemic cases and the evidence points to the presence of the infecting agent, probably a virus, being present in the human serum used and thus transmitted.

CLINICAL COURSE

Characteristically there is a prodromal period of five to ten days preceding the jaundice. The prodromal symptoms include marked anorexia, nausea and vomiting; severe retro-bulbar headache, fever, chills, muscle pain and abdominal discomfort. Any or all or none of these symptoms may occur but extreme anorexia is almost invariable. In some the prodromal symptoms are so severe that the patient is hospitalized as a fever of unknown origin, and in others the patient does not complain until he or his friends note jaundice. The anorexia may be attributed to the army diet and even dark urine often escapes the soldier's interest, if not his attention. A careful history generally elicits the information that the urine is dark and the stools light-coloured before jaundice was noticed. Jaundice develops very rapidly once it is noted and may be mild and transient or very severe and prolonged, varying from a few days to many weeks.

The physical finding vary in degree. *Jaundice* is usual but we have seen a number of undoubted

cases of hepatitis with all other signs which never became clinically jaundiced, although their icterus indices usually were above normal. *Fever* may be slight but is usually moderate and in a few cases, marked. In the average case the fever subsides within a few days of the jaundice reaching its height. Persistent fever was a most unfavourable sign. The *pulse* was relatively slow when the icterus appeared. *Pruritus* was not uncommon with the jaundice. The *liver* was generally enlarged and tender, sometimes very greatly. The *spleen* was quite commonly enlarged and tender too. *Icterus indices* were often quite high and I have seen readings well over 300. *Bile* was readily seen in the urine and the *stools* were completely clay-coloured and often costive.

Very often the severe symptoms started to subside when the jaundice appeared and a return of appetite was usually the first sign of beginning recovery.

TREATMENT

Complete bed rest was enforced until the temperature was normal, the urine free of bile and the liver no longer palpable. Diet was fat free and rich in carbohydrates and proteins were given as tolerated. Fluids were forced. Saline laxatives were frequently required. It was found that if the above criteria of recovery were not followed and the patient allowed out of bed that relapse was very likely to occur.

Convalescence. — Convalescence was usually prolonged. Fatigability was outstanding. It was policy not to force or accelerate convalescence for reasons indicated above.

Prognosis.—There was great variation. I know of cases, especially in enthusiastic field officers, who never went off duty and apparently recovered fully. These were undoubtedly very mild and the men exceptionally "tough" individuals. The jaundice stage commonly cleared in ten to fourteen days but I have known jaundice to persist for more than six months. The average case did not return to duty under ten weeks. Mortality was slight and probably less than 0.5%. However, the cases which did die were most memorable. The number which went on to immediate cirrhosis was probably small but such cases were seen by all hospitals. How many will subsequently develop cirrhosis is problematical but one cannot escape the thought that there may be a sizable number, particularly when one studies the very striking pathological sections. In this connection it is worth remembering that there is some evidence that a not inconsiderable number of cases of cirrhosis have a history of catarrhal jaundice earlier in life. I saw such a case in a young man a few months ago and there are others reported in the literature.

ALCOHOL

The question of alcohol and the possible part it plays in this disease arises. The time-honoured idea that alcohol is a direct liver poison has been questioned many times in recent years. Autopsy studies on known old alcoholics have usually failed to show liver damage. Recent dietary studies[7] suggest that cirrhosis occurring in alcoholics is due to dietary deficiencies, notably of methionine, etc., due to the chronic alcoholism in the same way that peripheral neuritis in alcoholics is primarily due to dietary deficiency. Soldiers are popularly supposed to be heavy consumers of alcohol and I suppose many are. Although I have no statistics to prove the point, I am sure that we had as high a proportion of hepatitis among teetotal soldiers as drinkers. An unkind person has suggested that the undoubted greater incidence of the disease among officers is due to the fact that officers consume more spirits than other ranks.

OFFICERS AND OTHER RANKS

The greater incidence among officers is a fact and a very puzzling one. One suggestion advanced is that officers use communal dishes in their mess and that the other ranks always use their own mess tins. In any case, it is interesting to speculate on this very curious phenomenon.

DIFFERENTIAL DIAGNOSIS

1. The *pre-icteric stage* which may last for six to ten days is often difficult to diagnose and must be essentially the problem of an undiagnosed fever. In the Central Mediterranean Forces we always had to distinguish this stage from malaria, sandfly fever and dysentery. Further, these diseases often co-existed with jaundice. The presence of a palpable, tender liver and bile in the urine were, of course, important differential points. Anorexia in soldiers is a rare complaint. When a soldier could not bear the sight of food, we were almost certain that he had hepatitis. Marked anorexia is undoubtedly the outstanding symptom and occurring as

it does in young people previously healthy, it is very striking.

2. *Jaundiced stage.*—When jaundice developed in an acute febrile form about the only disease with which it could be confused was Weil's disease or epidemic hæmorrhagic jaundice. I have seen cases of this disease and the diagnosis is rarely in serious doubt. They are always seriously ill, febrile, often delirious and, of course, are characterized by hæmorrhagic phenomena in the skin, scleræ, central nervous system, renal tract, etc. The organism, *Leptospira icterohæmorrhagica,* can occasionally be found in the blood or urine but is usually proved by guinea pig inoculation or by specific agglutination reactions. In the Central Mediterranean Forces, erroneous diagnoses of this disease were made in a number of seriously ill hepatitis cases because an artefact looking like a leptospira was found in dark field examinations of blood serum.

EPIDEMIOLOGY

I have referred above to various epidemiological features. The incubation period appears to be four to six weeks in naturally occurring cases but in those due to inoculation with human serum, the time varied from 30 to 120 days. Artificial infection of human volunteers by nasal washings from known cases has occurred in 30 to 50 days (Findlay and Martin[8]).

The route of natural entry of the infection would appear to be through the upper respiratory tract or via the food and the gastrointestinal tract. Present observations suggest strongly that patients are most infective in the pre-icteric stage. This presents a most difficult problem in control. An interesting sidelight on this is the fact that our surgical staff had a higher incidence of the disease than our medical personnel. It was thought that this was due to the fact that surgical patients, incubating the disease but not suspected until icteric, infected their attendants, whereas most jaundice patients admitted to medicine were past their heavily infective stage.

The recent work of Himsworth and Glynn[7] and many others, which shows that dietary deficiency plays some part in the so-called trophopathic hepatitis of animals, raises the question whether troops in the field have a deficient diet. Casein is the best source of the so-called protective factors and its source in soldier's diets is milk which is in very small supply and cheese which is available in moderate amounts. The question also arises whether explosives add their measure of chemical poisoning. Such factors are only surmises at the best and if they do play a part, they only increase the soldier's likelihood of acquiring the infection.

ETIOLOGY

The mass of evidence at the present time indicates that the infecting agent is a virus. For example, the disease can be spread by small amounts of convalescent serum. Further, very small amounts of serum used in the preparation of yellow fever vaccine have their infectivity greatly enhanced during the growth of the yellow-fever virus on the chick embryo. Findlay and Martin[8] have demonstrated that nasal washings from pre-icteric and early icteric cases will transmit the disease to humans when instilled into the nose. Although the virus has not been finally identified there seems to be little doubt that it is the etiological agent. So far, the disease has not been successfully transmitted to animals.

SUMMARY

1. Infective hepatitis is an outstanding disease of this war and Canadians have been heavily affected.

2. The disease is endemic in England, Europe, North Africa and the Middle East. Epidemics of varying degree occur throughout these areas. The disease is probably endemic in Canada and a small epidemic recently occurred in Ottawa and Montreal. Perhaps we will see more of this disease in the future.

3. The outcome usually is complete resolution with recovery. However, in a small proportion of cases the process may be fulminating, with resultant necrosis and death in a small number. Residual portal fibrosis may occur with clinical recovery and it is probable that residual fibrosis may lead to cirrhosis.

4. The clinical course has been outlined.

5. Problems of diagnosis are mentioned and the clear differentiation from hæmorrhagic jaundice (Weil's disease) emphasized.

6. Evidence is reviewed that the etiological agent is a virus.

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RÉSUMÉ

Ce qu'on appelait autrefois l'ictére catarrhal doit être maintenant désigné sous le nom d'hépatite infectieuse avec lésions primitives au niveau du foie et non au niveau des voies biliaires et du duodénum. Cette maladie a été relativement fréquente durant la guerre. Bien que son taux de mortalité soit bas, l'hépatite a une évolution longue et nécessite très souvent l'hospitalisation. Elle est endémique en Angleterre, en Europe, en Afrique du Nord et au Moyen-Orient. Des épidémies surviennent assez fréquemment. La maladie est probablement endémique au Canada. Bien que la guérison soit la règle, on a observé des évolutions vers la cirrhose. Quelques rares cas sont rapidement mortels. L'étude clinique est bien connue et le diagnostic n'est pas difficile. L'influence de l'arsenic, de l'alcool et de certains sérums est discutée. La maladie de Weil est facilement éliminée. Le traitement est essentiellement hygiéno-diététique. L'agent étiologique est à peu près certainement un virus; des arguments d'ordre expérimental l'ont abondamment démontré. JEAN SAUCIER

THE DIAGNOSIS OF OCCUPATIONAL ECZEMA*

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THE object of this paper is to discuss the factors upon which a diagnosis of occupational dermatitis can be made.

In the great majority of the cases, the skin reaction is of the true eczematous type; however there are numerous exceptions such as oily acne, ulcers caused by chromium derivatives, keratosis and epithelioma due to tar, soot, burns, etc.

The industrial eczema may be due to an almost interminable list of contacts. The elementary lesions are of a most ordinary type and offer no clue of an industrial or other origin and certainly do not indicate what industrial substance is their causative factor.

PREDISPOSING FACTORS

Certain causes contributing to the development of an occupational dermatitis should first be mentioned. Negroes are generally more resistant than white people. Women are more susceptible than men, and young people more than older ones. Blondes are more sensitive than brunettes.

Certain regions offer more susceptibility to reactogens. The flexor surfaces and folds are more tender than external portions of the skin. Although much exposed the palms are seldom affected. Excessive perspiration will increase the action of certain chemicals which become irritants only when moist; perspiration may also cause a certain degree of maceration of the epidermis which is an aggravating factor. Additional friction creates an ideal condition for a rash.

Cleanliness of body and clothing is of great importance. On the other hand the use of strong solutions, liquid soaps, turpentine, etc., for cleansing purposes is often the real cause of a dermatitis.

Ichthyosis, psoriasis, atopic dermatitis and seborrhœic dermatitis predispose the worker to develop a rash. The so-called "athlete's foot" must not be forgotten as it produces secondary eczematous eruptions.

A skin disease is not necessarily of an industrial origin because it occurs in a labourer in contact with irritating substances, or if occupational eruptions have been noted in the plant where he is working. Certain essential factors must be considered before a diagnosis of occupational dermatitis can be made: (*a*) the clinical diagnosis of the eruption; (*b*) the location of the lesions; (*c*) the history of the disease; (*d*) the "patch tests" (less important than the three first items).

THE CLINICAL DIAGNOSIS

First, and foremost, the correct diagnosis of the eruption is essential. It is important to determine if the rash belongs to a category known to be of an industrial origin.

We have seen cases of psoriasis, or lichen planus or pityriasis rosea mistaken for occupational diseases because the patient was in contact with explosives. We have seen cases of early syphilis in which the patients were given compensation because their rash was considered industrial.

We do not intend here to discuss all the various occupational skin hazards, as 90% of them are of the eczematous type, whatever the causative agent. We will limit ourselves to a brief description of eczema.

1. Let us recall that it can be one of two types: the *acute* and the *sub-acute* or *chronic*.

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