CHLORINATED NAPHTHALENE POISONING

BY

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Chlorinated naphthalenes in the form of waxes are now used extensively in industry for insulating wire and in the manufacture of electrical apparatus. Among workers exposed to these compounds an acneform skin eruption (chloracne) characterized by pustules, papules, and comedones is common. The comedones are often accompanied by a severe pruritus, and a paronychia of the fingers sometimes occurs. The eruption is characteristically present on the extensor surfaces of the arms, especially round the elbows (Mayers and Silverberg, 1938). Jones (1941) has reported a high percentage of chloracne in this country, and gives methods of effectively reducing its incidence. In addition a number of cases of toxic jaundice due to liver necrosis have been recorded in America among workers exposed to chloronaphthalenes: in one survey the incidence was as high as 9 cases out of 250 workers exposed in three different shops (Flinn and Jarvik, 1938). The belief that chlorinated naphthalenes were the responsible toxic agents has been substantiated by the production of liver necrosis in laboratory animals by administration of these compounds subcutaneously (Flinn and Jarvik, 1936), by inhalation, and by mouth (Drinker, Warren, and Bennett, 1937). The naphthalenes are used either melted by heat or dissolved in volatile solvents. Drinker *et al.* (1937) consider that the inhalation of the fumes from these processes is the mode of absorption in the cases with hepatic damage. Jones (1941) is of the opinion that the skin lesions are produced by direct contamination.

Toxic jaundice is notifiable. We regard the present fatal case of liver necrosis following exposure to chlorinated naphthalenes as worthy of record in that it is the first case of its kind notified in Scotland, and no mention has previously been made in this country of systemic effects from these substances, although they are now in fairly common use. In addition industrial plants using chlorinated naphthalenes are being put into operation in localities where the medical practitioner is not acquainted with their injurious effects.

Case History

The patient, an unmarried woman aged 41, was admitted to the Western Infirmary, Glasgow, with a history of nausea, vomiting, and jaundice of 4 weeks' duration. She had been employed for the past 6 months at a process which exposed her to fumes from chlorinated naphthalenes (C.K. wax), but not to any greater extent than in the case of the other workers, and no personal habit could be ascertained that would have involved greater contamination than usual. A number of workers in the same shop had developed an acneform dermatitis, but there was no other case of jaundice. Unfortunately the chemically significant facts in her history were ascertained only 2 days before death.

The woman gave a history of an attack of acute rheumatism 9 years ago, but there was no subsequent history of cardiac embarrassment until the development of her last illness. There was no record of any ailment that might have entailed liver damage. About 8 weeks before admission she began to feel "off colour" and noticed that in the evening her feet and ankles became swollen. The swelling disappeared after a night's rest. At the same time a permanent puffiness developed around the eyes. Two weeks later she became breathless on slight exertion. As stated, jaundice supervened 4 weeks before admission, and, though it varied in degree and was at no time very marked, it never entirely disappeared. Troublesome nausea, unaccompanied by pain or vomiting and unrelated to food, developed shortly after the onset of the jaundice, and she then gave up her work. In spite of the nausea her appetite remained almost normal and her weight was undiminished throughout the illness. Latterly the nausea was occasionally accompanied by vomiting of a greenish-yellow bitter-tasting fluid. After vomiting the patient's thirst increased. She noticed that her urine was becoming darker, while her stools were greyish in colour.

Examination on Admission

The patient seemed well nourished, showed no signs of any great discomfort, was cheerful, and was mentally alert. A definite but not deep icteric tinge of the skin and conjunctiva was present, and a faint purpuric rash on the legs and lower abdomen, slight oedema round the ankles, and puffiness of the loose tissues round the eyes. There was no cyanosis of the lips, and she was not breathless on making the movements necessary for clinical examination. The pulse was regular in rhythm and force and of normal rate (70 a minute). The blood pressure was 145/60. The temperature was normal and remained so until shortly before death. There was a slight increase in the area of cardiac dullness. The sounds were of good quality, but pre-systolic and systolic murmurs were audible over the apex. The liver dullness was slightly diminished. The urine was dark brown and contained bile; no abnormality was detected on microscopical examination. The blood serum gave an immediate direct positive van den Bergh reaction. Apart from a slight polymorphonuclear leucocytosis, the general blood examination revealed no abnormality, and there was no evidence of excessive haemolysis. A gruel fractional test meal showed a high total acidity with no free HCl in any of the specimens and no evidence of retention of fasting juice. Blood was present in all of the specimens. The stool was yellowish and well formed, and contained occult blood.

As the jaundice was not intense and the hazard of her occupation was not known, and as there was a history of breathlessness and oedema associated with a rheumatic history and with evident endocarditis, a diagnosis of rheumatic endocarditis and myocarditis with catarrhal jaundice and slight congestive cardiac failure was made. It was felt that if the jaundice and cardiac murmurs had been manifestations of a bacterial endocarditis other more obvious and diagnostic clinical features would have been seen. The patient was given a fat-free diet, with restricted fluids and diuretics.

On the third day after admission she became sick and drowsy and the jaundice increased in intensity. Muscular twitchings of all limbs developed. A patchy brownish discoloration of the skin over the arms and chest was noted. A great reduction in the extent of liver dullness was detected by percussion. The serious nature of the condition was realized and large quantities of glucose-saline (8 pints in 2 days) were administered. The muscular twitchings stopped, but the patient continued in coma, the pulse rapidly increased in rate, and she died on the fifth day after admission with only slight increase in the jaundice.

Post-mortem Findings

The body was that of a well-nourished subject. The skin showed a moderate icteric tinge. Examination of the *abdomen* revealed moderate bile-staining of adipose tissue. The peritoneum was normal, and 2 pints of straw-coloured fluid was found in the peritoneal cavity. There was marked oedema of the loose retroperitoneal tissues, especially along the connective-tissue planes of the pancreas, enlarging the gland and accentuating its lobulation. The *liver* (weight 650 g.—normal 1,500 g.) was very small, shapeless, collapsed under a wrinkled caspule, and of very soft consistency, with, in some areas, a few firmer nodules scattered throughout, varying in size from a few millimetres up to 2.5 cm. in diameter, mainly small. On section the nodules were of a dull yellow colour; the intervening soft tissues were mainly red, but in places were a pale green. The *gall-bladder* was normal. The *stomach* contained much dark-brown mucus. No other abnormality was noted apart from deep bile-staining of the kidneys. The *heart* (370 g.) revealed moderate hypertrophy and slight dilatation of the right ventricle; the other chambers were normal in size and structure. The aortic, mitral, and tricuspid valves showed chronic rheumatic endocarditis; the aortic and tricuspid only to the extent of slight thickening and increased rigidity. The mitral valve was distinctly stenosed (2.5 cm. diameter), with moderate irregular thickening and retraction of the flaps and thickening of the chordae tendineae. The *lungs* showed moderate oedema. Section of the *left femur* revealed fatty marrow with no more than the small amount of red marrow normal to the adult. The Prussian-blue reaction for haemosiderin was negative in spleen and kidneys.

Histological Examination.—The liver showed a varying picture of acute damage, fibrous proliferation, and regeneration: (1) large areas of autolysed necrotic hepatic parenchyma; (2) islets of surviving epithelial tissue disposed in irregular dislocated columns, and with the peripheral cells often necrotic or autolysed; (3) areas with absorption of dead liver tissue revealing collapsed sinusoids with zones of congestion, haemorrhage, and round-cell infiltration; and (4) groups of small islets of liver parenchyma surrounded by bands of young connective tissue containing many poorly formed bile ducts. Almost the entire right lobe showed acute damage, contrasting with the damage in the left lobe, which was mainly subacute. There was nothing of note in the *spleen* and *kidneys*. The *pancreas* showed minute areas of necrosis in the pancreatic fat, but there was no abnormality in the parenchyma or ducts of the gland.

Discussion

The clinical and pathological findings (apart from the endocarditis) are similar to those that have been described in America in chloronaphthalene poisoning. The patient did not have any chloracne, although this appeared in other workers in the same plant: no correlation has been found between the skin and the liver lesions (Mayers and Silverberg, 1938). Illness occurred in which jaundice eventually developed, but was never severe until the patient was near death. Greenburg, Mayers, and Smith (1939) record similar histories: their 3 fatal cases were treated at home (for catarrhal jaundice) for periods of from 6 weeks to 5 months; one patient continued to work for 5 months from the onset of the jaundice, and the necessity for hospital treatment was not realized until convulsions developed.

The liver findings are consistent with the length of the history; the histological picture is not of extensive liver necrosis of simultaneous production but of recurrent liver damage taking place over a short period. Thus recent necrosis occurs side by side with various stages of repair represented by fibrous proliferation and regeneration. The areas of recent damage are much more extensive than those in which repair is taking place and regeneration is not marked. Two of Greenburg's cases appear to have suffered at least one previous attack of acute hepatitis followed by some improvement before the onset of the fatal attack. In addition to the liver damage Greenburg *et al.* record more severe pancreatic damage than in the present case, in which it was confined to minute areas of fat necrosis. These changes are thought to result from the liver necrosis and not from the effects of the toxic agent. The retroperitoneal oedema found was probably the result of giving intravenous fluids in large quantities to a subject with cardiac decompensation.

In America no predisposing factor in the affected workers has been discovered. In the present case the endocarditis, with development of breathlessness, and oedema of the feet, which disappeared on rest, suggest cardiac decompensation as a predisposing factor, especially since in the latter the liver undergoes nutritional and vascular changes. It is possible, however, that liver damage initiated the decompensation, which clinically was not severe, while the valvular lesions were of moderate grade. The puffiness around the eyes is more indicative of oedema due to a cause other than cardiac.

Drinker *et al.* (1937) have shown that animals when exposed to low concentrations of the chloronaphthalenes may incur liver damage without presenting any clinical evidence. Furthermore, when animals of this group that give no evidence of liver damage are exposed to small doses of carbon tetrachloride, well tolerated by controls, they promptly die from acute hepatic necrosis, often with marked jaundice. This raises the question whether the chloronaphthalenes may only be one of two factors in the production of liver damage. Accordingly, Greenburg *et al.* (1939) suggest that neither anyone who at any time in the past has had any liver disease nor anyone with a history of typhoid, malaria, gall-stones, or other diseases known to affect the liver adversely should work with those substances. Likewise, persons receiving hepatotoxic drugs (e.g., arsenobenzol) should not be exposed to chloronaphthalenes, nor should chloroform, trichlorethylene, or avertin anaesthesia be given to chloronaphthalene workers. The present case may suggest that no one with organic heart disease should be allowed to work with the compounds.

It is unfortunate that the serious nature of the patient's illness was not realized earlier—a comment which applies to every case so far reported. This error would be eradicated if these workers were instructed in the peculiar hazard of their occupation, for not all of them have knowledge of the technical process and the chemicals involved, and probably few medical practitioners know of the chloronaphthalenes as hepatotoxic agents. Since experimentally a certain amount of liver damage may occur without visible sign, it is clear that workers in chloronaphthalenes should receive special attention on the least indication of ill-health apart from the jaundice. Furthermore, since the concentration of chloronaphthalenes in the air of the workshop in the present case was sufficient ultimately to produce fatal hepatic necrosis in one worker who presumably had a special predisposing factor, it is possible that recurrent subclinical liver damage may be occurring in others, leading to cirrhosis.

Summary

A case is described of fatal liver necrosis due to poisoning by chloronaphthalene. This substance is now extensively used in industry for insulating wire and electrical apparatus, and there is risk of its being absorbed by the skin or by inhalation of fumes. There is evidence, from cases described abroad, that the onset of the poisoning may be insidious: slight jaundice may appear unaccompanied by more clamant symptoms which would induce the individual to cease work. In the present instance the subject had been at risk of exposure for 6 months before the onset of any illness, but, though the first symptoms were very mild, death occurred 8 weeks later. The case was complicated by the existence of rheumatic cardiac disease.

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A COMPARISON OF DYSPEPSIA IN THE ARMY FOR 1940 AND 1941

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It was hoped that a comparison of data of dyspepsia in the Army for 1941 with those for 1940 might throw some further light on the subject; but there are so many variable factors bearing upon the question for which corrections cannot be made that it is impossible to draw many conclusions.

In 1940 8,702 medical cases were seen at the hospital, and of these 1,270 (14.6%) were suffering from dyspepsia. In 1941 5,606 cases were seen—2,000 less than in 1940—and of these 974 (17.4%) were dyspeptic. The drop in the total number of cases is because Dominion hospitals have claimed their own patients. A correction should perhaps be made as 76 cases were admitted to the gastric ward direct from near-by hospitals. These cases, however, were unselected and were in different stages of investigation and treatment, many of them undiagnosed. I have included them in the results. The patients were composed of Army Class 38%, Volunteers 30%, Reservists 16%, and Regulars and Territorials 8% each. These figures differ widely from those for 1940, but they are, I think, within reasonable expectations when one considers the class of troops in the area. There may be a reduction in the number of Reservists affected during 1941, but it must be remembered that many of this class had already been discharged in 1940. Actually only 99 (10%) of the cases in this series developed symptoms for the first time after joining the Army. In 17 of these the trouble was really anxiety neurosis.