# CARBON TETRACHLORIDE POISONING

## A REPORT OF THREE CASES WITH COMMENTARIES

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Carbon tetrachloride ($CCl_4$) poisoning is uncommon in our experience, but this may well be an underestimate of its frequency, since $CCl_4$ is in widespread use in South Africa, particularly as a dry-cleaning agent. Although a fatal case of poisoning in an African following the use of $CCl_4$ as a vermifuge was reported as long ago as 1931 from Southern Rhodesia,[1] we are aware of only one report from South Africa[2] dealing specifically with $CCl_4$ poisoning. The dangers of careless and indiscriminate use are not generally appreciated, and we would agree that $CCl_4$ is an underrated hazard.[3] In Canada it has been claimed to be the commonest medical cause of acute renal failure and that the diagnosis is frequently missed. Unless specifically enquired for, a history of exposure to $CCl_4$ may not be obtained. Not only may mild cases be unrecognized, but in addition inappropriate treatment and any delay in diagnosis may determine a fatal outcome.

During the month of November 1961, two patients were admitted to the medical wards of Groote Schuur Hospital suffering from $CCl_4$ poisoning, one by inhalation and one by ingestion. While both these patients recovered, in July 1962 a patient with massive hepatic necrosis was admitted in a moribund condition and died. The clinical presentation and course of these patients was considered of sufficient importance to warrant publication and, at the same time, to review present knowledge of this condition.

### CASE 1

A white male secretary, aged 45, had been perfectly well except for mild asthma. He had always been partial to alcohol and had indulged freely at a Mardi Gras celebration. About 12 - 15 hours later he attempted to remove a grease spot from his trousers with the aid of $CCl_4$ and a few hours thereafter developed severe nausea, retching, abdominal pain, headache, giddiness and malaise. On the third day of his illness the urine became dark and urinary output decreased progressively until his admission to hospital 2 days later.

On examination he was a relatively well-looking patient with mild jaundice. He had palmar erythema and questionable clubbing of the fingers. There were a few spider naevi on the anterior chest wall. There were no signs of dehydration. The blood pressure was 130/70 mm.Hg. The liver was just palpable and tender and the right kidney was easily palpable. Further systematic examination was normal. The urine contained 2-plus albumin and was of low specific gravity. It was dark-brown in colour, but bile, urobilinogen, porphyrins and haemoglobin were absent.

The haemoglobin level was 14 G. per 100 ml., the PCV 46%, and the ESR 15 mm. in the 1st hour. The leucocyte count was 11,000/c.mm., with 47% polymorphs, 46% lymphocytes, 1% monocytes, 5% eosinophils, and 1% basophils. The reticulocyte count was 1%, serum bilirubin 2·6 mg./100 ml., conjugated bilirubin 1·9 mg./100 ml., blood-urea level 182 mg./100 ml., serum albumin 3·4 G./100 ml., serum globulin 3·0 G./100 ml., thymol turbidity 1, zinc turbidity 11, cephalin cholesterol 3, serum sodium 130 mEq./l., serum potassium 3·8 mEq./l., serum chloride 95 mEq./l., serum cholesterol 180 mg./100 ml., and serum amylase 20 units/ml. The electrocardiogram (ECG) was normal. Chest X-ray showed some old scarring at the right apex. On X-ray of the abdomen only the right kidney was visible and was noted to be larger than normal.

*Course (Fig. 1)*

Despite an adequate intake of glucose and water only 30 ml. of urine were passed during the first 12 hours. Thereafter the conservative regime for the management of acute renal failure was instituted.[4] A serum-potassium level of 6·2 mEq./l.

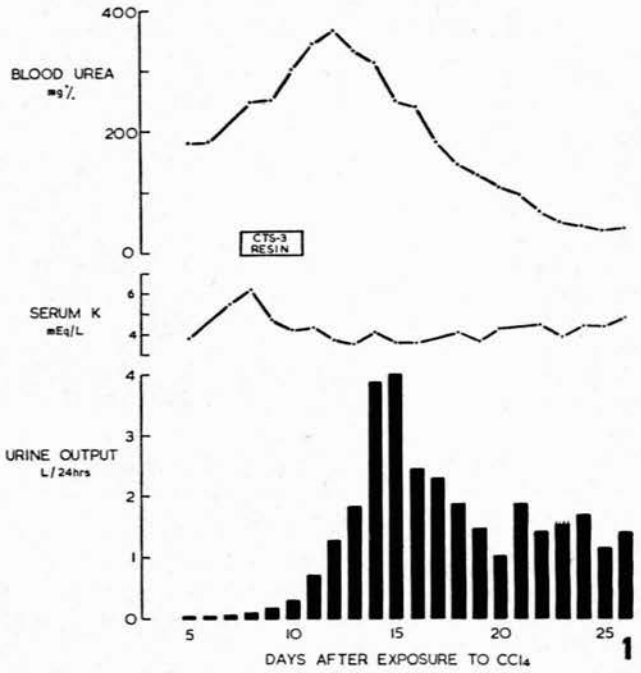


*Fig. 1.* This shows the effect of conservative management on blood urea and serum-potassium concentration, as well as the urine output in Case 1. Mild hyperkalaemia responded to treatment with CTS-3 resin.

associated with the ECG changes of severe hyperkalaemia necessitated the use of an exchange resin (CTS-3*).

Six days after admission and on the 11th day following exposure to $CCl_4$, diuresis commenced. Two days later the urine output reached 1 litre. The peak blood-urea level was 368 mg. per 100 ml. At the height of the diuresis, when the urine volume reached 4 l. a day, mild hypokalaemia developed. Eleven days later the blood urea had reached normal levels. The serum bilirubin and the serum electrolytes were normal by the 16th day after exposure. Three weeks after admission the right kidney was just palpable, the intravenous pyelogram was normal and the creatinine clearance was 65·9 ml. per minute. The urine was now protein-free. The patient had started to regain powers of urinary concentration. Blood pressure was normal and palmar erythema and clubbing appeared to be less prominent.

*Comment*

The following points are of interest:

1. *The brief nature of exposure to $CCl_4$.* At first it was felt that contact was too insignificant to warrant a confident diagnosis of $CCl_4$ poisoning. However, it was later established that the exposure took place in a small bath-

*Supplied by courtesy of Eli Lilly & Co.

room under conditions of poor ventilation. Cases of fatal poisoning have been reported following the use of $CCl_4$ in a small bathroom and similarly when grease spots have been removed from clothing in a closet.[5] The safe limit for acute poisoning is 1,000 parts per million (ppm) of air according to the National Safety Council of the USA.[6,7] For more chronic exposure a concentration of 100 ppm for 8 hours daily[6] has been considered a safe concentration, but more recently the tendency has been to regard 25 ppm as the safe level.[8,9]

2. *The history of alcoholism and previous alcohol ingestion.* The fatty liver of the alcoholic is said to be peculiarly susceptible to the effects of $CCl_4$. A history of alcoholism was obtained in only 9% of Smetana's cases,[10] but no less than 65% of Hardin's 77 patients[9] had such a history. It appears that ingestion of alcohol before exposure to $CCl_4$ increases its toxicity.[1,3,9-13] $CCl_4$ is soluble in alcohol and thus its absorption, either from the lungs or gut and its transport in the blood are facilitated. Renal excretion is also favoured under these circumstances, leading to an increased likelihood of renal damage. A history of previous ingestion of alcohol was obtained in 75% of the series of Guild *et al.*[11] They suggested that $CCl_4$ is oxidized to phosgene which can combine with ethanol to form ethylchloroformate. This may be more toxic than $CCl_4$. In the absence of ethanol, $CCl_4$ is oxidized to phosgene and ammonia, the latter being converted to urea. Only the $CCl_4$ itself is then likely to be the noxious agent.

3. *The method of poisoning.* There is no major difference in the symptoms of poisoning by inhalation, by ingestion or by absorption through the skin. After ingestion of $CCl_4$, its level is higher in the portal blood stream than in the systemic blood; thus the main effect of $CCl_4$ is manifested in liver damage. After inhalation, however, the blood concentrations reaching the kidneys and liver are the same and, by virtue of the fact that water is absorbed from the tubules, $CCl_4$ is more concentrated here and the chances of renal damage are higher. This is well illustrated in this case and is in conformity with the experience of others.[10]

4. *The dark colour of the urine.* This could not be explained by the usual tests, nor was there evidence of any indicator substance being present. The possibilities considered were the presence of an unidentified degradation product or an excess of urochrome.

CASE 2

The patient was a 36-year-old white male, a chronic alcoholic. He had previously undergone treatment for depression, having been admitted to an institution on 5 previous occasions. He had consumed immoderate quantities of liqour from 29 to 31 October 1961. In a fit of depression on 31 October he ingested about 150 ml. of $CCl_4$. He vomited immediately, but from then on he suffered from anorexia, nausea, vomiting, abdominal cramps and intermittent diarrhoea. On admission on 3 November he was an apathetic, depressed, thin man with a temperature of 100·4°F. The pulse rate was 95 beats per minute and the blood pressure 130/95 mm.Hg. There were no other abnormal signs apart from a 3-finger tender hepatomegaly, and a left sixth nerve palsy, left-sided deafness and a fractured mandible — residua of a motor-car accident. The haemoglobin level was 16 G. per 100 ml., the ESR 5 mm. in the 1st hour and the leucocyte count 12,000 per c.mm. There were 60% polymorphs and 40% lymphocytes. X-ray of the chest showed a normal heart size and clear lung fields.

*Course*

In the first 7 days his course in hospital was reported as uneventful, apart from intermittent nausea. During the first day he passed 240 ml. of urine and on the 2nd day 120 ml., but thereafter the daily urine volume was approximately 500 ml. On the 7th day he was reported to have had a small haematemesis and a haemoptysis, which were repeated on the 8th day in hospital. On the 9th day he suddenly became cyanosed and distressed, a marked tachycardia developed and his blood pressure rose to 140/110 mm.Hg. On day 10, the blood pressure was 160/125 mm.Hg, and acute pulmonary oedema supervened. His blood-urea level was then found to be 344 mg./100 ml. Total bilirubin was 1·8 mg./100 ml., conjugated bilirubin 1·1 mg./100 ml., alkaline phosphatase 3·8 Bodansky units, thymol turbidity 1, serum albumin 4·5 G./100 ml., serum globulin 2·4 G./100 ml., cephalin cholesterol 2, and thymol flocculation 4. The serum calcium was 9·7 mg./100 ml., serum sodium 132 mEq./l., serum potassium 5·4 mEq./l., and serum chloride 88 mEq./l. Serum bicarbonate was 21·4 mEq./l. X-ray of the chest now showed a uraemic lung picture, the ECG showed a sinus tachycardia, left ventricular strain and minor ST-T wave changes. The urine output on this day was 720 ml. Treatment of pulmonary oedema was undertaken. On day 11, when the blood-urea level was 334 mg./100 ml., the patient passed 3,000 ml. of urine. Urine examination was normal apart from a few casts.

At this stage the patient was referred to members of the renal unit as having acute renal failure following $CCl_4$ ingestion. It was agreed that this was the diagnosis, and conservative management was advised. In view of the pulmonary oedema and despite a 24-hour urinary output of 3 l., the daily fluid intake was limited to 1,500 ml. of 15% lactose. Three grams of sodium bicarbonate plus 3 G. of potassium chloride were given daily. His further treatment was as for patients in the diuretic phase of acute renal failure. Normal quantities of urine were passed 6 days after the onset of the diuresis. The blood-urea level was 43 mg./100 ml. 10 days after the peak blood-urea level. Initially there was mild hyponatraemia, hypochloraemia and acidosis, the lowest serum $CO_2$ being 18·3 mEq./l. The serum electrolytes were normal by the 18th day.

Treatment during the first 10 days included 50 mg. of 'sparine' *t.d.s.*, 50 mg. of 'benadryl' *q.i.d.*, and 'plebex', 4 ml. daily.

*Comment*

As in the previous patient, there was a history of long addiction to alcohol and recent over-indulgence. The evidence of hepatic damage was mild and renal involvement was not recognized until late in the course.

The main interest in this case lies in the development of pulmonary oedema 10 days after admission to hospital and 13 days after ingestion of $CCl_4$. After the first 2 days of oliguria the patient's urinary output varied between 420 and 1,050 ml. daily. The attending physician did not appreciate that a urinary output of this magnitude was compatible with acute renal failure, and hence the fluid intake was not restricted. The diagnostic pitfall of non-oliguric renal failure, although well documented,[4,14,15] is not sufficiently appreciated. As in this case, injudicious fluid administration results in the inevitable development of pulmonary oedema.

CASE 3

The patient was a 47-year-old white spinster who was partial to alcohol. Two days before admission to Groote Schuur Hospital she attended a celebration at which she decanted brandy from a gallon jar into a convenient 'half jack'. She failed to note that this bottle contained $CCl_4$. She became ill, with nausea and vomiting, and following gastric lavage at a local hospital was allowed to go home. The following day she claimed to be quite well, but the next afternoon she complained of abdominal pain and collapsed.

On admission, she was an obese, jaundiced woman. She was confused and noisy at first, but within half-an-hour became unconscious. The temperature was subnormal and mottled cyanosis of the extremities was striking. The pulse rate was 130 per minute and the blood pressure 130/90 mm.Hg. There were no abnormal physical signs except for absent reflexes and dilated pupils. The haemoglobin level was 14·5 G. per 100 ml., the ESR was 30 mm. in the 1st hour and the white-cell count was 10,000 per c.mm. Bladder catheterization produced only a few drops of urine. Coffee-ground material was aspirated from the stomach. Intravenous dextrose and hydrocortisone was administered. Although the state of consciousness fluctuated, there was no real improvement and she died 11 hours after admission.

Autopsy findings (by courtesy of Dr. P. A. Luckhoff) included widespread hepatic necrosis and diffuse fatty change. There were occasional scattered small islands of surviving cells at the periphery of the liver lobule. The kidneys showed degenerative changes in the tubules.

*Comment*

This patient, as in the case of the others, had been partial to alcohol and had indulged freely just before ingesting $CCl_4$. The early death on day 3 was the result of acute liver failure from massive necrosis of the liver. Oliguric renal failure was also present.

## DISCUSSION

It is not surprising that $CCl_4$ poisoning has figured prominently in medical literature, since $CCl_4$ is used as an extractant for fats and oils, as a solvent in rubber cements and textile soaps, as a cleaning fluid, and as a dry-cleaning and degreasing agent. Apart from its extensive use in fire extinguishers and as a fumigant for grain and silage, it has also been incorporated in hair shampoos and administered medicinally as a vermifuge.

$CCl_4$ poisoning is almost invariably caused either by ingestion or inhalation. Inhalation occurs most commonly while cleaning furniture, clothes or machinery under conditions of poor ventilation. The effects of $CCl_4$ poisoning are modified by previous ingestion of alcohol or fat which facilitate absorption. Active peristalsis at the time of ingestion of $CCl_4$ cuts down absorption from the gut and, therefore, diminishes the blood levels.[7]

A general account of $CCl_4$ poisoning is included in a Medical Research Council publication, 'Industrial Health Research Board, Report No. 80', by Browning.[6] Smetana, in 1939,[10] reviewed 141 cases, including 3 of his own. He drew attention to the importance of the renal lesion in $CCl_4$ poisoning. In 1949, Sirota[16] discussed the mechanism and picture of renal insufficiency in $CCl_4$ intoxication. Hardin,[9] in covering 77 cases, analysed the literature up to 1953 and discussed many aspects of $CCl_4$ poisoning emphasizing the greater frequency of alcoholism and renal involvement. Since 1954 there have been several general reports, including those of Guild *et al.*,[11] Shiels[17] and Joron *et al.*[3]

*Clinical Features*

The findings depend largely on the amount of $CCl_4$ ingested or inhaled and the time which has elapsed since exposure. The clinical presentation has been subdivided into acute, subacute or chronic poisoning.

*Acute poisoning.* A rapid onset and a short duration of symptoms characterize these cases. Sudden unconsciousness is followed either by quick recovery or sudden death. Some of the patients who recover are truly anaesthetized,[9] and death in the acute stage may be due to the anaesthetic effect of $CCl_4$.[18] However, it is known to cause acute myocardial damage,[7] and ventricular fibrillation is the probable cause of death.[2,9] Death in this phase has also been attributed to circulatory collapse owing to the effects of $CCl_4$ on the vasomotor system.[7]

*Subacute poisoning.* The 3 cases reported here are of this, the most important, type. The onset is slower and the duration of symptoms is longer. The initial symptoms which occur 1 hour - 6 days after exposure[11] are usually in the first instance due to the effects of $CCl_4$ on the central nervous system, i.e. giddiness, headache, ataxia and weakness, followed shortly by the effects of gastro-intestinal irritation — nausea, anorexia and vomiting — and later by symptoms of backache, abdominal pain and malaise. About 1 - 4 days after exposure, the patient may die of acute massive necrosis of the liver as in our case 3. This is the common cause of death.[11] If the patient survives, then 1 - 3 days after exposure hepatic and/or renal effects manifest themselves. The renal presentation is more common.[3] Oliguria may occur 1 - 7 (mean 3) days after exposure,[11] and the oliguric phase usually lasts 1 - 3 weeks, while the diuretic phase lasts 1 - 2 weeks.[9] Other effects at this stage include gastro-intestinal or pulmonary haemorrhage. Haemorrhagic diathesis: The mechanisms suggested include (*a*) hypoprothrombinaemia, (*b*) hypofibrinoginaemia and possibly hypocalcaemia, (*c*) uraemia, and (*d*) a direct effect of $CCl_4$ on the blood vessels. Pulmonary effects have been described.[19-21] In 4 out of 20 cases of $CCl_4$ poisoning, radiological changes varied from pulmonary infiltration to consolidation of 5 lobes.[19] One patient at autopsy was found to have an acute haemorrhagic pneumonia. The changes of pulmonary oedema and so-called uraemic lung account for most of the pulmonary findings. This is supported by the fact that in 27 men who died of $CCl_4$ poisoning, neither the anatomical nor the radiological alterations occurred before the 9th day, at which time uraemia was well advanced.[21] Myocarditis with ECG changes[9] and acute haemorrhagic colitis[9] may occur in $CCl_4$ poisoning and it is probable that pancreatitis is an accompaniment of alcoholism. The adrenal gland has also been found to be sensitive to $CCl_4$.[9]

*Chronic $CCl_4$ poisoning.* Systemic effects follow moderate exposure over a prolonged period. Contact with low concentrations of $CCl_4$ over a period of years is accompanied by such symptoms as giddiness, nausea, vomiting, headache and fatigue. The occurrence of dyspeptic symptoms, especially nausea and vomiting, in factory workers exposed to 45 parts of $CCl_4$ per million parts of air has been noted.[22] These symptoms disappeared when exposure to $CCl_4$ was stopped. Effects were thought to be due to $CCl_4$ stimulating the autonomic nervous system. There is a small group who develop partial loss of visual fields or even complete loss of vision. Optic neuritis and optic atrophy have been reported.[9,23] Although aplastic anaemia has been attributed to chronic $CCl_4$ exposure,[24,25] this is not generally accepted.[26,27] Severe hyperchromic anaemia resulting from liver damage or a direct effect on bone marrow,[7] and haemolytic anaemia, purpura and thrombocytopenia, have all been reported.[25,26] Finally, cirrhosis and hepatomas have been reported as long-term effects of exposure to $CCl_4$.[7,9]

*Diagnosis*

The association of hepatic failure and acute renal failure should always raise the possibility of $CCl_4$ poisoning. A history of exposure to $CCl_4$ should be sought in any case presenting with unexplained renal failure and/or hepatitis and/or haemorrhagic diathesis. Frequently, too, the onset may be suggestive of an acute abdominal gastro-intestinal illness — nausea and vomiting, and severe abdominal pain and tenderness leading to erroneous diagnosis and incorrect treatment.

Serum glutamic oxalacetic transaminase (SGOT) levels may be found to be raised in acute $CCl_4$ poisoning[28-30] and are an index of the degree of liver damage. If facilities are available, in doubtful cases blood levels of $CCl_4$ can be estimated with an infrared spectrophotometric technique.[31]

*Prognosis*

If a patient survives after a single episode of acute or subacute $CCl_4$ poisoning, recovery is complete. Most deaths in the subacute phase occur within 3 - 10 days from hepatic necrosis or acute renal failure. If death does not occur from massive hepatic necrosis, the patient has a 75% chance of recovering from the oliguric renal failure, according to the series of Guild *et al.*,[11] and probably a 100% chance of recovery from hepatitis. Regeneration after experimental $CCl_4$ liver injury is maximal 36 - 72 hours afterwards and repair is virtually complete after 120 hours.[32] In the series of Guild *et al.* the mortality was highest in those who ingested $CCl_4$, presumably because of the increased danger of acute massive hepatic necrosis under these circumstances.

*Mechanism of Action of $CCl_4$*

Much has been written on the mechanism of action of $CCl_4$ and even today this has by no means been elucidated. It would seem, however, that following the pioneering work by Christie and Judah[33] and many subsequent investigators, the solution may be near at hand. It should be noted that most of the experimental work has been carried out on rats.

Since the maximal effect of $CCl_4$ poisoning on the liver is on the centrilobular zone, Glynn and Himsworth[34] suggested that the necrosis was due to the anoxic damage caused by the swollen parenchymal cells impinging on the sinusoids, resulting in centrilobular cellular anoxia.

Christie and Judah, in 1954,[33] however, found that the earliest biochemical changes which precede the histological finding of cellular necrosis involve disorganization of mitochondrial tricarboxylic acid cycle activity. The enzyme systems first involved were those which required pyridine nucleotides for electron transport. On pre-incubation with $CCl_4$, liver mitochondria from normal rats produced a similar pattern of inhibition. They suggested that $CCl_4$ attacked mitochondria directly with loss of respiratory co-factors, thus inactivating pyridine nucleotide-dependent enzyme systems.

Dianzani[35] at about the same time found that $CCl_4$ uncouples oxidative phosphorylation and, in destroying mitochondrial function, deprives the cell of adenosine triphosphate with a secondary failure of fatty acid oxidation.

Calvert and Brody[36] agreed that the maximal effect of $CCl_4$ is on the mitochondria, but this results from anoxia owing to constriction of intrahepatic blood vessels, since mitochondria subjected to anoxia show the same changes as $CCl_4$ exerts on mitochondria.[37] They claimed that $CCl_4$ acts on the central nervous system causing a massive sympathetic discharge which results in: (*i*) constriction of intrahepatic blood vessels leading thus to anoxia; (*ii*) the stimulation of the adrenal medulla with release of epinephrine and nor-epinephrine, thus enhancing the vascular response;[36] and (*iii*) release of catecholanines at the same time which mobilize UFA* from the fat depots, with a rise in their blood level and resultant deposition of fat in the liver.[36,38] A serious objection to this theory, however, is the fact that no decrease in liver blood flow can be demonstrated after $CCl_4$ administration.[39]

Subsequent to 1958, Recknagel and his co-workers[40-44] described biochemical changes which took place in the cell *before* mitochondrial disorganization could be demonstrated. Gross mitochondrial changes occur only at 20 hours,[42] but before this electron microscopy shows an effect on the endoplasmic reticulum[45] and microsomal function has already declined.[46]

In 1961, Recknagel and Lombardi[44] showed that 1½ - 2 hours after feeding $CCl_4$ to rats, $CCl_4$ concentration is maximal in the liver and already microsomal enzymes and endoplasmic functions are disordered. At this stage, too, there is rapid accumulation of triglyceride in the liver. Based on the work of Byers and Friedman in 1960,[47] they suggested that a mechanism intimately associated with hepatic lipid metabolism is localized in the membranous component of the endoplasmic reticulum and is probably the key locus involved. They suggested that the formation of triglyceride by the liver is not interfered with, but that $CCl_4$ poisons the hepatic triglyceride secretory mechanism, thus leading to triglyceride accumulation in the liver. Judah and Rees,[48] however, showed excessive phosphatidic acid production in liver cells and, even with optimal supplies of choline, much of the glyceride is diverted to neutral fat.

The composite picture emerging, therefore, is that $CCl_4$ enters the liver cell by its effects on membrane permeability (perhaps because $CCl_4$ is a lipid solvent). As a result of the changes in the membrane permeability, the cell starts to swell and with the swelling there is a depression of microsomal and endoplasmic function leading to an accumulation of triglyceride. Secondarily, 20 hours after $CCl_4$ has entered the cell, there is significant mitochondrial swelling with disruption of the enzyme systems, especially those responsible for energy production. This leads to nuclear death and consequent cellular necrosis. Of importance is the work by Leduc and Wilson[49] who showed that the changes short of mitochondrial damage are still reversible. The centrilobular zones of the liver are particularly affected, possibly by a local anoxic effect or because these cells have an increased susceptibility to the action of $CCl_4$.

*Prophylaxis of the Effects of $CCl_4$ in Experimental Animals*

Initially the experimental use of various substrates, e.g. 'aureomycin', folic acid and cortisone, produced variable results,[50] but as an understanding of the mechanisms of $CCl_4$ action increased, so the attempts at prophylaxis in rats became more rational.

It was hoped that nicotinic acid and DL tryptophane would stimulate pyridine nucleotide formation and, therefore, maintain mitochondrial function, but these precursors were only helpful if given before $CCl_4$ administration.[51] Likewise, versene was used *in vivo* to block depression of DPN-linked dehydrogenase activity, but with little success.[52] Vitamin $B_{12}$ was claimed to assist in a non-specific way if given in massive doses. By increasing the levels of mitochondrial $B_{12}$ it may protect mitochondrial integrity.[53-55] In the same way sulphaguanidine[49] and 5-hydroxytryptamine[56] are thought to offer some protection by their non-specific action on mitochondrial integrity.

The most promising work in this field, however, is the observation that with the administration of 'phenergan' to $CCl_4$-poisoned rats there is no significant release of hepatic enzymes into the blood, and hepatic necrosis is almost completely prevented.[52] It thus maintains mitochondrial integrity, preventing swelling of the membrane and ionic shifts and their consequences. It does not act by detoxicating $CCl_4$ and has to be administered in very large doses. It is apparently effective, even if given after $CCl_4$ administration. If given immediately after administration and continued for 48 hours it almost completely prevents hepatic necrosis. It causes a delay of necrosis if given up to 6 hours after $CCl_4$ administration.

## MANAGEMENT OF A CASE OF $CCl_4$ POISONING

*Prevention*

Most important of all is prevention, and to date too little attention has been paid to this aspect. In terms of

*Unesterified fatty acids.

the Medical, Dental and Pharmacy Act, $CCl_4$ is classed as a 'poisonous substance'. The Act provides:

> that no poisonous substance shall be sold by retail by any person other than in containers (*a*) securely closed, free from leaks, and strong enough to withstand rough usage; (*b*) distinctly labelled with the name of the substance in English and Afrikaans; (*c*) conspicuously marked 'Poisonous — Dangerous' and 'Giftig — Gevaarlik'; and (*d*) bearing the name and address of the seller. Furthermore, where the substance is a liquid and the quantity is less than 30 fluid ounces, the container shall be distinguishable by touch from ordinary containers. Failure to comply with any of the above requirements is an offence punishable by a fine not exceeding fifty pounds (one hundred rand).[57]

This warning is, in our opinion, inadequate. All too often, especially with members of the lay public, the dangers of $CCl_4$ when used for dry-cleaning are not sufficiently realized. It is used carelessly without the necessary attention to adequate ventilation. It would seem highly desirable, therefore, that all containers in which $CCl_4$ is sold should in future be labelled in addition: 'Harmful vapour. Harmful if swallowed. Avoid prolonged breathing and prolonged contact with the skin. Adequate ventilation essential. Do not use in closed rooms'.

In industry, too, workers should be adequately protected with masks. Frequent checks on the concentration of $CCl_4$ in the atmosphere should be made, receptacles for dirty rags should be provided with lids and spilled $CCl_4$ should be carefully removed. Ventilation must, of course, be adequate. $CCl_4$, it is hoped, is no longer used as a vermifuge.

*Treatment*

In the event of poisoning, the patient should be removed from all contact with $CCl_4$. Dirty clothes should be removed and the skin cleaned, and, if the eyes are contaminated, irrigation with water is necessary. If $CCl_4$ has been ingested, Epsom salts should be administered following gastric lavage to increase peristalsis and to diminish absorption. The patient should remain in hospital under close observation for 3 - 7 days. At the onset, careful observation of pulse rate, blood pressure and level of consciousness is necessary. If there is vasomotor collapse, sympathomimetic drugs are not advised because of the danger of serious arrhythmia resulting from their effect on a depressed and sensitized myocardium.[7]

Evidence of hepatic involvement (SGOT levels if necessary) and renal failure (urine output and blood-urea levels) should be carefully watched for. Treatment of the hepatic disorder, the renal failure and haemorrhagic manifestations follows conventional lines. The place of phenergan needs to be established. It was thought to be of value in one patient.[30] In view of the experimental work it is doubtful whether it will be possible to administer this drug soon enough or in sufficient dosage in the average patient.


## SUMMARY

Some of the important effects of $CCl_4$ are illustrated in the presentation of three patients, two of whom recovered.

Interesting new developments in the understanding of the mechanism of action of $CCl_4$ and the possible prevention of its effects are discussed.


It is hoped that efforts will be made to inform the lay public of the care that must be exercised when $CCl_4$ is used, so that further cases of inadvertent $CCl_4$ poisoning may be prevented.

We wish to thank our colleagues for referring these patients to the Renal Insufficiency Service, which is one of the activities of the CSIR/UCT Renal-Metabolic Research Group. We are indebted to Prof. J. E. Kench and the staff of the Department of Clinical Pathology for many of the biochemical findings.

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