ABSTRACTS

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INDUSTRIAL TOXICOLOGY


After a review of the literature dealing with acrylonitrile, its properties and toxicity, and the methods in use for its determination in air, a new spectrophotometric method of estimation whereby very small quantities can be determined (20 to 60 litres for concentrations of 10 to 100 p.p.m.) is described in detail. The air to be tested is drawn at a rate of 1 litre per minute through two gas-washing bottles connected in series, each containing 300 ml. of water and being immersed in an ice bath. The quantity of acrylonitrile dissolved in the water is then estimated spectrophotometrically from the ultraviolet absorption spectrum, a wave-length of 210 m. being chosen. The methods of sampling and of estimation, the details of which are clearly described, were tested against the Kjeldahl (Petersen and Radke) method with satisfactory results. For the detection of acrylonitrile in blood, 1 ml. of blood is diluted tenfold with 0.1 N caustic soda and the solution heated to 30°C and aerated for 30 minutes in two narrow tubes, each containing 10 ml. of water, which are connected in series and immersed in an ice bath, the aqueous solutions being then examined spectrophotometrically in the same way.

Rats, dogs, and monkeys were each exposed for 7 hours to acrylonitrile vapour in air, the concentration being determined by the above method. No acrylonitrile was found in the blood of these animals, but estimations were made of the haemoglobin and methaemoglobin content, and of the concentration of cyanide in whole blood, erthrocytes, and plasma, and of thiocyanate in whole blood, plasma, and urine. Cyanide was present in high concentration in the blood of dogs exposed to concentrations of acrylonitrile from 100, 75, or 50 p.p.m. (all 6 dogs exposed to 100 p.p.m., and 3 of the 4 exposed to 75 p.p.m. dying), and in the blood of rhesus monkeys exposed to 75 p.p.m. (one of the 3 exposed dying). Only very small amounts were present in the blood of rats exposed to 100 p.p.m. (4 out of 20 dying) and none in that of rats exposed to lower concentrations. Most of the cyanide present in the blood was in the erythrocytes. Cyanmethaemoglobin was found in the blood of all these animals. Thiocyanate was present in very high concentration in the plasma of the rats and in low concentration in the plasma of the dogs, its concentration varying inversely with that of cyanide and with the severity of toxic signs. In the early stages of exposure the venous blood was hyperoxygenated and bright red in consequence of the histotoxic anoxia; later the blood became darkened. The animals severely exposed suffered brain damage characteristic of anoxia, the cortex being most severely affected. Similar changes, but of lesser degree, were present in those animals exposed to lower concentrations and which had shown no toxic symptoms. It is concluded that the toxicity of acrylonitrile is due to the formation of cyanide in the body. The cyanide is further metabolized to thiocyanate, which is excreted in the urine. Emergency treatment with amylnitrite by inhalation and sodium nitrite and thiosulphate intravenously is recommended in cases of acrylonitrile intoxication.

[This is an important paper.]

M. A. Dobbin Crawford.


Toxaphene, a chlorinated camphene with the formula C10H12Cl8, is one of the newer insecticides. It is an amber-coloured, waxy solid with a wild, pine-like odour and contains 67 to 69% chlorine. It melts at 70° to 95°C., is insoluble in water but soluble in oils and in the common fat solvents, and is practically non-volatile. It is a slow-acting, residual insecticide and is used in the form of a dust, emulsion, spray, or wettable powder. It has been widely employed for grasshopper control and as a supplement to DDT. It has also been used as a cattle dip, but should not be used for dairy cattle or in dairy cow-houses. It is not safe for household use, nor is it suitable for delousing, in spite of its persistence and its resistance to laundering.

Toxaphene causes a diffuse stimulation of the brain and spinal cord, resulting in generalized tetanoid or clonic convulsions which return at intervals of 3 to 5 minutes and terminate in respiratory failure. In experimental animals salivation and emesis precede fits, but these symptoms have not been observed in human beings. The lethal oral dose for man has been estimated as being
from 2 to 7 g. Toxaphene can be absorbed through the gastro-intestinal tract, through the respiratory tract, and through the skin. In solution it is readily absorbed; in the solid form it is absorbed in toxic amounts depending upon the species of animal and the concentration of the powder (dust) used. Toxaphene is approximately four times as acutely toxic as DDT to most animals. It is probably stored in the fat deposits of the body, and is believed to be slowly detoxified in the liver (as camphor is known to be) as analysis of the urine has yielded ethereal sulphates and gluconic acid conjugates of toxaphene. It is excreted also in milk.

When toxaphene has been ingested it is urgently necessary to evacuate the stomach and intestines by means of gastric lavage or induced vomiting, and saline cathartics. Oily cathartics are contraindicated, as they may possibly aid absorption. Early medication for the prevention or control of convulsions is necessary, and for this the barbiturates are effective. If given before the onset of convulsions the slow-acting depressants, such as phenobarbitone sodium, are the drugs of choice; if convulsions have already started, the quick-acting barbiturates such as pentobarbitone sodium are more effective, and full anaesthetic doses can be given if necessary. If convulsions have started, it is imperative to give sufficient barbiturate quickly, for the longer the convulsions persist the more difficult are they to control.

M. A. Dobbin Crawford.


"Toxaphene" (chlorinated camphene), one of the newer insecticides, is a convulsant drug which, having a specific effect upon the central nervous system, provides no warning symptoms such as nausea, colic, or diarrhoea. From 1 to 3 or more hours after the poison has been swallowed, the convulsions suddenly begin and there is loss of consciousness. In this paper 4 cases are reported in detail occurring in young children who had access to the insecticide; 3 of the children died from asphyxia during a convolution; the fourth recovered after receiving large doses of phenobarbitone and curare intramuscularly.

Also reported are two instances of group poisoning which followed the eating of green vegetables which had previously been sprayed with toxaphene. The vegetables had been washed in water and cooked before being eaten; in one instance they had been boiled for one hour with salt pork, and 3 of the people who partook of this food became convulsed; all recovered following treatment by gastric lavage or with apomorphine and sedation by phenobarbitone sodium. The published results of animal experiments are quoted. Toxaphene in an oily solution can be absorbed through the skin of rabbits, a dose of 250 mg. per kg. body weight causing death within 24 hours, but there is poor absorption by the skin if the drug is applied in an inert powder. Anaesthesia with barbiturates has protected dogs from the effects of supralethal doses. Where convulsions have already started, pentobarbitone sodium is the drug of choice.

No case of industrial poisoning is on record. Toxaphene has been produced and investigated during the past 5 years. M. A. Dobbin Crawford.


That advanced chronic nephritis is now rarely found in lead workers is largely due to the statutory measures adopted for their protection. The 3 patients whose cases are here recorded had each had prolonged industrial exposure to lead, and during the early years medical supervision was quite inadequate. Two of the men were employed in the recovery of lead from the gases evolved from the roasting ovens, hearths, and blast furnaces of a lead works. The fumes were led through pipes 40 cm. (16 in.) in diameter threaded with a high-tension cable whereby the dust, consisting of metallic lead, lead oxide, and lead sulphide, was ionized and deposited on the inner wall of the piping and on the cable itself, to be knocked off later. Exposure was severe. One man had been employed here continuously for 16 years, and the other for 22 years except for an interval of 2 years following an acute attack of lead poisoning. The symptoms of hyperpiesis eventually caused each of these men to consult his doctor, the blood pressure being 240/120 mm. Hg in the one and 250/160 mm. Hg in the other. At this stage their conditions were very similar, with headache, backache, defective vision (due to albuminuric retinitis), slight anaemia (though no stippled cells could be found), and albuminuria, the urine containing a few erythrocytes, leucocytes, and epithelial cells. One man carried on at light work, his working capacity being reduced by 75%, and a year later his condition showed little change. The other had two attacks of epileptiform convulsions and died within a year of diagnosis. At necropsy there was marked hypertrophy of the left ventricle of the heart and the changes typical of an intracapillary glomerulonephritis, many of the glomeruli being completely hyalinized and obliterated, while the arterioles were markedly sclerotic, the vasa afferentia alone escaping this change. It could not be determined whether the primary change had been a glomerulonephritis or a capillary injury due to the toxicity of lead.

The third man, aged 44, had been employed for 25 years at a lead-paint factory on the various processes (which are described) in the production of white lead 2 PbCO₃, Pb(OH)₂, which, although almost insoluble in water, is sufficiently soluble in the body fluids to be toxic. He suffered recurrent attacks of acute lead poisoning in 1927, 1930, and 1934. In 1938 an increase was found in the number of stippled erythrocytes in his blood, and severe hypertension with cardiac insufficiency developed. By December, 1949, his heart was dilated, his joints were swollen, and he had constant albuminuria. He died from ureaemia in February, 1950. His death was attributable to failure to recognize that his recurrent attacks of acute intoxication indicated a susceptibility to lead which required his removal from contact with the metal at an early stage.
These three cases emphasize the importance of regular and thorough medical supervision of all lead workers, and of their removal from hazard at the first suspicion of warning symptoms related to the urinary system. The issue may be fatal without the appearance of other classic signs of lead intoxication.

M. A. Dobbin Crawford.


The use of sodium thiosulphate in the treatment of lead poisoning was first reported on by Dennie and McBride (Arch. Derm. Syph., Chicago, 1923, 7 (63). Pincus published a short note of his experience in this form of therapy in 1936 (Med. J. Aust., 1936, 1, 463), and the present author outlines the work done at Mount Isa, Australia, in more detail. The lead-mine at Mount Isa employed about 1,200 men in 1935, and between 1931 and 1936 there were respectively 69, 95, 77, 71, 71, and 71 compensable cases of lead-poisoning each year. All these cases were examined by a medical board, but there was a number of milder cases in addition. The author has selected 18 cases to illustrate the value of sodium thiosulphate in treatment. All the patients received this form of therapy, but some were given calcium to control colic, while one case required morphine.

The effects of treatment were judged clinically by the medical board, who formed the opinion that the improvement under this method of treatment was more rapid than could be accounted for by removal from exposure to lead. The ratio between monocytes plus large lymphocytes and small lymphocytes was used to judge this improvement numerically. Before this treatment was instituted the average ratio for the 18 cases was 1:23, whereas after some days' treatment it rose to 3:22, which approaches the normal value for persons at Mount Isa who are exposed to lead but are without symptoms.

The injections consisted of 30 mg. of sodium thiosulphate in a few ml. of water, given on alternate days. Two or 3 to 12 or more injections were required.

W. K. S. Moore.


The toxicity of the following mercurials, all of which are used as seed disinfectants, has been examined: methyl and ethyl dicyandiamide, methyl mercury chloride, phenyl mercury acetate, and mercuric chloride. The LD50 for a single intraperitoneal injection in mice observed for 7 days was estimated for each drug, the results being 0.39, 0.38, 0.31, 0.26, and 0.14 mg. per kg. body weight respectively. Subcutaneous injection produced severe and widespread necrosis of the skin, while interpretation of the results of repeated intraperitoneal injection was difficult owing to the development of peritonitis. Mice were also exposed to air passed over the mercurials (but since no determinations were made of the vapour concentrations to which the animals were exposed, these experiments only demonstrate the order of volatility of the compounds). Determinations of the mercury content of tissues of rabbits after a single intravenous injection of methyl mercury dicyandiamide showed that the concentration in the kidney and liver fell appreciably over a period of 44 days, while that in the brain and muscles fell much more slowly.

W. N. Aldridge.


In this study 4 rabbits (Group 1) each received a daily dose of cadmium sulphate solution in water on 6 days a week for 10 weeks, the dose being 0.65 mg. of metallic cadmium per kg. body-weight. This contained the radioactive isotope 114Cd with a half-life of 43 days. At the start of the experiment the radioactivity measured about 0.25 mc. per g. of cadmium. The solution was given by subcutaneous injection and the total cadmium given was 40 mg. per kg. Another group of 4 rabbits (Group 2) was similarly treated, but for 4 weeks only; the total cadmium given was 15 mg. per kg.

Little cadmium was found in the urine during the first 6 weeks, but large quantities were excreted by the kidneys during the 7th and 8th weeks, up to 50 or 100 times the normal quantity. This coincided with the appearance in the urine of a protein of low molecular weight. Evidence is given indicating that a part of the cadmium may be bound to this protein. The animals were then killed by bleeding. The blood of the animals in Group 1 contained cadmium to the extent of 0.7 to 1.3 μg. per ml., all of which was in the erythrocytes; none was found in the plasma. Cadmium was found to be present in all organs of the body in both groups of rabbits (precise quantities are given) with accumulations in the liver, kidney, pancreas, and spleen.

M. A. Dobbin Crawford.


para-Phenylenediamine, which is extensively used in the dye industry, is known to be a strong sensitizer, though why compounds in the para position are important from the point of view of sensitization is not known. It would seem that sulphamides and p-aminobenzoic esters (for example, procaine), besides being strong sensitizers, will induce mutual sensitivity, and an individual sensitive to one of them will react positively to any of the others. From a study of 23 patients sensitive to the "para group" the author suggests that cross reactions can never be predicted, though by studying the occupation and enquiring about the use of procaine, for example, the original sensitizer can often be singled out. This may be important because on it depends to a certain degree the extent of the antigenic cross reactions. In one case 200 mg. of acid yellow or of amaranth, two common azo dyes used in foods, produced a rash in a woman sensitive to paraphenylenediamine, nylon dye, and other " para group " substances. A list of these substances is given in a table.

A. W. Frankland.