TOXIC EFFECTS OF ETHYLENE CHLOROHYDRIN

Part I.—CLINICAL

BY

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Literature

In spite of the toxic properties of ethylene chlorohydrin,* there is only one paper, so far as we know, which deals at all adequately with this compound. This is by Koelsch (1927) who refers to nine cases of which two were fatal; he also gives results of animal experiments. The circumstances in which these cases occurred are probably unlikely to be repeated—three cases (one fatal) during the use of the compound as a machine cleanser, and four others (one fatal) during its use as a solvent in a quick drying stain for oil-cloth.

The first victim, a man of 30 years, had been cleaning a machine with ethylene chlorohydrin and was exposed to a high concentration of vapour on a summer's day for some 2½ hours, and there must have been considerable contact with the skin for the job was done with a rag soaked in the cleansing agent. The symptoms which followed were nausea and vomiting, violent headache, and giddiness. The medical attendant noted no fever; cardiac action was normal; there were isolated pulmonary râles. Later in the day there was repeated bilious vomiting, followed by great thirst. Next morning the patient rose, drank some coffee, became unconscious and died shortly afterwards. Autopsy showed numerous ecchymoses, inflammatory detachment of large parts of the mucous membrane (and small isolated ulcers) in the respiratory passages, and pneumonia mainly in the right lung; there was evidence of old pulmonary tuberculosis and valvular disease of the heart; the gut was normal, but the liver was considerably enlarged; the kidneys appeared normal.

Of the other two men engaged on the same cleaning operation, but under much less exposure, one complained of nausea, vomiting, violent pre-cordial pain, giddiness, and weakness, but was quite well on the following day; whilst the second complained only of slight burning sensation in the eyes.

The second fatal case described by Koelsch was one of four men engaged in staining oil-cloth with colour dissolved in or mixed with ethylene

chlorohydrin. Exposure must have been considerable and the man developed nausea and signs of narcosis and had to stop work early in the day; the doctor held the condition to be of little moment, but in the afternoon dyspnoea set in and the man died in the evening. Autopsy showed cerebral and pulmonary oedema, acute gastro-intestinal catarrh, renal degeneration and disease of the cardiac valves and aorta as well as calcification of the arteries. The last of these findings was held (not by Koelsch, who merely quotes) to have been brought about by an acute poisoning. The remaining three men were relatively mildly affected, and although two required long treatment and convalescence, no permanent sequelae resulted.

Koelsch also refers to two other cases which had been reported to him, but although they had been severely ill, complete recovery occurred in both.

Reference must be made to the short note by Middleton (1930) on a fatal case of a lead burner. Two men were engaged in the repair of a leak in the lead lining of a still, which contained ethylene chlorohydrin. The men both had considerable direct skin contact with the water-chlorohydrin mixture which had to be removed before the leak could be repaired. When the chlorohydrin had been cleared, as far as could be judged by odour, the lead burner spent about 1½ hours repairing the leak with an oxy-hydrogen flame. His mate, who had done most of the mopping out of the still and hence had most of the skin contact, leaning over the manhole to give necessary assistance in the repair, experienced nausea. Both men, after the job was done, suffered severely from nausea, vomiting and weakness, the mate being the worse of the two. Both men had to be taken to hospital where the mate died after some ten hours; the lead burner recovered. No details of post-mortem findings are given by Middleton except that there were signs of respiratory failure. Middleton holds that death in this case was due to absorption of the chlorohydrin through the skin.

It will be observed that all the cases referred to in these reports were of the acute kind, that both Koelsch's fatal cases were already far from healthy subjects before the toxic event, that no clear picture emerges as to the cause of death, and that no histological evidence was obtained. It seems to us that Koelsch's two fatal cases died from cardiac failure. The symptoms of nausea and vomiting with sometimes giddiness and even mild signs of

* Ethylene chlorohydrin is 2 monochloro-ethyl alcohol (2 chloro-ethyl alcohol). Its chemical formula is $\text{CH}_2\text{Cl}-\text{CH}_2\text{OH}$. It is a colourless, mobile liquid with an odour difficult to describe but resembling a mixture of ethyl alcohol and ether. Sp. Gr. 1.213^{20°}₄.

It occurs in the chemical industry mainly in the manufacture of ethylene glycol and is widely used as a reactant in many organic syntheses. It is miscible in all proportions with water, ethyl alcohol, and ether. The boiling range of the highly purified material is found by us to be 129.1° C.—130.3° C. at 766 mm. Hg pressure.

narcosis are indicative of central action of the toxic materials. It will be seen that as far as human material is concerned, the cause of death is not entirely clear.

Koelsch's animal experiments deserve summary. He used two groups of animals: 1 cat and 2 guinea-pigs for acute exposures to ethylene chlorhydrin vapour, and 1 cat and 1 guinea-pig for chronic exposure. Of the former group, the cat was exposed to a concentration of 0.0045 g./lit. for 5½ hours daily for two successive days, when it showed general depression, slow and laboured respiration, the side position, repeated vomiting and it was unable to stand: death occurred 3 hours after the second exposure. Post-mortem examination revealed injected and collapsed lungs, tightly filled heart with some sub-epicardial petechiae and marked sub-endocardial haemorrhages: the liver and kidneys were congested and the brain showed punctiform haemorrhages. Microscopic examination confirmed these naked eye observations with, in addition, fine fatty deposits in the renal cortex, and granular masses in the tubules with some shadows of red blood cells. One of the guinea-pigs in this group was exposed to 0.0026 g./lit. during two succeeding days for 2½ and 8 hours respectively. Death occurred during the second night and post-mortem examination showed hyperaemic lungs, tightly packed auricles and punctiform haemorrhages in the brain. Microscopic examination confirmed these findings with, in addition, epithelial detachments in the trachea, globules of fat in the cardiac muscle, epithelial casts in the renal tubules and nuclear degeneration in the cells of Henle's loops. The second guinea-pig in this group was exposed for 15 minutes to a concentration of 0.0182 g./lit. and died after 30 hours. The post-mortem findings in the animal were similar to those observed in the former animal with, in addition, fatty degeneration of the liver.

Chronic effects were observed in a cat exposed to a concentration of 0.0025 g./lit. for 3 hours a day during 4 days. The animal showed some depression and loss in weight but no definite signs of illness until on the fourth day it vomited frequently and death followed. Macroscopically no great changes were noted except albuminuria and hyperaemic lungs, liver, and kidneys, but microscopically the kidneys showed breakdown of nuclei, the liver some nuclear degeneration, cellular swelling and some fatty changes in the lobules, whilst the lungs showed foci of bronchopneumonia and oedema.

A guinea-pig exposed to 0.0022 g./lit. for 3 hours a day during 4 days in one week and in the following week for 4 hours a day during 4 days (i.e. total of 28 hours during 21 days) lost weight, refused food and died. Examination of organs revealed pulmonary oedema and bronchopneumonia with hyperaemia of liver and kidneys.

In discussion of his findings, Koelsch emphasizes the fact that his animals showed no significant signs of illness during the period of exposure, these appearing some time after removal from the exposure chamber, death usually occurring during the night. The post-mortem findings are interpreted as indicating *death from asphyxia*, attention being specially drawn to local irritation of the deeper

respiratory passages, fatty changes in the cardiac muscle, liver, and kidneys. The loss in weight observed in his chronic experiments, he holds to be due to diminished food intake and perhaps also to specific metabolic disturbances. He concludes that ethylene chlorhydrin belongs to the metabolic poisons with special effects on the nervous system.

Experiments carried out at Koelsch's instigation confirmed that during an hour's exposure there were no significant signs of severe toxic action and only hours after removal from the chamber were the following signs observed: tremors, inco-ordination, paresis of extremities, later marked paralysis with side position, death occurring after several hours from respiratory paralysis. Cats showed vomiting, diarrhoea, paralyses, disturbances of equilibrium, sluggish dilated pupils sometimes with nystagmus, sometimes clonic spasms: death was due to respiratory failure. These workers (not named by Koelsch) stated that the nervous symptoms dominated the clinical picture in animals, but examination of tissues showed fatty changes in the liver and, in chronic experiments, nephritis. Changes in the lung were considered not striking and held to be secondary. Like Koelsch they found the compound could be absorbed through the skin.

In spite of the manifestly dangerous properties of ethylene chlorhydrin, no cases had been recorded in Koelsch's factories during twenty years of manufacture, a fact to be attributed to the totally enclosed plant effectively preventing any significant escape of vapour. In none of the cases cited above were the workers engaged in manufacture of the compound. The cases we shall describe were all engaged in manufacture. In Koelsch's and Middleton's cases the course was acute; in our cases the course was both acute and chronic.

Cases in Present Series

Case 1. G. D., aged 45 years. Foreman.

This man was a foreman of high repute and had been engaged on this particular plant for some thirteen years and was well acquainted with all the regulations, particularly that against the operation which he performed and which led to his death. The circumstances were as follows:—

Owing to a fault in a concentration tower for ethylene chlorhydrin, the foreman decided to find the cause of the trouble and to open an inspection door at the top of the tower. To perform such an operation whilst the tower was full of hot vapour was most strictly forbidden, but the foreman with the aid of a process worker did perform it, and in spite of what must have been an immense concentration of chlorhydrin and ethylene dichloride, managed to make the necessary adjustment, with the result that the process continued without obstruction. The incident occurred during a night shift in November, and the total time during which exposure to a high concentration of vapour continued was about 1½ hours. Half an hour later the process worker stated to the foreman that he felt sick and noticed that the latter looked ill. The process worker, whose exposure to the vapours had been much less severe, seems to have suffered no further, but the foreman,

on taking a cup of tea, was violently sick but was able to walk to the ambulance room an hour after the end of the exposure. Here he vomited and retched repeatedly and was very restless, refusing to lie down.

Two hours after the exposure he was still able to converse intelligently with the first-aid attendant but was still very sick, vomited bile, and was unsteady on his legs. The situation did not apparently strike the attendant as serious enough to call the medical officer at his home until some $3\frac{1}{2}$ hours after the end of exposure. Attempts to take a mixture containing a small dose of morphia were at first unsuccessful, but when some had been retained (probably about $\frac{1}{8}$ grain), the vomiting ceased and the patient became more comfortable and fell asleep. One and a half hours later the attendant noticed that the pulse was very weak. The doctor then appeared and found the patient very ill and unable to respond to questioning. The pulse was thready, poor in volume, and weak. Oxygen was administered through a B.L.B. mask, but this seemed to make him more restless with twisting and turning of the head from side to side and restless movements of the limbs. The pupils varied in size from pin-point to extreme dilation over periods of 2 or 3 minutes. Tendon reflexes were very sluggish. The blood-pressure, taken on three occasions, was difficult to read and the doctor considered it to be below 60/40. Some slight improvement of the cardiac action was obtained by injection of coramine and the patient seemed quieter. There were no abnormal physical signs in the chest other than a few râles at the base of the lungs. Throughout there was profuse perspiration. No urine could be obtained. Treatment in the ambulance room was continued on general lines with oxygen administration, but $11\frac{1}{2}$ hours after the end of exposure there was a turn for the worse. He was taken to hospital where he was put into an oxygen tent, but deteriorated rapidly and died 14 hours after the end of exposure to the toxic vapour. It is relevant to point out that on previous occasions this man had minor attacks of vomiting whilst engaged on this plant.

The autopsy report was in substance as follows:— 'The body was that of a man of very good average development and nutrition. Nothing abnormal was discovered in the mouth, oesophagus or gastrointestinal canal. The respiratory system, except for congestion of the tracheal mucous membrane, showed nothing abnormal. The heart was of average size with numerous petechial haemorrhages of the pericardium. The kidneys, liver, spleen, and pancreas appeared normal. The brain showed slight congestion of the cerebral cortex and marked oedema of the cerebral hemispheres. Death was held to be due to toxæmia from inhalation of poisonous fumes.'

A few sections of organs were sent to us and the following observations made: Lung—marked and extensive collapse, oedema, and great extravasation of blood into the alveoli (Fig. 1); liver—isolated areas of degenerative change: fatty degeneration, loss of cellular outlines and disappearance of nuclei; heart—cross-striation could not be seen: otherwise the muscle seemed normal; brain—the single section of brain tissue showed no significant changes.

It is not easy from these data to decide what the

decisive pathological change was which caused death. We are inclined to lay stress on the cerebral oedema, but whether this was a primary phenomenon due to attack of the toxic material on the vascular apparatus of the brain or secondary to organ changes, cannot be decided. Certain it is that neither the lung or liver changes were sufficient in themselves to cause death in so short a time. Kidney sections were not available.

Case 2. P., aged 40 years. Process worker.

This case occurred in another factory where ethylene chlorhydrin was being manufactured and where the workers were examined clinically both on engagement and subsequently.

On engagement the medical report was that he was a normal healthy man. He was examined, after entry, on four occasions in 7 weeks. Immediately prior to the last examination he had been behaving 'in a peculiar manner' on the plant. Urine and blood-pressure were normal. On the day following the last examination at the factory he visited his private doctor who diagnosed influenza. A week later, i.e. 2 months after starting, he went for a walk and collapsed in the street. He returned home to bed and complained of headache, dizziness, and vomiting. Two days later he left his bed and again collapsed in the street with similar symptoms. Four days later, his headache had become very severe and his mental condition very muddled; he was removed to hospital. While in hospital no definite physical signs were found, the urine was normal, and B.P. had fallen from the previously-recorded value of 140/90 to 120/80. Nine days after entry into hospital there was haematuria and death occurred on the following day, i.e. 11 weeks and 2 days after starting on this work.

The autopsy report was not satisfactory. Histological examination of tissues showed:—Heart and stomach—no abnormal features; spleen—congested and slightly hyperplastic; kidney—congestion affecting both glomeruli and interstitial tissue: convoluted tubules were severely damaged and showed necrotic changes with much debris in the lumen of the tubules, together with some blood cells; brain—a section from the basal ganglia showed gross oedema: the cells in this area showed degenerative changes. Unfortunately no lung or liver tissues were preserved.

The data on this case are somewhat deficient, but there could be no reasonable doubt that this man had been exposed some 2 months to concentrations of ethylene chlorhydrin (probably mixed with some sym-dichloroethane) which had produced symptoms of greater or less severity in a good many other workers. But in this case the fatal issue after only 11 weeks gives support to the suspicion of Koelsch that there is individual susceptibility. The man was, at the time of his entry, a normal healthy person, and there is no evidence that he had any greater exposure to the vapour than others working on the plant. This is quite different from case 1 in which the concentration of vapour to which the foreman was exposed was extremely high and would probably have proved fatal to anybody.

The cerebral symptoms were very marked in case 2. It is remarkable that no significant physical signs were observed in hospital, except the fall in blood-pressure. The sudden renal haemorrhage shortly before death has not been recorded in any

previous case, but the pathological changes in the kidneys of experimental animals (*vide infra*) render such a sign always a possibility. How far renal failure may have contributed to death cannot be said, but the absence of signs seems to make this improbable.

In this case also the case for attributing the death to cerebral changes seems to us good, but whether this is a primary effect of the poison or secondary to organ changes, which in the case of the kidneys were very severe, cannot be stated with certainty.

The following non-fatal cases are recorded in order to show the general features of the clinical picture which may be regarded as of little significance unless the relation to the toxic compound is realized. These cases occurred during a period in which a fault had developed in the plant; the average concentration of ethylene chlorohydrin in the atmosphere was about 18 parts per million.

Case 3. W. J. H. Male, aged 47 years.

This was a rather unhealthy type of man and alcoholic. While at work on a winter's day he developed headache, nausea, epigastric pain, and vomiting. He reported to the ambulance room but did not appear very ill. Vomiting became more severe and having passed a bulky motion, he suddenly collapsed into a state of stupor, from which, however, he could be roused. On examination his colour was very bad, the pulse was 68 and feeble. The heart was not enlarged and cardiac sounds were feeble. B.P. 100/80. A few scattered rhonchi were noted in the lungs and there was epigastric tenderness. There was generalized weakness. Cranial nerves and tendon reflexes were normal. The urine contained a trace of albumen. Coramine and strychnine injections were not followed by improvement. Administration of oxygen led to some improvement. He was removed to hospital by ambulance, where he collapsed again and received more oxygen. Recovery was slow and he was discharged from hospital after 10 days. B.P. on discharge was 140/90.

Case 4. N. Y. Female, aged 40 years.

This woman was of poor physique, but nothing specifically pathological could be recorded about one month before the present occurrence, when, with several others, she complained of abdominal pain and nausea. On going home from work, she began to vomit: this continued 'all night' but there was no collapse. She continued to experience nausea and anorexia for 7 days. Urine contained a trace of albumen. On return to work after this period, B.P. was 120/100, urine was normal, and general condition was fair.

Case 5. I. F. Female, aged 30 years.

Normal physique. In similar conditions to previous cases (3 and 4). Experienced nausea and vomited for some hours. Recovered after rest and ceased work for 3 days, after which she appeared quite normal.

Case 6. K. S. Female, aged 24 years.

Good physique when examined prior to engagement. Mildly affected: vomited once or twice. Went home to bed but returned fit to work next day.

Case 7. B. D. Female, aged 25 years.

Good physique on examination prior to engage-

ment. Mildly affected: nausea and vomiting. After rest at home returned to next shift.

Case 8. S. M. Female, aged 34 years.

Good physique. Slightly exposed but vomited profusely. Lost 3 shifts but there were no physical signs on return to work.

Case 9. S. T. L. Male, aged 47 years.

Good physique. Slightly affected. Nausea and vomiting for some hours. No other abnormal signs. Returned to work next shift.

Case 10. A. S. Male, aged 43 years. Fitter's labourer.

Poor physique, poor vision, bad teeth. B.P. 130/90 at time of engagement. When working on a night shift, felt sick at midnight but continued work for 2 more hours. Went to ambulance room with nausea, epigastric pain, and copious bilious vomiting. Treated by first-aid attendant with hot drinks, sodium bicarbonate, warmth, and rest for some 5 hours. Condition was not considered serious, but when allowed to rise from bed and dress, he collapsed. Very drowsy but could be roused. From time to time there was uncontrollable copious vomiting. Patient became cold, clammy, and shivered: grey-blue in colour: pulse 70 and feeble. Some 3½ hours later a bulky foul-smelling motion was passed and patient became alarmingly collapsed.

The medical officer found the patient sleepy but able to answer questions. Pulse 70 with very poor volume. Face grey-blue in colour, erythema over arms and trunk. Tremor of hands and head; loss of power in limbs. Cranial nerves and tendon reflexes normal; no sensory loss. The heart was normal in size; poor apical impulse and second sound could not be heard; B.P. 60/40. Pulmonary system apparently normal. Teeth very bad; tongue thickly coated with yellow, moist fur. Abdomen not tender but rigidity in right epigastrium. Liver one inch below costal margin. Urine showed faint trace of albumen. Treated with continuous oxygen through a B.L.B. mask with slow improvement.

Next day there were no abnormal physical signs; B.P. 100/70.

On the following day patient felt very well; B.P. 140/90.

Case 11. P. S. Male, aged 46 years.

Poor physique, very bad teeth. B.P. 140/100.

As in other cases, he complained during work of nausea, abdominal pain which later was accompanied by vomiting and an irritant cough. Treated in ambulance room with rest and warmth and improved symptomatically. Some hours later was transported home where he experienced intense headache, giddiness, and insecurity on his legs. Went to bed: vomited and defaecated and fell into a long sleep. On examination some hours later he was sleepy, complained of headache and there was a scarlet rash on the trunk: pulse 70, B.P. 100/70. Tongue was furred but moist; throat was injected and right epigastrium was tender. Liver was not palpable. Lungs showed a few scattered rhonchi. Nothing of significance in C.N.S. Urine showed trace of albumen.

Next day, great improvement: appetite returning; B.P. 140/100.

FIG. 1.—Lung of case 1 (human). H. and E. $\times 120$.

FIG. 2.—Kidney of rat exposed to 0.010 g./litre for 30 minutes. H. and E. $\times 120$.

FIG. 3.—Lung of rat exposed to 0.003 g./litre for 15 minutes on three successive days. H. and E. $\times 120$.

FIG. 4.—Kidney of rat exposed to 0.003 g./litre for 15 minutes on six successive days. H. and E. $\times 120$.

FIG. 5.—Liver of rat exposed to 0.003 g./litre for 15 minutes on eleven successive days. H. and E. $\times 375$.

FIG. 6.—Kidney of rat exposed to 0.003 g./litre for 15 minutes on eleven successive days. H. and E. $\times 120$.

Discussion of Signs and Symptoms

Summarizing signs and symptoms in these non-fatal cases, we have:—

Digestive system.—Nausea, epigastric pain, repeated vomiting (bile may appear), bulky offensive stools.

Circulatory system.—Depressor action on the circulation. Signs of shock in severe cases.

Nervous system.—Headache, giddiness, inco-ordination, confusion, mild narcotic effects.

Urinary system.—Slight albuminuria, disappearing on recovery, polyuria.*

Respiratory system.—Cough may be present. Rhonchi.

Skin.—Erythema on skin of arms and trunk in severe cases

* Some men complained of loss of sexual potency but it is difficult to interpret this complaint.

Symptoms and signs were worst in men of poor physical standard. Recovery in these non-fatal cases was complete; and in all except one (case 3) it was rapid.

From the nature of the work, it is certain that the route of absorption was the respiratory tract. The vapour absorbed was a mixture of ethylene chlorohydrin and ethylene dichloride, but the very minor narcotic effects observed lead us to believe that the latter was not the principal cause of the symptoms. The possibility of summation of toxic effects cannot be ruled out, and hence we cannot assert with certainty that the ethylene dichloride present was not involved in the production of symptoms. It is impossible with the data at our disposal to do more than suspect that ethylene chlorohydrin was the main toxic agent involved.

Since the events described above, regular estimations of ethylene chlorohydrin and ethylene dichloride in the atmosphere of the plant have been carried out. According to the results obtained, appropriate action is taken. The figures given in the table below (Table 1) show a marked improvement in conditions on one plant which was accompanied by definite falling off of symptoms of absorption by the workers. From the experience gained with these and from mild subsequent cases it seems to us that women are somewhat more liable to develop symptoms than are men.

The nature of the symptoms is clearly non-specific. Any of these signs and symptoms may be met with in poisoning by many of the chlorinated aliphatic hydrocarbons. This renders it difficult for us to be certain as to the relative importance to be attached to ethylene chlorohydrin and ethylene dichloride, to both of which all our cases were undoubtedly exposed (*vide infra*).

The course of the intoxication is such as to point to cumulative action and also to considerable delay between the actual exposure and the onset of symptoms. Even in the acutely fatal case (case 1) collapse did not occur during the exposure. Similarly with the mild cases in which symptoms often appeared only after the worker had reached home.

The regular occurrence of nausea and vomiting cannot be attributed to offensive or sickly odours. Men, who had worked previously on most offensive chemical processes without gastric disturbance, experienced these symptoms when on ethylene chlorohydrin. The odour of a mixture of ethylene chlorohydrin and ethylene vapours is characteristic but not frankly nauseating. Indeed, after a period in the shed the odour is no longer noticed. Hence we are of opinion that both the nausea and vomiting are central in origin.

The fall in blood-pressure noted in so many of these cases is an accompaniment of many intoxications with organic vapours. It will be shown below that ethylene chlorohydrin, in high concentration, inhibits the heart both by direct action on the

muscle and possibly also by some action on the vagal mechanism. The frankly cerebral symptoms, even to the point of psychological disturbance, leave no doubt as to the attack on the higher centres. The mild narcotic effect occasionally recorded was probably to be attributed mainly to the presence of ethylene dichloride. The occurrence of cerebral oedema in both fatal cases is additional evidence of toxic action on the vascular system, as are also the pericardial petechiae.

In none of the mild cases here recorded was there any marked attack on the respiratory system, but in case 1 the effect on the lungs was very evident. The presence of slight albuminuria even in the mild cases is significant, and in case 2 the toxic effect on the kidneys was very marked. Clinical evidence of toxic action on the liver in these cases was not obtained except in case 10, when there was some enlargement of the organ. Evidence from animal experiments with ethylene chlorohydrin shows marked effect on the liver. In case 1 there was also evidence of hepatic degeneration.

Summarizing the clinical features of the above cases, it may be said that the principal toxic agent was almost certainly ethylene chlorohydrin and that its toxic action in man is directed towards the nervous system, the cardio-vascular system and the kidneys: the secondary points of attack are the lungs and the liver. No irritant effects on the skin, eyes, and mucous membranes were observed.

Treatment

The treatment of all these cases was entirely symptomatic. In the mild cases recovery was in the main spontaneous, any measures taken being general and not significantly influencing the course of the intoxication.

The absence of physical signs even when as in case 2 death occurs later, renders it extremely difficult to decide what therapeutic measures are indicated. In case 1 some temporary improvement could be obtained by continuous oxygen administration and analeptics.

TABLE 1
CONCENTRATIONS OF ETHYLENE CHLOROHYDRIN (E.C.) AND ETHYLENE DICHLORIDE (E.D.) AT VARIOUS POINTS ON A PLANT WHERE MILD SYMPTOMS HAVE BEEN OBSERVED AMONGST THE WORKERS.

Sampling Point *	6th November, 1941		9th/10th April, 1942		6th/7th May, 1942		2nd/3rd July, 1942	
	E.C.	E.D.	E.C.	E.D.	E.C.	E.D.	E.C.	E.D.
	Parts per million. Vol./vol.							
1.	25	72	9	24	10	36	5	36
2.	8	15	9	84	10	48	5	48
3.	24	95	15	60	10	48	5	48
4.	16	152	20	143	10	72	5	24
5.	49	24	15	48	15	84	5	12
6.	20	131	25	72	20	84	0	48
7.	2	2	5	12	5	12		

* Sampling was carried out during the night shift.

Much more information on the nature of action of substances of this kind is required before a proper indication to treatment can be laid down.

Prevention

The usual formulae as to prevention of toxic events apply here, viz. that leaks, overflows, and escape of vapour should be avoided: good ventilation, draughting specially hazardous points, regular medical examination of workers, report by workers of untoward symptoms, detection of susceptible subjects, routine estimation of concentration of vapours at working places are all required. The main problem, as always, is design of plant. The necessity for periodic sampling from reaction vessels requires arrangements for sampling which do not involve the opening of points where escape of fume is inevitable.

The fact that ethylene chlorohydrin appears to be a cumulative poison renders it of the first importance to prevent even low concentrations in the atmosphere: we take the view that no concentration that is chemically determinable should be regarded as satisfactory. Table 1 shows the improvements obtained on one plant when the insidious nature of the poison was recognized as a result of experience in other similar places.

The improvement in the concentrations of ethylene chlorohydrin was very striking and resulted from simple plant measures and not from significant improvement in ventilation (in present circumstances the latter is seldom possible). The target set for ethylene chlorohydrin in the atmosphere is 2 p.p.m. but the attainment of this is likely to be very difficult.

This improvement has been followed by much diminution in the incidence of signs and symptoms among workers; but it is necessary to realize that where ethylene chlorohydrin is a toxic risk, determination of concentrations in the atmosphere must be continued as a routine as long as the process is continued.

Part II.—EXPERIMENTAL

BY

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The cases first recorded by Koelsch (1927) undoubtedly occurred because of the lack of knowledge of the toxic properties of ethylene chlorohydrin, which could have been realized by animal experiment. The very fact that the plant in which it occurred (probably as an intermediate in the manufacture of ethylene glycol) was so efficiently enclosed that no cases had been observed for 20 years, gave a false security which was dispelled only when clinical cases were met with during the utilization of the compound in open conditions. Whether these cases were indeed entirely due to the chlorohydrin it is difficult to say, for admixture with ethylene dichloride and even dichlor-diethyl ether seems

Summary

1. Two cases of death attributed to poisoning by inhalation of ethylene chlorohydrin vapour are described. One case was very acute in its course, the other sub-acute. The causes of death were not clear, but the associated symptoms and some histological evidence suggest that the compound is a violent cerebral and vascular poison. Pathological changes in the lungs, kidneys, and liver were marked.

2. Nine cases of non-fatal poisoning due to inhalation of the vapour are shortly described. The symptoms noted were non-specific and associated with all the main physiological systems in greater or less degree. Indications were obtained that men of poor physical standard are more readily affected than good specimens: women are thought to be more susceptible than men.

3. Some evidence was obtained that the substance is a cumulative poison.

4. It is held that in all processes in which ethylene chlorohydrin is used or appears as an intermediate stage in manufacture, every possible measure must be taken to control the concentration of the vapour in the atmosphere; since no concentration of the compound is considered safe if exposure is a daily occurrence. The diminution in the incidence of cases is soon manifest if even simple precautions are taken.

5. Treatment is purely symptomatic in severe cases. Mild cases in general soon recover but the likelihood of repeated attacks is always to be kept in mind. Some degree of personal idiosyncrasy is suspected.

Our thanks are due to Dr. Charles Cresdee for certain of the clinical data.

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highly probable, since the preparation of pure ethylene chlorohydrin requires considerable care and would probably not be worth doing for crude industrial purposes.

Our cases (see Part I) were certainly exposed to all three compounds, but the amount of the dichlor-diethyl ether was extremely small. We, also, were in a state of false security because of the absence of unfavourable events throughout years of manufacture.

As has already been stated, the relative parts played by the chlorohydrin and the dichloride in the production of the symptoms cannot be stated with certainty.