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THE GROWING MENACE OF BENZENE (BENZOL) POISONING IN AMERICAN INDUSTRY

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Up to 1914, comparatively little coal-tar benzene (benzol, C_6H_6) was used in the United States. Because of its solvent properties, it has long been employed on the continent and to a less extent in England in the manufacture of rubber goods and of quick-drying paints and for dry cleaning. But we had not yet begun to produce it ourselves; we imported it from Germany, it was more than twice as expensive as the petroleum solvents, and we therefore used the latter for the great majority of industrial processes.

The outbreak of the war did two things: It shut of the supply from Germany not only of benzene but also of amidobenzene, or anilin. which had become a valued ingredient of compound rubber, and it created a sudden demand for benzene and toluene for the manufacture of explosives, and of anilin for the manufacture of dyes as well as of rubber. Consequently, coke by-products plants were erected to secure benzene and toluene, and the latter was also obtained in the course of the production of illuminating gas. Then came the armistice, the sudden cessation of the manufacture of explosives, and the need for new markets for the great quantities of coal-tar distillates which were thrown back on the hands of the producers. These markets have been found in the rubber trade, especially for tires, footwear, and hose; in sealing mixtures for tin cans; in the shoe trade, for cement; in certain processes in the making of straw hats; as a solvent for fabrikoid, and as a substitute for gasoline in motor car fuel.[1] Benzene, which is a much more powerful solvent than petroleum benzin and naphtha for fats, gums and resins, is now below the latter in price, and the manufacturer has therefore a double temptation to use it. It is probabl that we shall presently find the petroleum distillate supplanted by the coal-tar in the making of varnish quick drying paints and shellacs, and in dry cleaning, f not in the making of spread rubber goods and dippe rubber goods, as is

Before the war, a few cases of chronic benzene poisoning had been reported by Selling[2] of Johns Hopkins from a can factory where rubber dissolved in benzene was used as a sealing fluid. No cases of severe acute industrial poisoning were then on record, but during the year 1915-1916 I reported fourteen instances of sudden acute poisoning with seven deaths[3] and since that time the danger of such an accident has become familiar to engineers and chemists and safety experts. The danger of chronic poisoning is less well known, and it seems timely to call the attention of the medical profession to this increasing menace in American industry, to describe the conditions under which it may be looked for, and the warning symptoms. It is important to take into account a possible confusion in names. Benzin is a petroleum distillate, far less toxic than benzene. Another source of confusion is the use in industry of the term "solvent naphtha" to cover, not petroleum naphtha, but a mixture of crude benzene, toluene and xylene.

ACUTE INDUSTRIAL POISONING

The German literature yields, as one would expect, the largest number of instances of benzene poisoning, both acute and chronic. The German factory inspectors' reports for 1912 contained three cases, two of them fatal. One man was painting with benzene tar paint the interior of a barrel; another, in a dry cleaning establishment, had climbed into the washing machine, which had a little residue of benzene at the bottom. The third, who was in charge of a distilling plant, had neglected to turn on the cold water for condensation, and the fumes that escaped killed him. A case similar to this was reported by the British factory inspectors[4] in 1918. An increase of pressure caused a quicker distillation of vapor than the condenser could deal with. The man, being overcome, revived with oxygen; but, when he returned to work the second night after, he was again overcome and died.

The earliest instances of acute industrial poisoning in American industry seem to have occurred in connection with war industries in 1915-1916. The men were pipe fitters or workmen engaged in distilling benzene or cleaning tanks or, in two instances, sulphonating benzene as a step in the production of phenol (carbolic acid). In more recent years a decided effort has been made to avoid such accidents; but, if a man is susceptible to benzene it rakes only a small quantity to poison or even to hill him.

EXTRAORDINARY SUSCEPTIBILITY TO BENZENE

In a case described by Lewin,[5] the benzene kettle had been empty for twenty-two hours, was washed out twice with steam and three times with cold water, and then it was allowed to stand all night filled with cold water. As the workman went in, a strong current of air was blown in through a pipe. In spite of all

1. The difference between the exhaust gases from gasoline and those from coal-tar distillate motor car fuel is described by Henderson, Yandell: J. Indust. Hyg. 3: 145, 1921.
2. Selling, L.: Bull. Johns Hopkins Hosp. 21: 33, 1910.
3. Hamilton, Alice: Industrial Poisons Encountered in the Manufacture of Explosives, J. A. M. A., 68: 1445 (May 19) 1917.
4. Annual Report, Chief Inspector of Factories and Workshops for year 1918, p. 78.
5. Lewin, L.: München. med Wchnschr., 54: 2377, 1907.

these precautions, he was overcome and fell to the bottom of the tank. Several of his fellow workmen tried to get him out, but all grew dizzy and confused, and had to give it up. Finally, an engineer in a diver's helmet succeeded in rescuing him, and he was revived; but one of the workmen who had helped in the rescue died within ten minutes of inhaling the fumes.

Even greater precautions had been taken in an English tank car which had been emptied of benzene, washed with water, then steamed out, then left for twenty hours full of water, washed out twice, boiled for twelve hours, and finally left for ten days with the 16-inch (40 cm.) manhole open. Nevertheless, the man who was sent in collapsed; and, although he was pulled out in time, one of his rescuers died.

In one of the great steel mills of Pennsylvania, two men were sent to change coils in a benzene tank which had been thoroughly blown out with steam. One of them was not affected at all; the other was overcome by the fumes, and died.

In a benzene refining plant in New Jersey, a man went to the top of a still to see what was wrong. There proved to be a bad leak, and he fainted almost instantly from the fumes; and by the time two others could come to his rescue, which was said to be not more than two or three minutes, he was moribund. Both men who went to help him fainted, but were revived.

The late T. F. Harrington of the State Labor Board of Massachusetts reported two serious poisonings, with one death, in steam fitters repairing pipes in a benzene still, 8 by 5 feet (2.4 by 1.5 meters) with a small manhole 15 by 11 inches (38 by 28 cm.) in diameter. There is no note as to the cleansing of this still, but a stream of compressed air under 60 pounds pressure was fed in by a 2-inch (5 cm.) pipe. At the end of forty-five minutes one of the men, aged 35, grew wildly excited, irrational, and finally lost consciousness. The younger man helped to push him through the manhole, which took twenty minutes, at the end of which time the younger man was found unconscious and dying.

PREVENTION OF ACUTE BENZENE POISONING

Such histories as the foregoing show how difficult it is adequately to protect men engaged in work in and about an apparatus that has been used for the production or storage of benzene. Even a Draeger helmet may not be enough, for a workman in a Pennsylvania plant who entered a tank wearing such a helmet was overcome by the fumes and died. The only possible explanation was that the nose-piece of the helmet could not have quite prevented nose breathing, but it shows that such a device is not positive protection. The best method seems to be that described to me by the men in charge of the safety work of the United States Steel Company's plant in Gary, Ind. After washing out the empty tank and steaming it out, they lower into it a cage of white mice; if the mice are overcome by gas, the process of flooding and steaming is repeated until the little animals can be lowered into the tank without showing any effect. If this procedure can be used in mine work for the detection of carbon monoxid, there seems no reason why it should not become general for the detection of benzene.

PATHOLOGY OF ACUTE BENZENE POISONING

According to Beinhauer,[6] in acute benzene poisoning the blood in the heart and vessels is fluid, in the veins of the abdomen, engorged. There are hemorrhages into the gastric mucosa, bloody foam in the air passages, no benzene odor, and no benzene demonstrable chemically. Sury Lienz[7] found conspicuous bright red spots over the body, the blood fluid and dark, petechial hemorrhages into the gastro-intestinal mucosa and pleurae, general venous congestion and bloody mucus in the air passages. Lehmann[8] of Würzburg, experimenting with cats, found a decided variation of susceptibility in individuals, but all of them showed signs of irritation of the mucous membrane, muscular twitchings, and a fall of body emperature. In large doses, there were convulsions, narcosis, very deep respirations first quick then slow, quickened pulse, and death from respiratory paralysis. A narcotic effect begins in cats after two hours' exposure to 20 mg. (⅓ grain) per liter (61 cubic inches) of air, and narcosis is complete in six hours. With 60 mg. (1 grain) the periods are fifteen minutes and one hour, respectively. In man, 15 mg. (¼ grain) per liter of air produces listlessness and confusion after half an hour, and exposure to from 20 to 30 mg. (⅓ to ½ grain, or from 2 to 3 parts per 100,000 parts of air) for a few hours may cause loss of consciousness.

CHRONIC BENZENE POISONING

The most famous cases of chronic benzene poisoning in the literature are Santesson's.[9] These were nine young women from 15 to 20 years of age with purpura hemorrhagica and hemorrhages from the mouth, the stomach, the nose or the uterus. They were employed in a velocipede tire factory in Upsala using benzene rubber cement. Four of them died after exposures of from three weeks to four months. The most striking finding in these cases was the fall in the number of red corpuscles and the almost complete leukopenia. Thirteen years later, Selling[2] described similar intoxications in girls, aged from 14 to 16, employed in a Maryland can factory in which the sealing mixture consisted of rubber and resin dissolved in commercial benzene. Three patients were brought to the Johns Hopkins Hospital with hemorrhages in the skin and from the gums and the nose. Here also there was evidence of profound blood destruction, the count in one instance falling to 640,000 red corpuscles, 480 white corpuscles, and 8 per cent. hemoglobin. In 1916, McClure[10] reported a case, from the same factory, of bleeding from the nose and mouth, black and blue spots over the body, secondary anemia, and breathlessness. This patient was saved by repeated transfusions of blood, and so was a boy of 17 who entered the hospital in a similar condition a year or so later. That same year, a woman of 57, also employed in this factory, died in the hospital after hemorrhages from the intestine, kidneys and nose, and into the skin.

Harrington[11] of Massachusetts reported five cases with three deaths, from an automobile tire factory. These men were using benzene in building automobile tires, applying it by a cloth to the rubber. Here, also, there were purpuric spots on the skin, hemorrhages from various mucous surfaces, extreme weakness and dyspnea. The red corpuscles in one instance fell to 944,000. In another, the white cells numbered 850, of which only 14 per cent. were polymorphonuclears.

6. Beinhauer, F.: München. med. Wchnschr., 43: 915, 1896.

7. Sury Bienz: Vrtljhrschr. f. gerichtl. Med. 49: 138, 1888.

8. Lehmann, K. B.: Kurzes Lehrbuch der Arbeits- und Gewerbehygiene, Leipzig, 1919. p. 249.

9. Santesson, C. G.: Pern. f. Hyg. 31: 336, 1897.

10. McClure, R. D.: Anemia Treated by Splenectomy and (Sept. 9) Often Repeated Transfusion of Blood, J. A. M. A. 67: 795

11. Harrington, T. F.: Boston M. & S. J. 177: 203 (Aug. 16) 1917.

Two hitherto unpublished cases of fatal purpura hemorrhagica caused by benzene fumes were brought before the New York State Workman's Compensation Commission in *1920.* The men had been employed on a machine for coating fabrikoid which is thus described: The fabric is fed in from the front to an endless traveling apron, which carries it over heated pipes. The coating mixture runs down from a can suspended above a 4 inch (10 cm.) hole in front, and the whole is encased in a wooden box. The temperature inside the machine is sufficient to volatilize all the solvent. The coating mixture consisted at that time of nitrocellulose, pigment, castor oil, grain alcohol, benzene and ethyl acetate. Fumes escaped from the hole in front, but still more the back, where the hot coated fabric left the machine. From evidence given at the hearing, it seems that nosebleed among the men in this department was of fairly frequent occurrence, and that the labor turnover was great. They worked eight hour shifts, sometimes sixteen hours, but the latter "not very often."

Both of the men who died were young and had always been strong and vigorous up to the time of their last illness. The first one worked for about nine months before he began to have bleeding from the gums, and he noticed small, red blotches on the skin between the ankles and the knees. Three weeks later, March 21, he had a severe nosebleed. He was taken to the hospital, March 24, and died. April 7, after repeated nosebleeds, bleeding from the mouth, temperature over 101, and the appearance of purpuric spots all over the legs up to the thighs. The second man worked for less than six months, sickened February 17, and died March *9.* He had been feeling ill, complaining of the poor ventilation in the shop and of loss of appetite, and was very pale. Then, on the night shift of February 17, he had what one fellow workman called a chill and another a convulsion, his nose began to bleed. and blood oozed from the gums, Evidence given by his physician shows that up to his death he had continual bleeding from the nose and mcuth, bruiselike blotches appeared on the legs and body, and the temperature ranged from *102* to over 104. In neither case was any blood examination made, and the medical details are very scanty,

The company had made tests of the air around the coating machines, for it was anxious to prevent the escape of the solvent, which it was trying to recover and use again. Something less than 5 per cent. was reported to be the highest concentration of benzene found in the air, and it is evident that the officials considered this amount too little to cause any anxiety.

Newton [12] of Akron, Ohio, has published the only article in American literature on the early stages of slow benzene poisoning. Three chemists were exposed to benzene vapors for about two weeks. Only *me* complained of ill health : headache. lassitude, anorexia and loss of weight. and then a sudden attack of pain in the abdomen, nausea and vomiting. Newton found the pulse and temperature normal, bur there was a marked leukopenia, 1.200. with 39 per cent. large mononuclears The erythrocyte count was 5.760.000, but the hemoglobin only 80 per cent. He then examined the blood of the other two and found white counts of 1,250 and 1,700. and a low red count. from 3.6 to 4 million Appropriate treatment resulted in a decided increase in the white cell count. showing the value of periodic examinations of the blood in workers exposed to benzene.

12. Newton, C. R.; Industrial Blood Poisons, J. A. M. A. 74: 114 (April 24) 1920.

PATHOLOGY OF CHRONIC BESZENE POISONING

Selling's [13] researches and those of Duke [14] show that the pathology of slow benzene poisoning consists in: (1) a direct destruction of leukocytes with reduced formation of new elements; (2) a destructive action on blood platelets and on the megacaryocytes of the marrow from which platelets are formed, and (3) destruction of adult red corpuscles and the prevention of the formation of new ones. These changes occur in the order given, the effect on the reds being especially characteristic of very slow poisoning, the last *to* appear and the last to disappear with recovery. Of the white cells, the polymorphonuclears suffer most. The blood picture, therefore, is largely negative; adult cells disappear and no young cells are formed. The destruction of platelets accounts for the abnormal fluidity of the blood.

Hektoen,[15] noting that Selling's experiments showed a selective action of benzene on the tissues and cells that are concerned in the production of antibodies and in defense against infection, studied the influence of benzene on the course of infection in animals, and found in rabbits an actual reduction of antibody formation, together with grave lesions in the marrow, a reduction in the number of leukocytes and a reduction in their phagocytic power. Rusk,[16] two years earlier, had shown that benzene-intoxicated animals produced hemolysins and precipitins less efficiently than normal animals.

The work of Weiskotten [17] and his colleagues, although not carried on with this in view, has a decided bearing on industrial benzene poisoning. They have found that the results of exposure of rabbits to benzene vapor are of the same general nature as those produced by subcutaneous injection of an olive oil-benzene mixture. Maximal sublethal dosage causes leukopenia, hemorrhages and slight anemia. After discontinuance of exposure, the total leukocyte curve rises to a permanent general level, lower than that existing before exposure. Their experiments also confirm those of Rusk and of Hektoen; for, during daily subcutaneous injections of an olive oil-benzene mixture, in four rabbits there developed evidences of active acute infection, and in at least *two* of these it seemed that infections present before the injections began had been "lighted up" by the benzene. In these animals, polymorphonuclear leukopenia did not occur; in fact, there was the usual leukocytosis of acute infection, and the animals died at its height. They conclude that the leukocyte count cannot be safely depended on in connection with the administration of benzene. It seems fair, therefore, to say that it cannot be absolutely depended on in the diagnosis of industrial benzene poisoning, although Newton's experience shows that it is of great value in detecting early cases. A year or so *ago,* a man employed in a Boston rubber works using benzene cement was taken with nosebleed, breathlessness and weakness, and bruiselike spots appeared over his body. The physician in charge, however, refused to regard the case as one of benzene poisoning because there was a high white cell count. One cannot help wondering whether careful examination might not have

13. Selling, L.: katr. z. path. Anat. u.z. allg. Path. 51: 576 1911.
14. Duke, W. W.: Causes of Variation in the Platelet Coun Arch. Int. Med. 11: 100 (Jan.) 1913.
15. Hektoen, Ludvig: J. Infect. Dis. 19: 69 (July) *1916.*
16. Rusk, G. Y.: Univ. California Pub. Pathology 2: 139. 1914.
17. Weiskotten H. G.; Gilles, C. E. F.; Boggs, E. O., and Templeton, E. R.; J. Res. 41: 425 (May) 1920.

revealed some focus of infection which would have accounted for this.

PREVENTION OF CHRONIC BENZENE POISONING

The question is, Can it be prevented? Is it possible in view of the marked susceptibility of certain individuals to benzene to protect workers completely against the effect of even small quantities of this poison? T. M. Legge tells of a man dying of typical benzene poisoning after employment for some months in a British rubber factory, yet analyses of the air at different points in the room showed only one part of benzene to 10,000 of air. Recently, I was consulted by a large industrial establishment as to the "possible danger" of exposing men and women to air containing one part of benzene in 200 parts of air, and at times one part in 100. It should be noted that Lehmann found that loss of consciousness might occur when them were from two to three parts in 100,000 of air.

Benzene is used in industry as a solvent, which means that the process is not complete till evaporation has occurred, till the solvent has passed off into the air. But the workman has tu breathe this air. Ideally, a strong suction exhaust should be installed at the point of origin of the toxic fumes; but how is this to be done in the varnishing of automobiles, removing shellac from the pews of a church. spreading fabrikoid on textiles, cementing the seams of boots. or building automobile tires? The practical difficulties are insurmountable. The surface covered with benzene is so big that no artificial exhaust can be so placed as to catch all the fumes. Moreover, benzene passes through the skin as well as the respiratory tract.

To the manufacturer, the introduction of this cheap and powerful solvent may seem an advantage; to the physician, interested in the producer more than in the product, it can only seem a disastrous innovation in industry.

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IS THE CONTROL OF DIPHTHERIA LEADING TO ERADICATION?

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The present procedures for the control of diphtheria do not seem to be leading toward the complete eradication of the disease. Since the case rate is approximately the same as that of thirty years ago, and the mortality rate has shown no appreciable reduction during the last few years, the factors utilized for control must be inadequate for eradication.

Eradication is here used as meaning such perfect control of the factors of a disease that epidemic spread becomes impossible. In this sense the term is applicable to the status of yellow fever in the United States, where, during the last century, it frequently reached as far north as Baltimore and Philadelphia in epidemic form; whereas at present its control is so perfect that this disease is no longer a menace to even our southern ports. Similarly, the control measures for typhoid are successful because both the case incidence and the mortality have been increasingly diminishing during the last twenty years. At the present rate of reduction typhoid as a cause of sickness and mortality should soon become practically extinct. Here the main factor would seem to be the successful prevention of transmission and a cumulative elimination of sources of infection.

At the present moment there are no indications that the control of diphtheria will parallel that either of yellow fever or of typhoid. If this be true, the present control measures for diphtheria are not successful.

True, the mortality from diphtheria and croup per hundred thousand population in the United States has been reduced 75 per cent. in the last thirty years (1890, 64 deaths per hundred thousand population; 1920, 15.3 deaths per hundred thousand [1]). Notwithstanding this reduction in mortality, the number of cases per hundred thousand would seem to be approximately the same as thirty years ago. This is asserted on the basis of the following consideration: During the early nineties, various authorities, from personal experience, placed the case mortality rate at from 25 to 40 per cent. On the basis, then, of an average 32 per cent. case mortality and a death rate of 64 per hundred thousand population (40,677 deaths, 62,947,714 population [2]) for 1890, there was an annual case rate for the total population of 200 per hundred thousand. It will be noted here that the case rate is determined from two fairly definite rates: case mortality and population mortality rate. So, then, we may say that in 1890 there was for the total population of the United States a diphtheria mortality rate of 64 per hundred thousand, a case mortality rate of about 32 per cent., and a case rate of 200 per hundred thousand.

In contrast to the rates for 1890, it is found that in the registration area (87 per cent. of the total population) there was for 1920 a mortality rate of 15.3 per hundred thousand, and, since the case mortality is about 8 per cent.,[3] the annual case rate for this average year is 200 per hundred thousand. As additional evidence that the rates for 1920 are approximately correct, the following is presented from a more elaborate report of 1919.[4] From sixty-eight cities with a combined population of 27,148,810 there were reported 65,823 diphtheria cases: a case rate of 243 per hundred thousand population. There were 5,404 deaths, making a case mortality of 8 per cent. and a population mortality rate of 20 per hundred thousand. This population is purely urban, and, to apply these rates to the entire United States. correction must be made for the rural population, where the disease is only 0.6 per cent. as prevalent as in the cities.[5] When this is done it is found that the case rate is somewhat over 200 per hundred thousand population, the case mortality 8 per cent., and the mortality rate slightly over 15 per hundred thousand.

Comparing the year 1890 with 1920, there is 75 per cent. reduction in case mortality (from 32 to 8 per cent.), which results in a 75 per cent. reduction in the mortality rate per hundred thousand population (from 64 to 15.3). But the disappointing feature is that the case rates per hundred thousand population would seem to be about the same (200) for the two average years in question.

RESULTS OF ANTITOXIN TREATMENT

During the last twenty-five years this reduction in mortality has been due almost wholly to the use of antidiphtheritic serum, although the more accurate—laboratory—diagnosis has been of great help. During the last twenty-five years, serum treatment has resulted in the saving of a million lives in the United States

1. Mortality Statistics. U. S. Bureau of the Census.
2. Vital Statistics. Part 1, Twelfth Census, U. S.. 1890.
3. Estimated from Pub. Health Rep., 1920.
4. Pub. Health Rep., Dec. 17. 1920. p. 3020.
5. Mortality Statistics, U. S. Bureau of the Census, 1910, p. 41.