BENZENE (BENZOL) POISONING*

REPORT OF A FATAL CASE WITH AUTOPSY FINDINGS

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It was Sir Wm. Osler who said, "It is the tragedy of today that man is so indifferent to the life of man. Yes; we surround the babe unborn with premonitory protection, deal wisely and gently with infancy and childhood and then hurl the product of a reasonably healthy youth into a maelstrom of blind chance, of dusts, fumes and fatigues, which wear down the stoutest body and cripple the most willing worker."

The current emphasis on production today which has come about through the war effort is throwing a much greater responsibility upon the medical departments of industrial organizations. Wherever workers handle toxic materials, even though mechanical and engineering protection is adequate, medical vigilance must be unrelenting.[1] To emphasize this point and to add to the literature on benzol poisoning we feel this report to be of particular interest because of the fact that (a) detailed studies had been carried out prior to, during and following a long illness, and (b) the concentration of benzol vapors in the working atmosphere were definitely known.

CASE REPORT

D. D., male, 35 years old; benzol poisoning chronic; hypoplasia red bone marrow, subacute bronchopneumonia; death; postmortem examination.

This man entered Corwin Hospital on April 18, 1942, because of a progressive weakness, dyspnea an exertion, rapid pounding heart, a slight bleeding from the gums of one day's duration and physical inability to perform his usual easy duties as a chemist in the by-products department of a coke plant where he had worked for eleven months. His symptoms followed a cold that had developed in February, 1942, and had persisted, though it was not particularly sevea-e.

The patient, working in a small room, had been in the habit of rinsing out distilling flasks with benzol six to eight times a day which required ten to fifteen minutes with each operation. The concentration of benzol vapors in the laboratory varied from 500 parts per million during the height of the operation to 30 parts per million five minutes after completion. Realizing *that* a definite occupational hazard was present'. crude solvent and cleaner's naphtha were substituted for benzol January 1, 1942. Physical examination and complete Mood examination on the patient a few days before had failed *to* reveal any significant physical findings or hematological changes. Inorganic urine sulfates were 72.7 per cent and 77.8 per cent on two occasions at this time aa determined by the method of Folin[2] and Yant, Schrenk, Sayers, Horvath and einhart[3].

Physical examination on admission to the hospital revealed a very well developed, well nourished white male. He appeared chronically ill for the skin was lemon yellow and almost transparent, or wax-like. The mucous membranes were pale as were the conjunctivae but no signs of bleeding were noted. Cardiac pulsations were visible in the neck and were heaving over the precordium. The pulse rate was rapid and there was a soft hemic apical murmur. The spleen and liver were not palpable nor was there any adenopathy.

Laboratory Findings.—Urinalysis: The specific gravity of the urine was 1.017. No albumin or pus was present. Inorganic sulfate was 92 per cent (taken three days after last exposure to benzol)[4].

Blood: Hemoglobin was 31 per cent; red blood count 1,550,000 with 3.7 per cent reticulocytes. The white blood count was 3,450 with 10 per cent stab forms, 40 per cent segmented forms and 50 per cent lymphocytes. Platelet count was 171,000. Bleeding time was 3 minutes, 10 seconds and the coagulation time was 3 minutes, 45 seconds. The Kahn and Kolmer were negative.

Treatment and Clinical Course.—The patient was immediately started on supportive therapy including a high vitamin, high caloric diet, yellow bone marrow by mouth, liver extract intramuscularly, vitamin C and B by mouth and parenterally. hematinic plastules with liver and strict oral and personal hygiene with much fresh air and sunshine. In addition, blood transfusions were given weekly. In spite of a feeling of well-being on the part of the patient, his progress was unsatisfactory. On Aug. 20, 1942, the hemoglobin was 74 per cent; red blood count 3,390,000; white blood count 5.100, with 4 per cent eosinophils, 7 per cent stab forms, 43 per cent segmented forms, 43 per cent lymphocytes and 3 per cent monocytes. The patient, although only slightly improved, was very anxious to go home for a few days. Permission was reluctantly granted on Sept. 11, 1942; however, he returned fourteen days later with a severe chest cold of five days' duration.

Physical examination at this time revealed an acutely ill patient. His temperature was 102.8 F., pulse rate 100 per minute and respiratory rate 28 per minute. He complained of masked substernal tightness and coughed intermittently Producing a thick greenish yellow mucoid material. The lung fields were filled with coarse crackles throughout with scattered areas of bronchial breathing. Roentgen examination failed to visualize any pneumonic process but there was a mild increase in the peribronchial markings.

Laboratory Report.—Urinalysis: The specific gravity was 1.033.

Blood: The. hemoglobin was 79 per cent; red blood count 3,650,000; white blood count 3,300 with 12 per cent stab forms. 53 per cent segmented *farms,* 32 per cent lymphocytes and 3 per cent monocytes.

Sputum: Repeated typings were negative for pneumococcus.

The patient was thought to be suffering from a pneumonic process but in view of *the* serious blood findings sulfanol drugs were contraindicated. He was placed in an oxygen tent and previous

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therapy was resumed. His course was septic, the temperatuie showing a daily elevation to 104 F., with a corresponding increase in respiration and pulse rate. Because of the poor progress of the patient, sulfadiazine later was administered, 2 gm. initially with 1 gm. every four hours. This produced no relief of symptoms or seeming effect on the blood picture. The last blood study performed on Oct. 26, 1942, revealed a hemoglobin of 54 per cent: a red blood count of 2,630,000; a white blood count of 4,600 with 3 per cent eosinophils, 19 per cent stab forms, 35 per cent segmented forms, 40 per cent lymphocytes and 3 per cent monocytes The patient died on Nov. 3, 1942, after an illness of appioximately nine months.

Autopsy Observations

Autopsy was performed twenty-three hours postmortem and twenty hours after embalming. An abstract of the important findings follows:

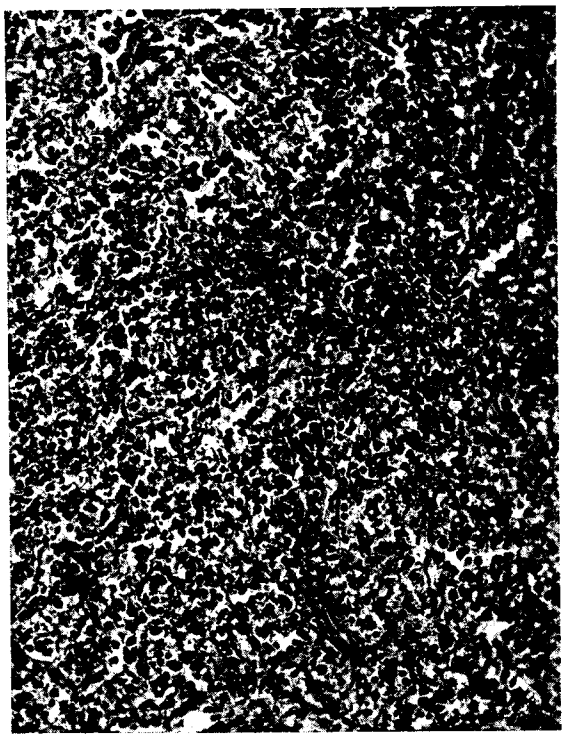

Fig. 1. Spleen. Lymphoid hypoplasia. x150.

Gross Examination.—The body was that of a well developed and well preserved young adult male. The skin had a pallid, rather yellowish tint. No free fluid was present in the body cavities but all organs had a pale appearance.

Lungs: The right and left lungs presented similar changes. The visceral pleurae were mottled with a dark anthracotic pigment. A few friable adbesicns joined the left lower lobe to the diaphragm. To palpation firm nodular areas were noted with intervening crepitant areas. The lower lobes were heavy and many more nodular areas were present. The cut surface of the sectioned lungs was reddish brown, exuded a reddish frothy fluid and the nodular areas were conspicuous. From the cut smaller bronchi a white mucoid material could be expressed which was similar to material in the trachea and bronchi.

Spleen: This organ was not enlarged. To palpation it was very flaccid. The cut surface of the sectioned organ was a deep reddish brown and very soft.

Liver: The liver was not enlarged, but the external surface was a pale reddish brown. The cut surface was not remarkable.

Bone Marrow: The appearance of the marrow obtained from ribs, sternum, and vertebrae was similar. It was grayish red, moist and abundant. Marrow obtained from the upper tibia was of the yellow adipose type.

Microscopic Examination.—Lungs: The bronchi were slightly to moderately dilated. The mucosa was intact but was extensively infiltrated with leukocytes including lymphocytes and monocytes, with scattered granulocytes. The bronchial lumina almost all contained mucopurulent exudate in large quantity. Some of the small bronchi were partly filled with granulation tissue as well as exudate. The lung parenchyma showed a patchy exudate, more or less purulent and partly

Fig. 2. Lirer. Fatty metamorphosis. x175.

organized, tilling scattered groups of alveoli. There was moderate anthracotic pigmentation of the interstitial tissue and atelectasis and emphysema were present throughout.

Spleen: In some areas the sinusoids were empty, dilated with large lining cells, and elsewhere were ccmpressed. The pulp spaces contained normoblasts, myeloid cells and occasional megakaryocytes and also many phagocytic cells loaded with brown granular pigment. Malpighian bodies were reduced in number. Those remaining were small and were without germinal centers.

Liver: Contained abundant pigment of two types. One was seen in liver cells and bile canaliculi. It was dense, yellow-green and hyaline. The other was brown, granular and appeared in sinusoidal lining cells. Liver structure was not normal. The central veins were not well defined, and the lobules were correspondingly distorted. The liver cells were coarsely granular, with unevenly stained irregular nuclei. Fatty metamorphosis was present

in many. The sinusoids were compressed and thin. The blood present within them was scanty with very few leukocytes.

Bone Marrow: There was a reduction in total number and irregularity in distribution of the myeloid elements. The adipose tissue stromal cells and blood vessels did not appear to be significantly altered. The erythroblastic elements were represented by small clumps of small dark staining cells, chiefly normoblasts. Megakaryocytes were numerous, irregularly spaced, with

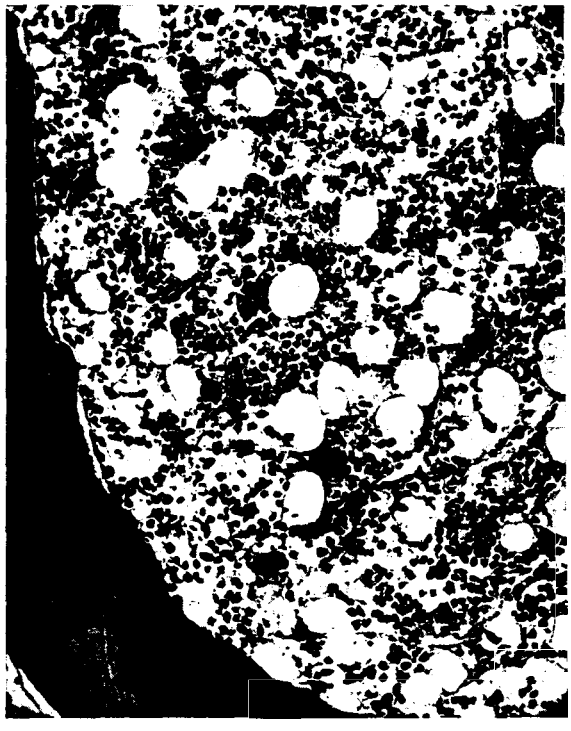

Fig. 3. Vertebral bone marrow. Hypoplasia of erythroblastic elements. x175.

marked variation in size, shape and nuclear configuration. All of the myeloid elements were present, but mature granulocytes were less numerous than normal. Eosinophilic granulocytes were present but were proportionately reduced in number. The predominate cell was undifferentiated non-granular with a large reticular, round, oval or indented nucleus. Pigment deposition was not demonstrable in the bone marrow.

Comment

Continued or intermittent exposure to benzol produces in certain individuals irreversible changes. These changes depend upon duration; exposure concentration of the vapors and individual susceptibility. The last factor seems to be important for it has been our privilege to study men who have worked daily for months and even years in high concentrations of this aromatic hydrocarbon and yet show no deleterious effect. The blood picture in benzol poisoning also varies but the usual finding is depression of the blood-forming organs[6]. A white count of 5,000 or less is indicative of benzol poisoning, and as has been shown by Hunter[5] and Von Oettingen[7], a decrease of the polymorphonuclear percentage is the best index of early poisoning. These same authors also report cases with increased leukocyte counts, eosinophilia, thrombocytosis and thrombopenia. There may be a tendency to polycythemia but the usual tendency is for a progressive anemia to develop with a corresponding depression of the hemoglobin.

The pathology of this condition has been admirably described by Mallory, Gall and Brickley[8]. They describe the entire hematopoietic system undergoing marked changes. Long exposure to benzol produces extreme marrow hyperplasia and extramedullary hematopoiesis and is the more common finding. Short or long exposure may produce a severe hypoplasia of the hematopoietic tissue or there may be an intermediate reaction.

Summary

1. A fatal case of benzol poisoning has been presented with autopsy observations.

2. The duration of exposure, concentration of the vapors and clinical course are discussed.

3. The pathological changes present in this case are consistent with the findings of Mallory, Gall and Brickley[8] in chronic exposure to benzol in what they describe as the intermediate group of cases.

4. Bronchopneumonia was a complicating and terminal factor.

5. Prevention of this condition must be brought about by more efficient medical and engineering control and by education of the worker.

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MANAGEMENT OF THE SILICOTIC PATIENT

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Silicosis, by the very nature of the disease, does not lend itself to effective treatment and our efforts, once the disease has been acquired, must necessarily be directed toward halting the process short of disablement. The problem therefore resolves itself into one of proper management of the patient rather than of treatment in the usual sense of the word.

That the problem of adequate supervision and treatment of workmen in the dusty trades is the problem not only of the industrial physician but of the general practitioner as well is indicated by the results of a recent survey of the industrial hygiene problem in fifteen states, including Colorado, Idaho, and Utah'. From these results it was estimated that over 1,000,000 workers in the United States are exposed to silicious dust. Of special interest to the mining West is the fact that of 55.676 workers in 548 plants devoted to the extraction of minerals. not more than 40 per cent had the services of a plant physician either part time or full time.

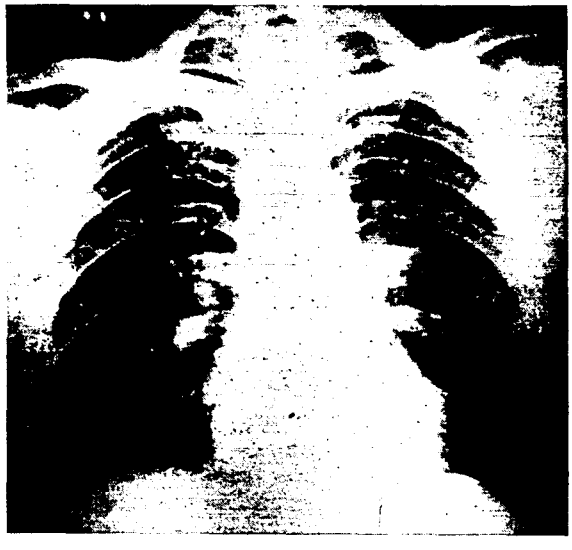

Fig. 1

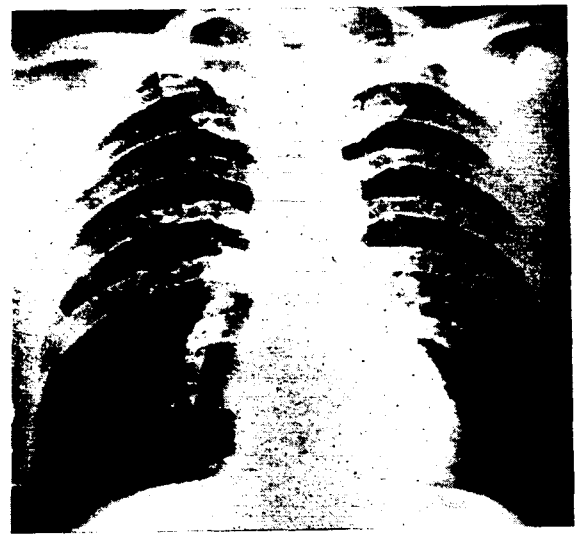

Fig. 2

With these conditions aggravated by the war. the family physician must inevitably assume a greater share of the responsibility for the proper management of silicotic patients.

Good practice in the management of the silicotic as well as in the solution of the whole problem of silicosis demands that physicians assume a greater responsibility for the conditions under which their patients work. It should be required that the air these patients breathe be made to conform to established minimum standards of freedom from dangerous dusts. The physician who fails to do this is not justified in permitting the patient to continue in his hazardous employment. Unfortunately, the removal of the silicotic worker will only result in a healthy worker being exposed to the same hazard and the physician thereby contributes to the perpetuation of the disease.

The primary responsibility of the physician who undertakes the management of the patient with silicosis is to advise him intelligently and truthfully as to the necessity for

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