OCCUPATIONAL ANAEMIAS

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The subject of industrial anaemia, without definite limitations, lends itself to broad interpretation, for in the general sense there are countless anaemias which are industrial in origin. Some may be accounted for by long hours of labor, too little fresh air and sunshine, poor hygienic conditions; others may be secondary to industrial disease which primarily has no relation to the hemopoietic system, as for example pneumoconiosis. Still simpler would be anaemias, secondary in nature, following accidents in which there is great hemorrhage. Innumerable instances may be thought of wherein anaemia may be produced. A study of all these would be as broad as the science of industrial medicine itself, since the blood picture is so usually affected in any debilitating disease. However, this paper has for its aim a discussion of anaemias proper, anaemias in which the blood destruction is a primary phenomenon, brought about through direct action of poison on red cell or poison on hemoglobin. In other words, this paper shall consider only those anaemias that have for their etiology a direct poisonous action on the oxygen carrying facilities of the body.

There are a good number of hemotoxic agents used in the industries, and many of them are employed in manners which make poisoning comparatively easy. Certain of these compounds have received a large amount of notoriety and are well known, the literature being filled with them. An example of such a toxin is lead. Conversely there are certain extremely dangerous substances about which very little has been written, and such is vanadium. It would, of course, be the more easy and logical thing to discuss the well known poisons to great length, since

their literature is so abundant while that of the little heard of poisons is so meagre, but rather than do that it has been deemed advisable to do just the opposite - - - if not to produce more about the less known things, at least to give them more time in the study of the literature.

The industrial poisons which will be considered are arseniuretted hydrogen, benzol, toluol, xylol, aniline, nitrobenzol, dinitrobenzol, dinitrotoluol, nitro-toluol, trinitrotoluol, toluidine, naphtha, gasoline, benzine, vanadium tetrachlorethane, carbon-monozide,and lead. In certain instances where there is a chemical relationship between substances and where their reactions are almost identical, these substances will be considered together.

ARSENIURETTED HYDROGEN ANAEMIAS.

Arseniuretted hydrogen poisoning gives evidence of assuming greater and greater importance in industrial medicine. With modern industrial procedures tending more and more to the use of those processes in which arseniuretted hydrogen is produced, more cases are to be looked for, and with clearer and more accurate knowledge of the clinical manifestations of this condition fewer will be erringly diagnosed.

HISTORY.

Twenty years ago arseniuretted hydrogen poisoning was all but unknown. Koelsch[3] found but one hundred thirty cases in the entire German literature. In 1908 Glaister[1] states that but one hundred twenty had been registered in Great Britan, and in the years between 1900 and 1914

there were but fifty three. Of late years, numbers of poisonings by this chemical have been reported, and rather exhaustive work has been carried out regarding the production of the gas, the signs and symptoms of the poisoning, the pathology; but there is yet a large field of prevention to be worked out.

PROPERTIES OF CHEMICAL.

Arseniuretted hydrogen, also known as Arsine and Hydrogen Arsenide, is a colorless gas which gives off an odor of garlic. It liquifies at -40°D. and is very soluble in water, five volumes of the gas being soluble in one volume of water. Its production is usually accompanied by much heat, and this causes it to be somewhat unstable. The usual manner in which arseniuretted hydrogen is formed is by the action of a strong acid (most often hydrochloric or sulphuric) on one of the heavy metals - zinc, tin or iron, when one of the components of the reaction has arsenic as an impurity. It is rather the common thing for zinc, tin or iron to have arsenic in combination with them. Analysis of samples of sulphuric acid has shown that the crude acid may contain 0.045-0.140 per cent of arsenious acid as an impurity. Crude hydrochloric acid has 0.0014-0.641 per cent of arsenious acid in it.(1) The reaction for the formation of the gas is.

$$H_2SO_4 + Zn = ZnSO_4 + H_2$$

$$2\,As + 3\,H_2 = 2\,AsH_3$$

TOXICITY.

The gas is extremely toxic. Dr. Alice Hamilton in her monograph "Hygienic Control of the Aniline Dye Industry in Europe" states that

the hundredth part of a milligram of arsenic taken as arseniuretted hydrogen is rapidly fatal for human beings. Wignall[7] does not agree with this statement, drawing his conclusions from the amount of arsenic obtained from the urine of patients who recovered. He believes that far greater amounts may be taken. According to investigations of Joachimoglu reported by Koelsch[3], the fatal dose of arseniuretted hydrogen for man is .1 to .15 grams. Dubitzki says concentration is more important and believes the danger begins when the air contains 0.05 parts per thousand; 0.03 parts per thousand will produce poisoning after several hours.

PATHOLOGY.

Pathologically, the primary effect seems to be not on the tissues of the naso-pharynx or even on the lungs. Post mortem examination revealed only a hypostatic congestion of the lung tissues.[8] Guelman[1] states that the lungs act as an open gate to the gas, allowing it to pass as freely as oxygen itself and with no more ill effect on the structures. The primary damage is to the red blood cells, arseniuretted hydrogen acting as a powerful solvent to them. Albrecht and Hedinger quoted by Guelman suggest that the lecithin coat is dissolved from the corpuscles. The latest work found on this subject[9] states that arsine or arseniuretted hydrogen is oxidized by oxyhemoglobin to a colloidal form of arsenic and that this destroys the red blood corpuscle structure. Naegeli believed that arsine destroyed that hemoglobin which was dissolved in the blood plasma earliest, thus accounting for the color index of over one. Simultaneous regeneration and destruction also quite likely takes place. Guelman believes that the products of red cell destruction stimulate cell proliferation, thus accounting for the leucocytosis which was observed in all his cases.

With cell destruction, hemoglobin is excreted in the urine and by way of the bile. Accordingly, the greatest of the pathological changes are in the kidneys and liver. The kidneys are also called upon to excrete the arsenic. The kidneys grossly are enlarged and very dark on their external surface. The cut surface is pale and fatty. Microscopically there is a thin capsule and increased parenchymal connective tissue. The malpighian bodies are seen in a state of hyaline degeneration. The capsular surface is uneven due to swelling of the convoluted tubules. The epithelium of the convaluted tubules is of the low cuboidal instead of the tall columnar. Thus there is a large lumen. The secreting cells form a spongy mass and are vacuolated. There are pigment granules in the convoluted tubules. The cells all seem in incipient necrosis. Delepine (8) believes the necrosis to be usually more advanced than apparent.

The surface of the liver grossly is smooth. The cut surface is pale and shows signs of a fatty fibrosis. Microscopically the blood capillaries are very much distended and contain decolorized red cells, which are greatlyswollen. The walls of the capillaries are distinct. The liver cells are shrunken, many are vacuolated; those especially in the portal zone give a spongy appearance of vacuolization. The nuclei of these cells are indistinct, the vacuoles do not take the fat stains. Many of the cells are pigmented with a finely granular pigment -- especially those in the hepatic and portal zones of the lobule. In short, then, the liver may be said to be in a state of dropsical degeneration with considerable atrophy, pigmentation, some necrosis and very slight fatty degeneration of the secreting epithelium.

Of the other organs, the heart grossly is soft and the wall appears to be slightly fatty. Microscopic examination shows that there is some slightly increased segmentation; striation transversely is indistinct while that running longitudinally is exaggerated. Some of the fibres may be granular and give a fat reaction. The spleen grossly appears darker than usual but microscopically shows nothing. The other organs are negative of significant findings. No record was found of examination of the bone marrow. This would have been interesting.

SIGNS AND SYMPTOMS.

The length of time after exposure to the gas until symptoms begin is difficult to determine, since there is no distinct feature of the physical properties of the gas to make it noticed. The garlic odor is scarcely ever remembered in those who have been poisoned. Legge (2) gives an account of a case in which a man was poisoned and the time of exposure was taken as that time when there was frothing of the contents of a vessel with which he was working. Symptoms came on in six hours in this case. Generally it may be said that several hours elapse between exposure and the onset of symptoms.

The classical symptoms are: Abdominal pain, headache, vomiting, chills (1)(2)(3) and diarrhoea. The abdominal pain becomes acute and griping in character and tends to be somewhat localized to the epigastric region. There is tenderness here on palpation. The patient becomes weak and drowsy, his skin early shows a deep pallor and in some cases a copper-red cyanosis is described. In the very acute cases there may be oppression in the chest, great apathy, confusion, burning pains in the throat and dyspnoea. Depending upon the severity of the poisoning, jaundice and hematuria may develop

within a few hours, but it commonly does not appear until eighteen hours have elapsed. At this time there is kidney tenderness and there may be diffuse hemorrhages from the conjunctiva. The pupils may be contracted, the tongue scarlet in color, the abdomen sunken and the liver enlarged. There is frequent vomiting and hiccuping of bile. The reflexes sometimes are hyperactive, less often are hypoactive. As the condition goes on the jaundice deepens, the feces become darker and more blood stained. Acute oliguria usually with the urine blood-red comes on late. The patients are observed to pass out in convulsions. Gerbis (4) has added to these symptoms great thirst, pain along nerves, paraesthesias, tingling of extremities. Dudley (5) observes that while in some red cell destroying diseases, such as blackwater fever, the blood pressure is low, but in this condition it is generally somewhat increased though the pulse and respiration are but slightly higher than normal.

Dudley (5) in a very interesting and dramatic report of arseniuretted hydrogen poisoning in a submarine describes a number of cases of a less severe type, none of which were fatal. His cases showed a slight increase in pulse rate, no fever. A number of the cases developed a soft systolic murmur which he calls haemic due to the anaemia. The dyspnoea occurred only on exertion. All had vomiting, burning upper abdominal pain, dryness and burning in the throat. Here there was sometimes diarrhoea, sometimes an obstinate constipation. Edema of the fact and jaundice were constant -- the crew of this submarine were called by their mates the "Chinese crew". There was a mild degree of hematuria and some bile was found in the urine. This cleared up very rapidly when the poison was removed. Neuritis and a peculiar muscular weakness were especially marked in these cases.

The laboratory findings on examination of the urine of these cases usually shows diminished quantity, thick consistency with a specific gravity of around 1.020, color a brownish-red, reaction slightly acid, albumin five per cent or less, Gmelin's reaction at times positive and at times negative, an average of two kidney epithelial cells and four erythrocytes to each field, and some granular casts. The blood examination shows reds diminished often to as low as 810,000 cells per c mm. Hemoglobin is usually under forty per cent and goes as low as sixteen and eighteen per cent. The leucocyte count is always increased and counts of 30,000 are common. Neutrophiles usually predominate, making about eighty per cent of the whites. The color index is most often over one. (Dudley, however, does not agree with the other workers in some respects. He finds a leucopenia in his cases and about forty per cent of the white cells are lymphocytes). Stained films of the red cells show many microcytes, macrocytes and a few nucleated red cells. One of Dudley's cases with a red count of two million cells, a high color index, advanced degeneration of red cells with erythroblasts and megaloblasts more numerous than normoblasts and with a bile stained serum gave an appearance so much like pernicious anaemia that he asks whether this does not point to a toxaemic cause for pernicious anaemia. Fragility of red cells was decreased, suggesting that there was a survival only of the fittest of the cells.

INDUSTRIES WHERE THE ARSENIURETTED HYDROGEN HAZARD EXISTS. PREVENTION.

As previously stated, the poison gas, arseiuretted hydrogen, is usually formed in processes in which there is a reaction one with the other of either acid or metal in which arsenic is found as an impurity. Thus

(6) Kunz-Krause, H. gives a very interesting account of his own experience with arsine poisoning.

Legge[2] cites cases in chemical works where arsenic is being extracted from acids to make chemically pure acids. He also mentions an instance where large tanks were being cleaned by acid which was carried in in galvanized iron pails and in which arsenic was present either in the acid or the pail. In another instance workmen entered to clean a large vat which had contained sulphuric acid, but had supposedly been flushed. Residue remaining in the bottom of the tank was still giving off sufficient arsine to fatally poison two of the men.

Industries making or using hydrogen have to their credit a number of deaths from this poison. Hydrogen is made chiefly by the action of hydrochloric acid on zinc, both of which may contain arsenic as an impurity. Thus the hydrogen used in the oxyhydrogen often is contaminated and workers using the flame are among the victims. Toy balloons which are filled with hydrogen and also the large balloon industry which also uses hydrogen have among their workers a few score of fatalities.

Other cases are seen in the process of picling iron previous to galvanizing. Gases were reported in the bleaching powder manufacture when men were sent to clean acid tanks with iron shovels. In the production of acetylene by decomposing impure calcium carbide and ferrosilicon others were seen.[1] In the process of bronzing art metal there are cases reported. While arsenic is no longer used in colors in the dying industry, there are still numberless processes of reduction where acid and metal meet that give chances for poisoning. During the years of the war when metals and acids were likely to be more than usually crude, there were many more cases of poisoning than formerly.

Dudley recounts a tale of wartime poisoning which would do credit

to a popular fiction writer. Two submarines, the "D3" and "D4" were experiencing very distressful occurrences. At every return to the submarine base, numbers of the crews would be ill. Other submarine crews dubbed them the "Chinese crew", for their skins had all assumed a jaundiced cast. Headaches, insomnia and often diarrhoea were bothering the men. Three of the members became so ill that upon their return to port they were sent to the base hospital, the fleet surgeon diagnosing carbon monoxide poisoning. However, at the hospital a clinical diagnosis of arsine poisoning was made and extensive investigation started as to the source of the poisoning. The crew members blamed a new fuel, but further investigation developed that actually the storage batteries were responsible. The makers of the batteries blamed the sulphuric acid which was being used and analysis of the acid did show traces of arsenic, but new acid did not relieve the situation. Further investigation developed that the antimonial lead allow surfacing the plates had been deeply corroded and that an arsenic impurity of the plates themselves was being rapidly dissolved. With new plates the trouble was alleviated.

And so, storage batteries are also a potential danger especially when used in closely confined places. However, it is stated in the Oxford System of Medicine, volume 4, page 621, that there usually is no ill health in connection with the forming and charging rooms of an electric storage battery plant, but Rambousek tells of an instance of arseniuretted hydrogen poisoning in this department of a German plant.

(10)

The MacArthur-Forrest cyanide process for recovering gold and silver from the poorer ores is also one fraught with dangers. A stage of this process at which the double cyanide of the gold or silver and potassium with water is filtered through zinc dust will produce arsine if

the zinc dust contains arsenic. Several fatalities have arisen from this process. With the English process of making benzidin in which for the alkaline reduction with zinc dust and caustic is followed by the addition of acid. If the zinc contains arsenic, arsine will be formed. Frequently the poisonings attributed to benzidin in those who clean the tanks after the reduction process in the anilin industries are arsine poisonings.

Prevention of the arseniuretted hydrogen hazard seems to resolve itself to intelligent study of chemical methods employed with an understanding of where the danger exists, for the first step toward prevention must lie in an appreciation that a danger exists. Ideal would be methods where-in arseniuretted hydrogen would not be formed. Substitution of electrolysis for the acid-metal method of hydrogen production or the use of de-arsenated chemicals would, of course, be the theoretical answer to remove the danger. Practically such procedures are obviously impossible. Koelsch (3) suggests that prevention consist of the use of closed apparatus wherever possible and that where this cannot be done ventilation must be provided. With fairly definite figures as to the toxicity and the toxic concentrations, exhausts, ventilators, hoods and the like should be employed and should be so efficient as to leave a large margin of safety. Koelsch gives a method for detecting the gas; mercuric chloride is turned yellow by very slight concentrations of arseniuretted hydrogen. A solution of this on filter paper would make a very simple and valuable means for detecting the danger. Yet another small point which neverthe less is of importance is the speed or rate with which arsine producing chemicals are brought together. Many of the fatalities recorded seem to give a history of a sudden evolution of gas which was brought about by the rapid addition

of acid to metal. With ventilators competent to care for an average evolution of gas, a sudden and profuse outpouring of it would probably overload the atmosphere for time long enough to have bad effects. The fatal cases are not those of continued exposures to small amounts, but rather seem to be the sudden, single, overwhelming blasts of the chemical. Thus another point in prophylaxis is the regulation of the speed of reactions, adjusting the ventilators to the maximum production and not to the average. A further suggestion that is made by many of the authorities is for periodic urine and blood examinations. Workers who are exposed to toxins of this kind give early evidence of their danger by decreased red counts, decreased hemoglobin and by their urinary findings.

ANAEMIAS CAUSED BY BENZOL, TOLUENE AND XYLENE.

Benzol poisoning in America previous to 1914 was little heard of. Selling (12) had reported a few cases in a can factory where benzol had been used as solvent for rubber used in sealing, but not until certain effects of the World War had made themselves felt did benzol poisoning make itself familiar to all connected with industrial medicine. Dramatically, almost uncannily, did the cases then appear. The reason for this sudden flood of accidents came on the heels of the adoption of the chemicals into American industry. The war as explained by Hamilton (13) did two things: First the supply of benzol from Germany was cut off and with it aniline which was used in rubber compounds could not be procured; second, there was a sudden demand for benzol and toluene for the manufacture of explosives. Consequently coke by-products plants were erected in order to procure benzol and toluene; the latter was also obtained from illuminating gas.

Then came the armistice and a sudden cessation in the manufacture

of explosives. With it came the need for a new market for the enormous quantities of benzol that war-time industries had required. Benzol, a cheap solvent acting more efficiently than petroleum benzin and naphtha for fats, resins and gums and now at a lower price than these latter, naturally was looked upon with great favor by manufacturers wherever it could be used. As a consequence benzol became a part of a great many industries and processes. With little knowledge of its activity and its dangers, multitudes of accidents were bound to follow. True to expectations many cases did occur, and with a study of the literature of the past ten years, it is striking how the deluge of literature came forth on a subject that previously had been a rarety in this country.

PHYSICAL PROPERTIES AND CHEMISTRY.

Benzol or benzene (C_6H_6) is a colorless liquid, boiling at 79.6°C., obtained from the distillation of coal tar and from the strippings of coke oven gas. It is highly insoluble in water, slightly soluble in alcohol, and completely miscible with ether, acetic acid, carbon disulphide, and a large number of organic substances. Many substances are commercially known as benzol, some of which contain benzene and some do not. All are to be sharply defined from benzine which is a petroleum product (a mixture of C_6H_{14} and C_7H_{16}). Benzol was discovered by Faraday in 1825 in the liquid produced by the compression of illuminating gas from certain oils. In 1865 Kekule[14] announced its structural formula.

Toluene is a limpid liquid, boiling at 111°C. and smelling like benzene. It has a specific gravity of 0.88 at 0°C. and does not solidify at 120°C. This hydrocarbon is found in the light oils from coal and wood tar and also among the products of dry distillation of balsam

of tolu and other resins. It has been formed synthetically by adding sodium to a mixture of brombenzene, methyl iodide and pure anhydrous ether, and keeping the mixture cold.

Xylol, formerly regarded as a pure compound, later researches have shown to be a mizture of two dimethyl benzenes. They are colorless liquids boiling at 136°C., solidifying at 15° to a crystalline mass and possessing a peculiar smell which is quite different from that of benzene. Fuming nitric acid converts it into two dinitrocompounds, which are separated by crystallizing them with alcohol.

TOXICITY.

Hamilton (13) states that in cats a narcotic effect begins in two hours after exposure to 20 mg. per liter of air. In six hours narcosis is complete. With 60 mg. per liter the narcosis comes on in fifteen minutes and is complete in an hour. In man 15 mg per liter of air produces listlessness and confusion after half an hour, and exposure to 20-30 mg per liter may cause loss of consciousness in a few hours (2-3 parts per 100,000 parts of air). Legge (15) cites a case of poisoning where the concentration was 5.5 parts per 10,000 when the room was ventilated and 168 parts per 10,000 when it was not.

The toxicity of toluene and xylene are very comparable to that of benzene. They produce the narcosis spoken of above, but do not produce delirium or convulsions. The action may be described in a word as being similar to that of benzene, idffering only in severity, benzene being more toxic. Toluene and xylene have not near the industrial importance of benzol.

PATHOLOGY.

To demonstrate the toxic and pathological actions of benzol, Fontana (16) injected guinea pigs with the chemical using 1 cc per kilo of body weight daily. Death was found to occur in from four to ten days, and it was demonstrated that at the moment of death, leucocytes and granular erythrocytes were completely or almost completely absent from the circulating stream. As the leucopenia was being produced, it was found that the polymorphonuclear leucocyte was the type of cell most extensively reduced. With a rapidly fatal case, however, this inversion of the leucocytic formula failed to appear. The effect on the red cells was not so great. Hemoglobin was reduced by about one tenth, and in four days the red count lowered to around 3,000,000. The granular red cells always diminished progressively and finally disappeared. Only about half of the animals showed a diminution in the platelets. The volume of the spleen was reduced in all, the bone marrow was sometimes normal, sometimes gelatinous. Subseral ecchymoses were frequent and sometimes there was parenchymal hemorrhage. Microscopic examination of the femoral medulla showed scarcity of leucocytes, megokaryocytes among the red corpuscles and some polychromatophilia. There was increase in the medullary fat, also congestion and small hemorrhages and sometimes atrophy. Smears from the spleen showed numerous white elements, chiefly mononuclears. The spleen was usually congested with subcapsular hemorrhages and atrophy of the malpighian corpuscles with sometimes a diffuse sclerosis. The lymphatic glands frequently showed small hemorrhages and the channels seemed empty of cells. Small hemorrhages and slight fatty infiltration was all the liver showed.

Zenoni (17) describing three of his cases histologically says they are characterized by: noticeable hypoplasia of the bone marrow with toxic

leukolysis, disappearance of megakayocytes and scanty production of erythroblasts; parenchymatous atrophy of the spleen with a corresponding increase of the fibrous and reticular tissues, presence of many plasma cells and considerable amounts of blood pigment; fatty degeneration of the wall of many small blood vessels. Zenoni thus thinks the histopathological picture of this affection is noticeably different from pernicious anaemia.

(18)
An autopsy report by MacCallum quoted by Underhill and Harris is as follows: Anatomical diagnosis: Purpura Hemorrhagica (probably toxic), hemorrhages in the skin, viscera and serous surfaces, pallor of the organs. Muscles a deep red color. Blood pale and watery. The heart muscle and to a less extent the liver show some fatty degeneration. Bone marrow of femur fairly consistent; it is of a dull ochre yellow color with no abundance of bloody supply. It does not look like markedly hyperplastic marrow. Microscopic report gives hyaline necrosis of malpighian corpuscles of spleen. Smear of the femur marrow shows very few cells of any kind. The predominant cell is the normal red, which is pallid and slightly basophylic and shows no great irregularity. Leucocytes are extremely scanty. They are mostly of the lymphocytic or myeloblastic type. They are characterized generally by a very definitely reduced chromatin in the nuclei. Many nuclei show vacuolization and the cytoplasm is thin, fragile and poorly stained. One megalocaryocyte seen. Suggests an aplastic bone marrow.

(12)
Selling has evidence that benzol destroys the platelets; Underhill
(18)
and Harris conducted a series of experiments demonstrating that benzol acts not only on the blood elements but exerts a catabolic influence on body

tissues as a whole. (14) Winslow states that benzol acts as a cerebral depressant giving anesthetic effect, and also is a nerve irritant producing spasmodic movements, and actual damage to nerve tissue. He says the early leucocytosis is due to a compensatory production of more white cells due to the destruction of those already in the blood stream, but that leukopenia is the true picture. (19) Rohner, Baldridge and Hansmann believe that the endothelial leucocyte and the adult erythrocyte are immune from the action of benzol, and that the effect of the chemical is on the bone marrow alone. (20) Forbes and Hompe find that benzol has little effect on blood coagulation time, quite in contrast with Hurwitz' (27) belief and that of most others. (21) Weiskotten, Gibbs, Boggs and Templeton find that the cell showing the greatest decrease is the small mononuclear, and that after recovery there is a permanent leukopenia due to the fact that the small mononuclears never reach their former level. (22) Gettler presents a method for analysis for benzol from post mortem organs. He finds benzol in liver, brain, blood, heart and lungs in measurable quantities. His method should be of importance medico-legally.

SIGNS AND SYMPTOMS.

Both acute and chronic cases are described. The acute cases, however, are much more rarely seen. (14) Winslow states that the common symptoms of the acute intoxication are: (a) dizziness, faintness and drowsiness-culminating in unconsciousness and coma; (b) pallor of face and cyanosis of lips and finger tips; (c) feeble and rapid pulse; (d)breathlessness and a feeling of tightness in the chest, sometimes culminating in immediate death from respiratory paralysis; (e) visual disturbance with nervous excitation, tremors and convulsions, and more rarely mania or delirium; (f) reddish

spots on the skin and internal surfaces due to small hemorrhages in the tissues; and (g) where the substance has been taken in by mouth, symptoms of acute gastric irritation. Death may occur within five minutes or the patient may apparently recover and succumb several days later. Vigorous muscular exertion renders the toxin more potent.

The chronic condition is better known. Starr (23) in attempting to arrive at early diagnosis, objects to the belief that a leukopenia is of early enough significance (as stated by Newton (24) since there is often an earlier leucocytosis, leukopenia not arriving, according to Hektoen, (25) until after hemorrhages have begun, decides on the following as being very useful where benzol is known to be in use: irritation of the mucous membranes of the respiratory tract, nausea, vomiting, burning sensation in the upper epigastrium, frequent urination, giddiness, slight air hunger and weakness - - - all of which tend to become worse when leaving the benzol atmosphere. Winslow (14) summarizes the more commonly observed symptoms as follows: (a) general systemic disturbance as evidenced by headache, dizziness, weakness, anorexia and loss of weight; (b) pallor, shown by blood examination to be true anaemia; (c) marked reduction in white cells; (d) bleeding from nose, gums, vagina and bowels, with development of purplish spots caused by small hemorrhages within the tissues; (e) sore throat and spongy gums, and burning of eyes and throat; (f) shortness of breath and tightness of chest; (g) sometimes abdominal pain, nausea and vomiting; (h) sometimes, slight tremors, visual disturbances, and abnormal sensitiveness to touch; (i) rarely convulsions, delirium and skin eruptions. Brucken (26) reports a case having headache, somnolence, exhaustion, palpitation, cough, temperature 101°F., pulse 100, excessive menstruation, hematoma, (on touch) blood in stools, leucopenia, anaemia, polychromasia, anisocytosis and pro-

longed bleeding time.

Of the laboratory findings, only the blood picture is significant. The anaemia depends on the severity of the poisoning and the red count may vary from a few thousand to 4,000,000. The white count at first shows a slight leucocytosis as a compensatory phenomenon, but the true picture is a leucopenia. (16) Fontana states that in the very acute cases blood taken at the moment preceding death often shows no leucocytes or granular erythrocytes. The more usual experience is to find from 500 to 5,000 white cells. (29) A lymphocytosis is characteristic.- - - forty percent of the total whites are lymphocytes, and in many cases the polymorphonuclears make up but fourteen per cent of the total. The hemoglobin is generally such as to make the color index less than one. Much work lately has been done toward arriving at some means whereby blood findings could be taken as an index of early poisoning. The polychromasia, anisocytosis and prolonged bleeding time are found in the later cases, but early in the disease are not prominent enough to be of value. Paul, Friedlander and Mc Cord, believing that leucopenia is too deceptive a guide, searched for some earlier and more reliable finding, placing their observations on the red cell. (28) Immaturity of red cells in the circulating stream is accepted evidence of anaemia. Many evidences of immaturity are to be found. They range from nucleated red cells to the Isaac body, which is apparently lost as a last step prior to maturity. Between these extremes, a stage occurs in which all or a large number of the forming red cells contain basophilic material. These cells are also called "reticulated cells" or "basophilic aggregations". They are generally accepted as evidence of regeneration. (28) Three technical procedures are utilized in

determining the presence of basophilic material: (a) enumeration of red cells containing basophilic material; (b) basophilic aggregation test; (c) Wright's stain for polychromatophilic cells. These are described in the article of Paul, Friedlander and Mc Cord,(28) and they conclude after a study of both clinical cases and test animals that in benzol poisoning there is an increase in basophilic material early and it can be used as early evidence of benzol poisoning where there has been frank exposure to benzol.

INDUSTRIES USING BENZOL, TOLUOL AND XYLOL.

Benzol is used in two very distinctly different types of processes.(14) In such industries as (a) the distillation of coal and coal tar in the production of benzol, (b) the blending of motor fuels, and (c) the chemical industries, including oil extraction, dye and dye intermediates, manufacture of paints, varnishes and stains, and of paint and varnish removers, benzol is used in large quantities, but the very nature of the industry demands that it be kept in a closed pipe line system, any openings representing a loss of valuable vapors, and making the system an inefficient one with a correspondingly large financial loss.

In the second group of processes represented by the use of benzol (a) in the rubber industry, (b) in artificial leather manufacture, (c) in sanitary can manufacture, (d) in dry cleaning, and (e) in connection with the handling of paints, varnishes and stains, benzol is employed chiefly as a solvent or a vehicle, and as a part of the process it must be removed so as to leave the originally dissolved substance in place. The method of removal of the benzol is usually to permit it to evaporate; in most cases this is done in the cold; in some cases, however, the compound maybe

warmed - - - a procedure which naturally removes the benzol with greater rapidity.

Aside from the cases noted above, there is always the danger of benzol fatalities wherever workmen must enter to clean or repair the benzol kettles or vats. The earliest instance of an acute poisoning in American industry is reported by Hamilton (13) as occurring in a pipe fitter and workmen cleaning tanks of benzol in one of the explosives manufacturing companies. The step of sulphonating benzol in the production of phenol has given several accidents. The most peril, of course, is present in the open processes as enumerated above.

PREVENTION.

The recommendations of the National Safety Council in regard to the use of benzol are as follows: "As has already been pointed out, benzol is used in industry under two more or less distinct sets of conditions. In the manufacture of benzol from coal and coal tar, in the blending of motor fuels, and in the chemical industries, the solvent is necessarily handled in closed containers and pipe systems. Here chronic poisoning is unlikely to occur and the chief hazard arises from acute poisoning due to carelessness in the cleaning of tanks, breaks in the apparatus, and similar accidents.

With regard to this type of process, it seems certain that with proper care in construction, maintenance,and operation the use of benzol can be made sufficiently safe to warrant its employment. It is true that fatal accidents have occurred, and will no doubt continue to occur, in these processes, just as these accidents occur and will continue to occur from the use of steam boilers. The danger is, however, in both instances

a controllable one to be met by careful attention to safety provisions and not by the abandoment of the substance or the device in question.

The chief measures of protection which should be enforced in industries in this type are: (a) Regular and systematic inspection to insure against breaks or leakage. (b) The greatest possible care in freeing tanks or other receptacles which have contained benzol from all traces of the substance before they are entered for cleaning or repairing. (c) The protection of workers entering enclosed places liable to contain benzol fumes by the use of positive pressure air helmets or hose masks; and the conduct of all such work by teams of two or more men who are familiar with the dangers involved.

Where used as a solvent in the rubber industry, in the artificial leather manufacture, in sanitary can manufacture, in dry cleaning, and in the use of paints and varnishes, benzol is employed as a solvent or vehicle under conditions which almost of necessity permit more or less evaporation of the solvent into the atmosphere. Here there is relatively little danger of acute benzol poisoning, but very great danger of chronic poisoning, arising from prolonged or repeated exposure to the fumes.

In order to minimize such hazards as far as possible, there are two general types of precautions which should be taken, tending respectively to decrease the degree of exposure and to detect and control incipient poisoning in its earliest possible stages. 1: To diminish exposure, enclosed processes should, of course, be used wherever possible and whenever containers are cleaned or apparatus repaired the special precautions discussed above dealing with closed systems should be observed. Wherever employees are likely in the course of their work to be exposed to benzol

fumes, as in the ordinary solvent and evaporating processes, or in handling the products of such processes, they should be protected by the most effective local exhaust ventilation designed according to the following general principles: (a) Where benzol is evaporated at room temperatures air removal by local exhaust ventilation with down draught is recommended, although in certain enclosed processes direct ventilation with upward draught may be indicated. (b) Where localized heat is applied in the evaporation of the benzol, hoods or enclosures should be provided with up draught local exhaust. This draft should be sufficiently intensive and applied so closely to the point of origin of the evaporating benzol as to insure the complete removal of all the benzol before the heated surface is removed from the hood or enclosure. Masks and respirators should not be relied upon to protect the worker against ordinary routine exposure to benzol fumes, since such devices cannot be made efficient without at the same time making them too uncomfortable to wear all day. 2: To detect incipient poisoning at a stage when its effects can be minimized, it seems essential to the committee that all workers to be employed in processes where exposure to the fumes of this solvent is involved should be given a thorough medical examination before employment and should be re-examined, with systematic blood counts once a month thereafter. In addition to this, absence from work should be promptly followed by some persons conversant with the symptoms of benzol poisoning; and the employees themselves should be made familiar with the symptoms which are most likely to occur. No worker showing organic disease of heart, lungs or kidneys, hemorrhagic tendencies or anaemia should be employed. Any worker showing any of the following symptoms should be promptly excluded from benzol exposure: hemorrhages from mucous membranes, white count decreased by 25% of previous

count or white count under 5,000, red count reduced 25%, hemoglobin below seventy per cent.

Starr quotes Sommerfield and Fischer (23) as believing that women should not be employed where there are benzol fumes, since during their developmental period and especially during menstruation they are susceptible in an extraordinary degree to the vapors of benzol. Starr suggests that wherever benzol is kept there should be a label on it stating the dangers when it is exposed to air. This he also applies to all benzol containing products,such as rubber cement. Legge (15) suggests the use of xylol and toluol since they often can replace benzol and are but very slightly toxic themselves.

ANAEMIAS FROM THE NITRO AND AMIDO DERIVATIVES OF BENZENE, TOLUENE AND THEIR HOMOLOGUES.

Obviously there exists a multitude of compounds which could be included in the category set forth in the title of this section. Some would be in use industrially, more of them would not. Their actions as toxic agents in the human body, however, seem to differ only in degree. It would be an endless task to try to consider all of them separately, and for that reason, first, only those compounds that have industrial importance will be considered, and,second, since the pathology, symptomatology and toxicity are so comparable mention of individual characteristics will only be made when something of differential importance exists.

Those substances which enter the class designated above, and which are of sufficient industrial and clinical importance to find themselves in the literature of the last fifteen years are: anilin, dinitro-

benzene, dinitro-toluene, nitro-benzene and trinit-rotoluene. (For consideration of a number of the rarer substances, reference may be made to an article by Wells.(30) Of these, there is trinitrotoluene whose importance industrially has in the last ten years rapidly faded. Trinitrotoluene as an explosive reached its ascendency during the years of the World War. With the United States' entrance to the war, the prevention of poisoning among American workers presented a problem of considerable importance. Protection of the health of workers was a matter of great concern, and much time and study was put into the problem. However, with the end of the war this need for protection of workers ceased as suddenly as it began, so that today the problem of trinitrotoluene poisoning is not much more than a story.

Aniline, however, and nitrobenzol, dinitrobenzol and dinitrotoluene show very much the reverse reaction. In dyes, photographic materials, rubber compounds, all of them are being used to greater and greater extent and consequently with the war's end, rather than ceasing to be a problem, became a greater problem than ever before.

CHEMICAL AND PHYSICAL PROPERTIES.(31)

Aniline is a colorless, refractive liquid, boiling at 181°C. and solidifying at -8°C. to a crystalline mass;when exposed to the air and light it assumes a brown color. It has a peculiar, not unpleasant,smell and is very sparingly soluble in water, but freely in alcohol, ether and benzene. With acids it forms salts, most of which crystallize well. It is generally produced commercially from benzene which is first converted into nitrobenzene by acting on it with a mixture of sulphuric and nitric acids. Then mixed with acetic acid and iron filings, a solid mass is

formed which after the addition of lime and distillation produces aniline, which is usually contaminated with amidotoluenes and other bases.

Nitrobenzene has generally a brown color, but when quite pure is a pale yellow, strongly refractive liquid, boiling at 220 C. It has a burning sweet taste and a smell resembling that of oil of bitter almonds and of cinnamon. Benzene dissolves in concentrated nitric acid with the evolution of heat. On the addition of water, nitro benzene is precipitated as a heavy oily liquid.

Dinitrobenzene is formed by boiling nitrobenzene with strong nitric acid. It crystallizes from nitric acid or from alcohol in long, glistening, colorless meedles, melting at 86°C.

Toluidine crystallizes from aqueous alcohol in large transparent, shining plates, melting at 45°C and boiling at 202°C. It possesses a peculiar odor and is sparingly soluble in water. Its reactions and production are exactly parallel to aniline.

Nitrotoluene crystallizes in colorless prisms, melting at 54°C and boiling at 237°C., is formed and reacts similarly to nitrobenzene.

Dinitrotoluene crystallizes from alcohol in long colorless, brittle needles, melting at 71°C. Its production and chemical characteristics are comparable to its benzol brother.

Trinitrotoluene is formed by boiling toluene for some days with a mixture of fuming, sulphuric and nitric acids. It is sparingly soluble in alcohol, and forms long needles at 82°C.

TOXICITY.

There are a few general rules regarding the toxicity of the amido and nitro derivatives. First the entrance of the nitroso group and the nitro group increase toxicity always, whether they enter the ring or a side chain, but it is not necessarily true that an increasing number of nitro groups increases toxicity; thus it was the experience of the French during the war that picric acid or trinitrophenol was not nearly so poisonous as one of the dinitro-phenols. Also reduction of the nitro group to NH_2, as in changing mononitrobenzene to aniline, mononitrotoluene to toluidine, lessens toxicity. It is not necessarily always the most toxic substance that causes the most sickness. A study of the sickness records in a dye works shows that mononitrobenzene does not give nearly so many cases as does dinitrobenzene, yet mononitrobenzene is a liquid and so more apt to be toxic. Dinitrobenzene, a solid, however, requires being transported and handled in the open, and always causes more poisoning. Thus the factor of exposure is a large one. (32)

Anilin's exact toxicity is rather difficult to state, since its effect is often felt after entrance through the skin; in fact this is the common mode of entrance. There is a great variance in the time of reaction of any drug through the skin, the skin offering the slowest and least uniform absorption. It is stated, however, that several drams by mouth is necessary to afford a toxic dose. (33)

Eight to ten drops of nitro benzene have caused death. The mode of entrance is most often the skin and death may appear very rapidly, two hours, or it may not arrive for a day or two. Dinitro-benzene closely resembles nitrobenzene in toxicity, and it to may either be inhaled

or absorbed through the skin.

The toxic effects from trinitrotoluene are usually of a chronic nature. Little can be said authoritatively concerning the amounts of trinitrotoluene that will cause death or symptoms. It is stated that the toxic dose for an adult man is probably less than 180 mgs.(34) Variations in susceptibility are marked. Susceptibility seems to be increased by anaemia or infection. It seems possible to acquire a certain tolerance for the substance. A meat diet seems to have prophylactic value. Alcoholics have increased susceptibility.

PATHOLOGY.

Poisoning from the nitro and amido derivatives produces in general much the same clinical picture, differing in some details and with a few striking exceptions. According to Curshman(32) there is an important difference between the nitro and amido compounds, in that the latter are simply blood poisons and all the symptoms produced by them may be referred to their action on the blood, while the nitro compounds have in addition a direct action on the central nervous system. That this is true of the nitro compounds is undisputed, but Heubner believes it is true of the amido derivatives of benzene as well as the nitro.

From aniline, very few fatal cases have been reported since its influx in 1917 into American industry. Aniline, nitrobenzol and dinitrobenzol enter the body most frequently following an accident in which some is spilled on clothing or skin to allow absorption through the skin. No histological changes are reported except those of the blood. Of these there are many.

In acute intoxication the changes in the blood seem first to be

the formation of methemoglobin and the destruction of red cells. The blood count and the hemoglobin fall. Microscopic examination shows that the red cells are altered in size, shape and staining properties. The cells are pale, and there is some fragmentation and polychromatophilia. Early in the attack, the blood becomes chocolate colored and thicker than normal. Hudson (35) says nitro compounds are more apt to give the chocolate color early since they give more hemolysis than aniline. The spectroscopic examination may reveal lines which are said to be those of methemoglobin, or rather lines situated between the methemoglobin and oxyhemoglobin, and therefore not quite typical. Later in the attack it is usually not possible to detect these lines. Indeed, Curshman (32) says that when cyanosis is developed, it is impossible to detect methemoglobin.

The evidence of cell destruction is succeeded in a few days by the evidence of active regeneration, and the blood picture may then be very much like that in pernicious anaemia, with variations in staining and size, and with the appearance of stippled cells and nucleation. The changes in the white cells are less characteristic, but during the acute attack there is usually a polymorphonuclear leucocytosis. Later in the chronic forms there are fewer of these cells and more of a lymphocytosis. In the slower forms, the destruction of red cells may act as a stimulant bone marrow production, and an increased red count may be found. Minot believes that with minimal dosage of T.N.T. a polycythaemia is first developed. At times an unusually marked strain appears to be placed on the marrow, so that what has been termed a lowered marrow threshold occurs, as evidenced in the peripheral blood by the occurrence of blasts, Howell-Jolly bodies, and perhaps atypical mononuclear cells and abnormal appearing polynuclears.

(36)
Minot states that the first evidence of the marrow's failing to act is seen when there is relative increase of lymphocytes, with decrease of polymorphonuclears. Further evidence is seen in the diminution of platelets.

(37)
Hayhorn describes the microscopic changes in experimental T.N.T. poisoning. Sections of the brain, heart, and skeletal muscles showed no convincing changes. The lungs were in part collapsed and often oedematous. One or two instances of early pneumonia were seen and some of the lobules were hemorrhagic. In the animals in which T.N.T. was forced into the lungs, large phagocytic endothelial cells were found in the alveoli and these contained both black granules due to anthracosis and coarse yellowish granules which did not give the iron reaction.

The liver lesions were of several kinds, varying largely with the duration of poisoning. The earliest lesions seen were small sharply defined foci of necrosis, varying in size from the size of a few cells to about a third of a lobule, and were located near the central vein. Some of these lesions resembled the necrosis of eclampsia save that none of them were found near the periportal connective tissue. In the animals where the poisoning was carried out over a more prolonged period, the liver lobules showed advanced fatty changes of both globular and granular types. The globules were found in the cells about the central vein and in some instances wre seen to some extent throughout the whole lobule. Associated with the fatty changes often there were large areas of necrosis. The third type of lesion was similar to focal necrosis, save that it was diffuse and involved a number of lobules. One animal that recovered showed a liver the periportal bundles of which approached each other much more nor-

mally, suggesting that repeated T.N.T. injury and repair may lead to cirrhosis.

In the spleen the blood sinuses became enlarged and quite definitely outlined. Large phagocytic cells filled with red cell debris replaced the red cells in the sinuses. The arrangement of these cells was in a way suggestive of Gaucher's spleen.

The kidney lesions were constant. The glomeruli were congested and the glomerular spaces dilated and filled with cellular debris, free pigment granules and occasionally with the shadows of red blood cells. The convuluted tubules were dilated and filled with cells, granular material and often were so swelled that the lumens were closed.

The bone marrow always showed less than the normal amount of fat. Some showed no fat granules, some had vacuoles widely separated. The megakaryocytes and multinucleated giant cells were numerous and often appeared in rows of three or four. Many large groups of nucleated reds were found and they appeared to occur in nests. Of the myelocytic sries the coarsely granular eosinophilic myelocytes were the most common cells and they constantly occurred in nests. A few polymorphs, eosin staining, were among them. A large endothelial phagocyte able to phagocyte nucleated reds as well as debris was occasionally present.

The pathogenesis is summed up by Voegtlin(38): The blood destruction is due to an injury of the red blood corpuscles leading to increased phagocytosis of these cells in spleen, liver and bone marrow. He states that T.N.T. is changed in the body and is not excreted as such. Reduction and axidation may take part in this transformation. The reduction

product, trinitrobenzoic acid is much less toxic than T.N.T.

SIGNS AND SYMPTOMS.

Poisoning from the nitro and amido derivatives of benzene and toluene may be acute as is most often seen with anilin, nitrobenzene and the dinitro compounds where spilling and contact with the skin is the large factor, and it may be chronic as is most often the case with trinitro-toluene. In a light case of the acute poisoning, the face flushes, there is a sense of fullness and a throbbing in the head, burning in the throat, tightness in the chest, and then a violent headache may come on accompanied with dizziness, roaring in the ears and some disturbance of sight. The flushed face next becomes livid, with bluish lips and tongue, and there is a sensation of weakness in the knees, a staggering gait. With prompt removal of the poison the attack may last only a few hours, but the cyanosis of lips and tongue usually last for several days.

In the severer acute cases, the color of the face is gray-blue, the lips and tongue are more deeply cyanosed, the muscles tremble, the man staggers and feels as if his knees were caving in. He is nauseated and may vomit and complains of cramps in his abdomen and of extreme weakness. Consciousness is often lost a few hours after the attack begins, respiration is shallow and quick, the pulse is small and fluttering, irregular and enormously accelerated; the skin is cold and the blood pressure usually low. If coma persists, the respiration and pulse grow slower and slower, there is involuntary defecation and urination, and convulsions usually come on just before death. It is characteristic that these attacks never come on while a man is at work but generally strike while he is on his way home or even hours later.(32) Neuhof(39) adds formication as a prominent symptom.

In the fatal cases jaundice may also appear.

Among the more chronic cases of anilin poisoning there is noticed a pallor and blueness of nails and gums. A blue line at the gum margin is present.(40) There is a loss of appetite, lassitude. In the rubber industry, Davis(41) has found many other evidences of the chronic poisoning. Slight insomnia, mental uncertainty, headache, joint and muscle pains, scotomata, rarely hematuria and hyperacidity of the stomach, constipation or diarrhoea. Macular skin eruptions are noted. Hemoptysis appears late. Employers recognize that thereis a lassitude among the older employees that makes them less efficient. There also is recognized what is known as an anilin grouch; men long in the employ of anilin processes become very irritable and hard to get along with. Cords(42) gives account of the eye symptoms of chronic nitrobenzol poisoning. The optic nerve seems especially vulnerable to this poison.

The laboratory findings in regard to the blood have been described under "Pathology". The urinary findings have differed among different observers. In general the specific gravity is not constant, the reaction is usually acid. Albumin usually is not present unless there is marked anaemia. Commonly the urine is a dark brown in color. It may be the color of port wine or a smoky red. In such cases methemoglobin or unchanged hemoglobin or blood pigment, bile pigment or hematoporphyrin may be detected. Mohr found hydrobilirubin in dinitrobenzene poisoning. Not infrequently the urines from these poisonings reduce Fehling's solution. Neubauer found anilin unchanged in the urine. Hematin can be demonstrated in all.

In T.N.T. poisoning individual susceptibility plays a very large

part in determining what the symptoms shall be. The cleanliness of the individual, of his surroundings are important. Hot weather and a moist skin favor the absorption of the poison. Young men are apparently more susceptible than full grown adults. Negroes are perhaps less susceptible than whites.

Of the early symptoms of T.N.T. poisoning, breathlessness on exertion seems the earliest. Next in order comes dizziness on stooping over and more or less persistent headache. Loss of appetite, morning nausea, foul tasting mouth were all early symptoms. Cramps in legs, fatigue disproportionate to the work done, chest tightness are all complained of. Very early the patient notices a change in the color of his urine; it becomes a clear brown, at first about as dark as weak tea and increasing to coffee color. By the time the doctor is consulted the patient presents an expression of dullness and weariness, heavy eyes, drooping lids, sclerotics slightly yellow, lips and mucous membranes blue, the face leaden or ashen. Occasionally serious changes may occur without giving much in the way of suffering; Hamilton describes a case which was accidentally picked up and which showed all the signs of intense intoxication, but complained only of headache and dyspnoea. (43) Some workers describe a toxic jaundice in T.N.T. poisoning,but Hamilton reports not seeing one in a survey of five large plants during the war. Alcohol has a marked effect on the symptomatology; many tales are told of men falling to the saloon floor after a drink of liquor. They very rapidly developed the picture of the poisoning.

British reports seem to be filled with stories of toxic jaundice in connection with T.N.T. poisoning. The absence of this symptom in America is attributed to a closer medical supervision. British statis-

tics show that the jaundice appeared only after three or more months of contact with T.N.T. (44) Putnam and Herman present the symptoms of T.N.T. poisoning as being of two orders: irritative and toxic. Of the irritative symptoms there are those respiratory symptoms of nasal discomfort, sneezing, coryza, epistaxis, smarting and watery eyes, frontal headaches, sore throat, tightness and pain in chest, dry cough. The irritative symptoms of gastro-intestinal origin are constant bitter taste, spasmodic epigastric pain, nausea and vomiting, anorexia, constipation, diarrhoea, Cutaneous eruptions were also present. Of the toxic symptoms there were bilious attacks, nausea, vomiting, anorexia, constipation, jaundice, heartburn. There were faintness, giddiness, flushes, pallor, cyanosis, bradycardia, palpitation, air hunger, swelling of extremities, non-traumatic bruises. There was drowsiness, apathy, loss of memory, blurring of vision, peripheral neuritis and as a terminal event delirium, coma, convulsions. There is then but slight difference between chronic poisonings of the different nitro and amido derivatives.

INDUSTRIES USING THE NITRO AND AMIDO DERIVATIVES. PREVENTION.

T.N.T. is valuable only as an explosive; in civil life its use is extremely restricted since it is not more valuable than the other explosives and is decidedly more dangerous. T.N.T. in civil life then does not constitute a serious problem, for its production is as limited as its use, and few workers come in contact with it. Masses of work done in regard to it in war time have, however, given much information that is not entirely useless, for as is seen in a description of the pathology, symptomatology and chemistry associated with the chemical, most facts referable to T.N.T. are as true for the other nitro and amido derivatives.

Anilin is used in the rubber industry, in the dying industry; it is present in paints, in dressings. Chemical plants prepare it and in all its use is rather widespread. (41) Davis who makes his observations from a rubber plant suggests as a method of avoiding intoxication that first the employees be instructed regarding the hazard of aniline contact. He requires forced ventilation to avoid fumes and vapors, and all aniline compounds are handled in closed receptacles. He restricts the time during which workers may remain exposed to the fumes of aniline, and he insists on improved personal hygiene. If any aniline or its derivatives are spilled on a worker or his clothing, an immediate bath is demanded. Rubber gloves and shoes that will resist the chemical are worn.

Some employers give milk to the employees to keep the general health on a high level. The constipating qualities of milk, however, do not always make this a wise procedure, for it may block one of the most efficient routes of aniline excretion. Some employers give a dram of vinegar to each employee every morning, with the idea of forming anilin compounds that the kidney can excrete. Davis gives lemonade and Epsom salts enough to creat sufficient alkaline reserve and to cause diuresis and evacuation daily. Periodic health examinations are required and should include urine and blood examinations. Alcohol is forbidden all employees.

(45) Cronin concludes that if aniline must be used it should only be used by experienced workmen. There should be hooding and ventilation. He suggests rotation of employees.

(46) Oppenheimer warns of aniline tumors of the bladder which become rapidly malignant. He advises thorough investigation of all bladder symp-

toms in aniline workers, and thorough removal of the tumor when it is first found.

In regard to T.N.T. poisoning, it is suggested by Voegtlin (38) that precautions should be taken to prevent dust inhalation, entrance by the gastro intestinal tract and skin absorption. Clean clothing, personal cleanliness, gloves should be insisted upon. Voegtlin says respirators are of no value. Floor ventilation by forced draft should be installed. The diet should be nutritious and it should contain large amounts of meat, since it has been noticed that a meat diet makes one less liable to intoxication. Routine weekly examinations should be held; no one with previous anaemia should be employed. Intermittent employment reduces the health hazard. In an earlier paper Voegtlin (34) suggested relief from work of all showing a reduction in hemoglobin of 20%. He suggested a meat diet of 150 grams minimal. He also gives a varnish to paint on the hands to prevent skin absorption.

Nelson's System (47) gives the following precautionary measures: 1: Alternation of employment. 2: Mechanical means for filling shells. 3: Reduction of hand labor. 4: Locally applied exhaust ventilation wherever dust or fumes are given off. 5: No dry sweeping. 6: Protective clothing and washing facilities.

THE ANAEMIA OF CHRONIC BENZIN POISONING

(NAPHTHA, GASOLINE)

Chronic poisoning by members of the petroleum series is so little recognized as to be denied existence by some, passed over lightly by others. The acute intoxication is striking, but is devoid of fatal consequences and

may be quickly recovered from. Chronic poisoning, however, though the symptoms do not seem characteristic, is probably more common and its consequences more serious. The physicians of many rubber centers refuse to admit that a thing such as chronic naphtha poisoning can exist, claiming the trouble is due to indoor work or faulty hygiene. Recent work, however, rather points to the error of this view.(48)

CHEMISTRY AND PHYSICAL PROPERTIES.

Gasoline, naphtha or benzin is a mixture of the lower boiling hydrocarbons, usually coming off between temperatures between 40° and 150°C. Gasoline and its products are mostly mixtures of C_6H_{14}, C_7H_{16}, C_8H_{18}. Commercially the distinction between gasoline, benzine and naphtha is a matter of boiling point - - - naphtha and benzine being the higher. These substances are colorless, have a characteristic acrid odor, are inflammable and explosive when vaporized with the proper amounts of air. They are but sparingly soluble in water, and are themselves excellent solvents of fats, resins and oils.

TOXICITY.

Three drams of naphtha have caused death within three hours.(33) Aside from that statement, very little is to be found concerning the toxicity of these compounds. Apparently this study is but beginning, and a hazard little realized previously is coming to be suspected. Certainly, in most cases the toxicity is not great; chronicity seems to be the greatest factor.

PATHOLOGY.

Instances having the earmarks of chronic benzine poisoning that have been reported are few.(49) Haden gives an account of one, the blood

of which showed a red count of 4,300,000 with 70% hemoglobin. There was a leucopenia with reduction of the polymorphonuclears. Post mortem findings in cases of benzine poisoning seem not to exist; death probably does not come from this sort of poisoning. The symptoms seem out of proportion with the actual damage done, thus giving warning early.

SIGNS AND SYMPTOMS.

There seems in the rubber industry among those who are exposed to naphtha fumes to be a large number of minor symptoms which perhaps constitute slight benzine intoxication. There is a loss of health, loss of vigor and energy, headache or only a feeling of oppression in the head, listlessness, dullness, restless sleep, loss of appetite, disturbed digestion, gastric pain, constipation and many obscure complaints. Some are sleepy in the daytime, cannot sleep at night; others have sore throats and cough. There are paraesthesias, muscle weaknesses - - - all of these occurring too frequently to be incidental. Hamilton quotes a case reported by Dorendorf (48) in which four men had lancinating pains in the limbs, coldness of the hands, loss of strength and loss of memory. Potts (50) reports a case of a man exposed to gasoline who fell unconscious, waking up with cerebellar gait and localized paralyses. Neuritis seems common among the workers in cleaning establishments where gasoline is used.

Haden (49) tells of a rather acute case of poisoning where at the end of two months of employment exposed to gasoline a patient developed nausea, vomiting, dizziness, confusion, weakness. He became unable to work more than a few days a week, became so drowsy that he would fall to sleep quite easily. His hands and feet were heavy and cold, he had pains and muscular cramps and dimness of vision. He was found so mentally dull that a

history was difficult to get. His skin was jaundiced, lips purplish. There was a sweetish odor to the breath. There was a tremor to eyelids and lips. The liver was enlarged and tender; the urine almost black with bile. Kraus (51) reports a similar case but balances between gasoline and gas poisoning as a diagnosis.

INDUSTRIAL USES. PREVENTION.

Petroleum distillates have an extensive use in industry and also in private life. Used as fuel, everyone owning or operating an automobile comes in contact with them. Garagemen, filling station employees and all the network of employees concerned in the production of gasoline are endangered to the poison. As solvents gasoline, naphtha, benzine are used in connection with fats, gums resins, rubber, gutta-percha in countless industries. Gasoline and the other distillates are used for illumination and are part of lubricating oils. In cleaning as in dry-cleaning processes, in dissolving inks, oils, etc. there is a large field for its use.

Pumping, refining and distilling processes have apparently gone for years without investigation. That poisoning may occur there is attested by reports of two physicians: Mitchell (52) and Sharp. (53)

As to prevention, only the obvious things can be suggested. Use of as much as possible of mechanical handling of gasoline and like substances should be encouraged. Proper ventilation by forced draft should be required where evaporation processes are used. Personal cleanliness, encouragement of health habits are important. What is perhaps most needed is more study and definite knowledge concerning poisoning by petroleum

distillates. Systematic checks on workers in plants where exposure is known to occur, more knowledge of the blood picture are needed. With more knowledge at hand better methods could be devised for combatting the poison in industry.

ANAEMIA FROM VANADIUM

There is an extreme paucity of observations and investigation regarding vanadium poisoning. Hamilton (54) in her book on industrial poisoning states that there is but one original article in the literature previous to her own. Dutton in 1911 first reported the toxic action of vanadium.(55) A search of the literature reveals no other work than that of Dutton and Hamilton. As would seem obvious, there are but few industries where vanadium is used. Hamilton states that but two factories exist where vanadium steel is manufactured, however these factories are in one of the largest industrial centers in America. Vanadium poisoning serves as an example of industrial hazard such as the medical profession knows nothing about.

THE CHEMISTRY AND PHYSICAL PROPERTIES.

Vanadium is more like phosphorus than any other metal in its physical and chemical properties. Vanadium was first described by Sefstrom in 1830 and named in honor of vanadis the Scandinavian godess of fortune. Vanadite which is a combination of vanadium and lead compounds is quite abundant in nature. Pure vanadium is very difficult to prepare. The pure metal is a brilliant, silvery substance, crystallizing in the hexagonal system like phosphorus. It is very hard and very brittle and has a density of about 6.02. It melts at 1720°. By reducing a mixture of the oxides of iron and vanadium an alloy called ferro-

vanadium containing about thirty per cent vanadium is formed. This alloy is used in making vanadium steel, which is very tough and strong.

TOXICITY. PATHOLOGY.

Little is known as to the toxic dose or action of vanadium, but Dr. Omar Cruickshank has experimented with the action of vanadium compounds on dogs, and he finds that the symptoms produced in dogs are the same as those observed in humans. No autopsy reports are recorded, but the blood picture early shows an increase in red cells and in hemoglobin, while later there is a marked reduction in both. At times there is disintegration of the red cells. Symptomatically Sutton concludes that the principle lesions are found in lungs, kidneys and gastro intestinal tract. The lungs are congested and show a marked destruction of alveolar tissue. The kidneys are congested and at times show acute hemorrhagic nephritis. The gastro intestinal tract shows evidence of irritation and inflammation. There is said to be much tuberculosis among the employees in vanadium mills, and it is thought that vanadium dust predisposes one to tuberculosis. Elimination is by urine, feces, sputum and saliva.

SIGNS AND SYMPTOMS.

A prominent and characteristic symptom is cough. It is dry, irritating and paroxysmal, becoming so intense that hemorrhages are frequent and severe, even causing death. Emaciation, irritation of the nose, eyes and throat are always in evidence. There is anorexia, nausea and often diarrhoea, though an obstinate constipation comes on later. Albumin, casts and blood are often present in the urine.

Continuous exposure to the poison leads to fine tremors of the extremities, headache, neurotinnitus, amaurosis, vertigo, hysteria and

melancholia. Fatal termination is frequent as a result of continuous exposure to the poison.

INDUSTRIES USING VANADIUM. PREVENTION.

The production of ferro-vanadium in the United States amounts to 12,000,000 pounds annually. In plants making this compound, the crude vanadium ore comes in sacks, and the emptying of these sacks in charging the furnaces is admittedly a dusty process. The metal itself is said to be of no importance technically, though its various forms are valuable. The pentoxide is used in photography as a developer, vanadium chloride and trioxide are used as a mordant in printing fabrics, thus making possible poisoning from wearing,certain of these materials. The trioxide is used also in the manufacture of steel, in making easily maleable and ductile alloys. Vanadium pentoxide has been used medically in diseases of deficient metabolism.

For prevention, first employers must be made to see the dangers, employees must be warned and educated to carefulness. Means to allay and carry off the dust and fumes should be employed, constantly. Perfect ventilation and respirators are imperative. The nasal and oral cavities should be thoroughly cleansed with some efficient alkaline spray, such as the ordinary Dobell solution, followed by a mentholated oil spray. The stomach should be washed out and the intestine freely evacuated with a saline laxative. The cough may be allayed by giving terpin hydrate gr. one-fourth, heroin grain one-eighth and creosote minim one-half every two hours with counter irritations of iodine and mustard applications over the chest. Inhalation of stimulating vapors is salutary. Tonics and iron preparations for the anaemia, cod liver oil, baths, exercise are all indicated.

TETRACHLORETHANE ANAEMIA.

Used in the manufacture of airplanes and non-inflamable motion picture films, tetrachlorethane becomes a poison of most recent and widespread hazard in a modern world. Along with numerous other chemicals appearing as inovations in warfare, tetrachlorethane first lumed into importance during the World War. The first reported case of such poisoning occurred in Germany in an airplane plant in Johannisthal. Fortunately this country profited by the mistakes of the Germans and the British and was protected from fatalities during the war chiefly through the use of good substitutes. However, with the knowledge gained from the use of tetrachlorethane during the war and with, in addition, increased care in its use in peace times, it becomes an entirely feasible material with which to work.

THE CHEMICAL AND PHYSICAL PROPERTIES.

Tetrachlorethane (acetylene tetrachloride), a saturated hydrocarbon of the methane group, is a heavy, colorless, oily liquid with a boiling point of 147.2°C. and a specific gravity of 1.6208 at 4°/4°. It is non-inflamable and has a sickish sweet odor suggestive of chloroform. It is insoluble in water, but soluble in alcohol, benzene and acetone. It is an excellent solvent for cellulose esters, dammar, sandarac, copals, etc.

TOXICITY.

Lehrmann (56) states that he found that air containing as little as 0.001 to 0.002 parts per thousand over six or seven hours would cause the minor symptoms.

PATHOLOGY.

Minot (57) in a description of the blood states that the blood changes can generally be observed before the symptoms appear. There is a progressive increase in large mononuclear cells often reaching 40 per cent, which is most valuable and very early. Many immature large mononuclears appear; there is a slight elevation of the white count and a progressive but slight anaemia. He also observes a slight increase in the number of platelets. His final conclusion is that a large mononuclear count of over 12 where there is known to be exposure is proof of intoxication. When the mononuclears begin to show destruction, the process is advanced.

Wilcox (58) quoted by Parmenter ascribes the jaundice observed in tetrachlorethane poisoning to a cholangitis set up in the smaller bile-ducts causing an obstruction to the flow of bile to the liver. There is present also a marked fatty infiltration and degeneration of liver cells which in severe instances is followed by necroses of the liver cells and symptoms of autointoxication identical with those of acute yellow atrophy. If the necrosis is survived, fibrous tissue replaced the injury.

Hamilton (56) states that repeated exposures cause profound disturbances in metabolism and evidences of destruction of the red cells in the circulating blood with formation of new cells and basophilic granulation. There is a fatty infiltration and degeneration of the liver and numerous minute hemorrhages into the mucous and serous tissues. Animals in experimental poisoning show changes more extreme than in any other form of poisoning except phosphorus. There is flabby yellow heart muscle and acute degeneration of the kidney epithelium. The effect resembles

delayed chloroform poisoning, but the hemolytic power is seven times that of chloroform.

Wilcox makes the assertion that contrary to the other workers' belief the jaundice is not hematogenous but a true biliary jaundice with the earliest changes appearing in the bile capillaries, and that there is no appreciable anaemia nor are there changes in the red blood corpuscles. The work of Minot and others somewhat over-balance this opinion.

SYMPTOMS.

(58)
Parmenter says that the symptoms may be divided into three groups - - - general, nervous and gastric symptoms. In many cases the nervous overlap the gastric. The general or preliminary symptoms consist in an abnormal sense of fatigue and a general discontent which passes as a continual "grouch" among the patient's friends. Associated there is an inability to concentrate. Men say they cannot keep still, and that five minutes is long enough to be doing any one thing. Profuse sweating on any exertion accompanies a feeling of being easily tired. Occasionally nocturia or polyuria are complained of by those never before so affected. Distaste for food and nervousness are also early symptoms. In the mild cases there may be no other symptoms, and with history of exposure, these together with a blood picture are enough for a diagnosis.

The nervous symptoms are perhaps next in appearance and importance. They are complained of in detail as headache, weird dreams, loss of sleep, and a general feeling of nervousness which is noticed by friends as well as by the person suffering from the poisoning. General nervousness in the subjective sense and the excessive dreaming are often among the earliest signs noted. The actual loss of sleep comes somewhat

later, and with still severer poisoning there is often exhaustion on slight exertion, or more especially vertigo on stooping or leaning forward from a sitting posture.

As for gastric symptoms, which appear either with or following the nervous symptoms, a loss of appetite appears and is accompanied often by nausea which is constant except at night. There is a sensation of fulness in the stomach, gas and frequent sour eructations. The gas and eructations are nearly always more prominent after the ingestion of food. There is an occasional diarrhoea, but constipation is more often complained of. Rarely there is generalized abdomiaal pain, sometimes and in the most severe poisoning the pain localizes in the right upper quadrant.

The signs are few, consisting chiefly of a loss of weight, and a very slight jaundice. The loss of weight varies from 5 to 15 pounds over a period of time from two weeks to two months and usually precedes the jaundice. The jaundice at this stage is not sufficient to eause bile to appear in the urine, and is generally noted as only a very slight tinting of the sclerae. It usually does appear just before the onset of the gastric symptoms, but never does it become more severe than to involve the face and chest. The jaundice is significant in that it indicates the amount of liver involvement. Occasionally the liver may be found enlarged, and frequently there is liver tenderness.

The urinary findings are usually not of aid except where bile does appear in the urine. The blood is of most importance and is discussed under the heading "Pathology".

Leri reports a peculiar form of polyneuritis caused be tetrachlorethane and characterized by a paralysis effecting the interosseal

muscles of hands and feet and to a lesser degree the extensor muscles of the feet and flexor muscles of the hands, an anesthesia in the region of the interosseal branches of the extremities, abolition of the tendon reflexes, paralysis of the soft palate associated with suppression of the pharyngeal reflex and paralysis of the orbicularis oculi andoris. There was also inequality of the pupils.(59)

INDUSTRIES INVOLVED. PREVENTION.

Tetrachlorethane is the best solvent for cellulose acetate that industry has, and because it is non-inflamable it may be used for purposes for which the inflammable cellulose nitrate or celluloid is not adapted. Thus it was the chief constituent of the coating or "dope" which was applied to battle planes, and is now used to make non-inflammable motion picture films. It is employed in one process of artificial silk manufacture and is a constituent of certain lacquers. The rubber industry also makes use of tetrachlorethane. It is used in the extraction of certain alkaloids and oils. Lithography makes use of it. A number of deaths have occurred in the manufacture of artificial pearls from fish scales dissolved in tetrachlorethane.(60)

Frois(60) states that general measures of ventilation are not enough and that the fumes should be removed by exhaust near the points at which they are liberated. He suggests the use of a cage with a glass top and front, with holes for the arms of the worker. Downward exhaust, maintained at low pressure,would remove the fumes without causing too rapid evaporation of the solvent with consequent chilling of the arms of the worker. Parmenter(58)(61) believes that a person showing the early symptoms should have his blood examined and if it is abnormal should be laid off for a time not ex-

ceeding a week. At that time he might return and be watched. In a case of severe poisoning the subject should be excused from work immediately and should later have a blood examination. His return to work should be governed by his symptoms. Some should be laid off indefinitely. Two mild attacks should lead the employer to get the man work outside the plant. Masks should be recommended in certain exposed places. He gives suggestions that general working conditions should be the best, with due regard to vacations, habits of eating, hours of work, etc. He thinks it is entirely inadvisable to dispense with tetrachlorethane in industry, since it can be handled safely. In a later paper Parmenter gives a form for taking histories of tetrachlorethane poisoning. He gives the work of Minot a prominent place in detecting early cases - - - stating that a mononuclear count of over 12 made the diagnosis.

As for active treatment, Fiessinger and Wolf (62) advise early and prolonged use of liver organotherapy, with abundance of sweetened beverages. Alkaline treatment giving about 2 gm. each of sodium citrate and sodium carbonate every two or three hours is advised. This was often supplemented with small glucose and sodium bicarbonate enemata.

ANAEMIA OF CARBON MONOXIDE

That carbon monoxide poisoning is of growing importance is attested by a recent editorial in the Journal of the American Medical Association.(63) Its menace, it might be thought, has been brought sufficiently to the mind of the public to avert frequent disasters; however, this seems not yet to be the case. Carbon monoxide is the oldest of industrial poisons, since it must date from man's discovery of the use of fire. Incomplete combustion of carbon, burning in an atmosphere without

sufficient oxygen, results in the production of CO instead of CO_2 and water. This gas, odorless, non-irritating and, therefore, giving no warning of its presence, is responsible for more deaths than all other gases put together; (64) but the greater number of these, in the United States at least, are not of industrial origin, but are caused by the accidental or deliberate inhalation of illuminating gas, which in this country commonly contains a high percentage of carbon monoxide. Perhaps of even more importance recently is the danger supplied by the automobile. According to Henderson and Haggard (65) the exhaust gas from the internal combustion engines contains carbon monoxide in percentages ranging from a fraction of one per cent to seven per cent or even higher.

PHYSICAL PROPERTIES AND CHEMISTRY.

Carbon monoxide is a colorless, practically odorless gas. It is 0.967 times as heavy as air and is so difficult to liquefy that it was formerly regarded as one of the permanent gases. Its critical temperature is about -141°C. and its critical pressure 36 atmospheres. It is almost insoluble in water, but is absorbed by a solution of cuprous chloride containing either hydrochloric acid or ammonia. It is very active compound, combining directly with a great many substances. It has a marked affinity for xoygen and burns with a blue flame. It is, therefore, a strong reducing agent. Carbon monoxide also combines with chlorine, sulphur and some of the metals, such as nickel and iron.

TOXICITY.

Carbon monoxide is the gas known as "after damp" in the mines. The toxic action of the gas is exhibited through its affinity for hemoglobin with the formation of methemoglobin. A proportion of 0.5 per 1000

parts of air is enough to cause disturbance; 2 to 3 parts per 1000 is dangerous to life.(66) Henderson et al(67) state that 400 parts of carbon monoxide per million of air is a maximum that may be endured by persons for one hour without noticeable effects, and a hundred parts per million may be taken as a maximum for continuous exposure for about seven hours a day without noticeable effects.

PATHOLOGY.

Regarding the action of carbon monoxide on the body tissues, there are two beliefs. There are those on the one hand who think that the gas has a definite toxic action for many tissues and that the lesions found at autopsy demonstrate such action. The other group feels that all the pathological changes may be explained through simple anoxemia. This latter view is supported by Haggard as reported by Hamilton.(64) He feels that death from carbon monoxide is due directly to failure of respiration, for if respiratory failure is prevented by means of administration of 8 or 10 per cent carbon dioxide, the carbon monoxide combination with hemoglobin may rise to an unusually high percentage without any evidence of impairment of the heart function. The lack of oxygen resulting from the formation of CO hemoglobin induces excessive breathing, and, as a result, excessive loss of carbon dioxide and failure of respiration.

Geppert, as reported in the Oxford System,(66) thinks there is more than this and points out that while anoxemia acts as a respiratory accelerator,(66) CO does not. Sibelius believes that the lesions caused by CO may be accounted for through changes in the vessels, fatty degeneration of capillaries and of the muscular cost of the arteries.

The primary danger lies in the great affinity that CO has for

hemoglobin. This affinity is 200-300 times greater than that of oxygen. However, the CO-hemoglobin combination is not very stable, and the CO may be rapidly washed out when the hemoglobin is exposed to oxygen. Henderson (65) nevertheless reports that CO has been found in the blood five days after the poisoning; he finds a nerve lesion that seems progressive even after the gas has been washed out.

Considering now the pathological picture, the lungs are involved in about 75 per cent of the cases.(66) Symptomatically there seems always to be an excess of fluid in the lungs as evidences by mouth frothing, rales, etc. There seems constantly to be congestion and edema in the fatal cases. Compensatory emphysema is often observed. Atelectasis is also seen. Evidence of bronchitis and broncho-pneumonia is very common. Hypostatic pneumonia is not rare.

Lesions of the heart and vessels seem to be of a fatty degenerative nature. Heart block is often the immediate cause of death and the fatty changes of anoxemia are seen in the conductive tissue.

The nervous system presents many and interesting pathological changes. Klebs is credited with having first described in 1865 encephalomalacie following CO poisoning. In one of his cases the softening was in the lenticular nucleus.(66) Cases reported by Simon showed softening in the cerebral hemisphere, corpus striatum and optic thalmus. Sibelius believes that the effect is a disseminated encephalitis, akin to that caused by alcohol, and sometimes complicated by areas of ischemia caused by degenerative changes in the arteries. He believes that there is a specific toxicity about CO.

Kolisko reported by Hill and Semerak (68) believes that there is

always a bilateral softening of the lenticular nucleus; later work by Hill and Semerak who had opportunity to see 32 cases in the Cook County Hospital strongly confirm this. In addition, these cases all showed hyperaemia of the brain substance. In 21 there was internal hydrocephalus. The pathology in the lenticular nucleus was sometimes evident to the naked eye, and the area even seemed mushy in the extreme cases. All showed areas of necrosis on microscopic examination. Age, in so far as it affected the state of the vessel walls, seemed to be the factor in determining the extent of lenticular pathology - the older individuals showing more. Other factors were the duration of the poisoning and the amount of the gas inhaled. Hill and Semerak explain this peculiar localization of effect through anatomic peculiarities of the circulation in these areas. The gas is thought to produce a thrombosis and degeneration of the vessel walls. These authors do not feel that CO poisoning have anything to do with the cause of arteriosclerosis; however, they state that various paralyses and mental conditions may be traced to previous CO poisoning.

The blood in cases of CO poisoning where the poisoning is slow enough for blood changes to take place always shows a polycythemia, compensatory in character. (66) Afelback and Karasek found a count of over six million in 665 of their South Chicago cases, the highest being 9,676,000. The hemoglobin runs from 95 to 125 per cent and usually thereis an eosinophilia of about 5 per cent. No poikilocytosis or nucleated reds is found. The blood is observed to be a cherry red in fatal cases; this gives a peculiar lifelike appearance to one who has died of this poison. Spectroscopic examination gives the typical bands of methemoglobin.

It has been recognized quite some time that pregnant women exposed to CO are apt to have premature labors. Lewin believes that CO

poisoning that is insufficient to give symptoms in the mother may often result fatally for the fetus, since such poisoning in women employed where CO exists often have still-births. Nicloux says that the blood of the fetus usually contains the same amount of CO as does that of the mother. (64)

SIGNS AND SYMPTOMS.

Acute Poisoning. The onset of symptoms may be most sudden and instantaneous. Victims commonly are found in natural positions, instruments of trades in their hands, seemingly about to perform the act they intended when the poison struck them. Usually, however, there are at least slight warning symptoms even with exposure to high percentage of the gas. Pressure and throbbing in the head, a feeling of knees caving in, blurred sight, roaring in the ears, dryness or constriction of the throat, nausea, stomach pain or a peculiar sweetish taste is often an early symptom. Other observers add to this list giddiness, swimming sensation, pounding of the heart, constriction of the chest. Early there is a dullness of the mind of such character that the victim realized his peril but makes no effort to escape it. Intelligence is blunted, will and energy lost. There is a loss of power in the lower limbs, followed by absolute muscular helplessness. Unconsciousness when it does come is not accompanied by convulsions, but unconsciousness is rare in industrial cases. According to many authorities, in carbon monoxide coma the lips should be rosy red and there should be an appearance of perfect health, but in industrial poisoning this is rarely true. (64) Men are usually pale or livid, with blue lips and red blotches on the skin, or even actual hemorrhages under the skin. Often at this time the patient is mentally confused, his respiration is stertorous, rapid and deep, his pulse from 80 to 120 - neither weak nor bounding. Many industrial surgeons feel that if death from gassing is not

immediate, the patient will recover without treatment. In some cases there is a stage of violent, maniacal delirium in which the patient struggles and seems to have hallucinations. Commonly he has vomiting and rectal incontinence accompanying this stage. After two to eight hours the patient usually has no other symptom excepting a severe headache. According to Glaister (64) the course of the poisoning determines the after effects. Slow gradual poisoning gives more serious permanent damage than does the rapid poisoning, even though there be delirium and convulsions in the latter. Weakness of the heart, pneumonia, paralysis and mental disease may be the lot of the subject of slow intoxication. Splitting headache, dizziness, muscle weakness so that the patient is unable to hold up his head, anesthesias, paresthesias are all the after effects of the poisoning. The immediate sequence of an industrial gassing is often pneumonia, which is said by some authorities to be a deglutition pneumonia or caused by the irritation of the lung tissue by the gas, while others believe the underlying cause to be a paralysis of the vagus, like the pneumonia of high altitudes described by Mosso. (66) The pneumonia develops rapidly, is lobar in type, caused by the pneumococcus, extensive, with an unusually low temperature and a pulse rate out of proportion to the fever, and it runs a rapid course, frequently ending in death.

Chronic Poisoning. Whether or not continued exposure to small quantities of CO produces chronic poisoning is still a matter of dispute. The poisoning cannot be an accumulative poisoning obviously for to attain that there would need be a constant exposure with a gradual building up of the amount of gas until the threshold for symptoms was reached. There are no workers but what have some hours away from CO and these serve to wash all the CO from the blood. Any accumulation must then be functional.

Lewin does not think vasuular changes occur in the chronic poisoning as they do in the acute, but believes that the injury is one from long continued anoxemia. It is probable that the chronic poisoning is more common than the acute. Grawitz found bakers and tailors with an anaemia resembling pernicious anaemia and which he attributed to CO. Studies of men in steel mills where there is exposure to small amounts over a long period of time showed their blood to polycythaemic with a distinct eosinophilia. This has been obtained also with experimental animals. At times there is pallor and loss of weight. Apfelbach and Karasek (66) found a definite loss of muscular power in men exposed to CO, especially among the men over 40 years of age. Multiple sclerosis and mental deterioration have been described as a result of long continued exposure to CO. (66)

INDUSTRIES WHERE CO IS A HAZARD.

In the steel industry, the modern blast furnaces give off 150,000 to 200,000 cubic feet of gas per ton of fuel consumed. The charging is done automatically and the gases are used for fuel and are treated to remove the various by-products of them such as benzene. With the higher temperatures in the furnace, most of the gas given off is carbon monoxide, and it is easily appreciable how dangerous the top filling furnaces can be. Some of the most serious accidents occur when the flues are cleaned out, there often being pockets of gas which the flushing will not remove. Men who clean the furnaces and work at the open hearths also have dangerous jobs. The Illinois Steel Company, which has three large plants near Chicago, has records of the cases of gassing which have occurred. Among 1,112 men who were employed at blast furnaces in the period from 1912 to 1915, the average number of cases requiring medical attention was 66, and the average number of deaths 3.25 - giving a mortality rate of 5 per cent

which is lower than the British rate of 22.8 over a similar period of years. Nevertheless every now and then some extensive and serious accident does occur from this gas.

In mining the gaseous impurities come from blasting, from the burning of wood and pyrites or native sulphur, from accidental explosions of coal dust and from gases given off by shale. Blasting is a normal process in mining and the gases formed are of greater importance than those from accidental occurrences. Detonation of explosives gives off more CO than does burning of the explosives. T.N.T. gives off 57 per cent CO and dynamite gives 34 per cent. Picric acid gives 61 per cent CO. Next to blasting in the production of CO is the slow combustion of coal itself, the CO working into the mind from being incompletely walled off. The gasoline engine used in mines for pumps and locomotion is another danger. The danger of CO in mines increases as the mines grow deeper since ventilation becomes more difficult and there is more chance of men being walled off.

The manufacture of illuminating gas seldom produces CO fatalities or poisoning. Practically the only employees who meet with accident are those who are doing the extension work, laying new lines and putting in meters. It is common practice to allow themen to work until they start staggering and then to pull them out and send someone else in. The officials explain that there is no other way, and the intoxication is looked for. Rarely does the effect become so marked but what there is quick recovery on removal from the gas. In the four years, from 1915 to 1919, there were but four fatal gas poisonings in the entire gas industry in the United States. (64)

Today the automobile supplies the greatest danger from CO poisoning. A variation of from a fraction of one per cent to seven per cent CO

depending on the proportion of air and gasoline in the carburation, is to be found in the exhausts of automobiles.(67) The automobile produces 28 liters of carbon monoxide for each 20 horse power --- thus making the atmosphere of a single garage deadly in five minutes.(63) In traffic congested streets the content of CO is 100 parts per million, sufficient to give at least slight toxic symptoms after a few hours. Traffic policemen are said to show a mild chronic poisoning.

Industrially the large commercial garages present the greatest problem. With many engines running idle for the purpose of testing them, and often running several minutes and without proper hose connections to the exhaust to transport the fumes, the air quickly becomes dangerous. Harris of the New York City Health Department conducted a series of investigations of garages in 1918. He found many cases of poisoning and ascribes the increased CO content of the air to the lack of heat. Engines are hard to start in cold weather, and when started are kept running several minutes to warm them to a smoothly running temperature. Tests made by the United States Bureau of Mines in 1919 indicated a concentration of CO as high as 19.8 parts per 1,000 after an engine had run 10 minutes and 32 parts per 1,000 after 35 minutes. An idle engine produces more than when under a load.

Aside from garage men, there are numerous other workers who are exposed to more or less CO. Laundry workers, especially ironers, pressers in tailor shops, furnace tenders, painters working in which salamanders are kept burning to dry the walls, printers - especially linotypists, and men working at type melting kettles heated with gas, molders of metals where gas is used for heat, workers in canneries on soldering machines and many other unusual sources too numerous to mention.

PREVENTION.

The prevention of CO poisoning obviously revolves around the removal of the gas as it is formed, recognition of its presence and danger when it cannot be removed and frequent physical examinations of those who are exposed to it. Also knowledge of the early symptoms should be impressed upon any of those workers who are known to be exposed to CO.

(69)

Nelson's Loose Leaf Living Medicine gives the following precautionary measures. "The structural conditions should be such as not to entail unnecessary risk; thus: 1. (a) The suction or other gas engine should not be confined as in a basement or sunken room, but in a room or shed properly lighted and adequately ventilated (by special openings and a fan where practicable) to the outer air, and either without doors or with doors cut out at the bottom. (b) The vent pipe through which the gas main to the engine is cleared of air, or any similar vent pipe, should never end inside a building, but always outside, and at least six feet from the ground. (c) The openings giving access to any part of the gas circuit should be few, and in positions as safe as possible, and opened only in cases of real need, and by responsible persons. 2. A competent person should be made responsible for inspection at stated short intervals all valves and connections, to see that there is no leakage, and for keeping a signed and dated record of such inspections. 3. A notice mounted on a board should be affixed in the engine room or gas plant house as recommended above. 4. No person should be allowed to execute work single handed in a place where exposure to the poisonous gas is to be anticipated. 5. No workman should enter or approach the holder or other parts of the gas circuit, when opened, until the gas has been well flushed out by fresh air. 6. Life belts should be provided for rescue purposes, and the place where they are to be found stated in the notice. When dangerous work is foreseen, special rescue appliances should

always be used. 7. A cylinder of compressed oxygen, fitted with a main valve (preferably worked by a hand wheel), a pressure gauge, a pressure reducing valve, a flexible bag and a mask with necessary tubing, should be kept in constant readiness in the ambulance room. The apparatus should be in charge of not less than two person well instructed in its use. At least once a month the equipment and the rubber parts especially should be examined by them. 8. Further notices should be affixed in the works, explaining the deadly nature of the gas and the symptoms of the poisoning and means of rescue and first aid. 9. The workmen should be practiced in rescue drill, including the use of the appliances provided. They should be further instructed by a medical man in artificial breathing and the administration of oxygen. They should be especially warned of the danger of exposing a gassed person to cold and of walking him up and down. Investigation of all cases of gassing should be as much a matter of routine inquiry by the Safety Committees formed on the works as investigation of accidents. 10. Men in charge of any engine worked by a poisonous gas, or of any apparatus in which such gas is stored, or otherwise exposed to risk of inhaling it, should be free from any disease of the heart or lungs. Employers would do well to cause such persons to be medically examined and certified."

LEAD ANAEMIA.

The most promient and distinguished of industrial poisons is lead. Lead enjoys this dignity out of deference for its age, first, for its use is as old as civilization itself, and so likewise is knowledge of its toxic effects. Next, lead is important because of its widespread and diversified uses. No other chemical with equally dangerous potentialities can in any way compare with lead in this respect. Literally thousands of

industries and processes are concerned with lead; practically every living person is in some way intimate with it. The literature concerning lead poisoning is almost without limit; an attempt to review that of even recent years would be a thesis in itself, and nothing so comprehensive shall be attempted here.

Lead came into use very early in history; its poisonous effects were soon discovered. Greek, Latin and Arabian physicians knew that lead would cause colic if swallowed. Dioscorides, in the first or second century after Christ, accurately described not only lead colic but paralysis following the swallowing of lead, and also knew that the breathing of lead fumes would cause the same disorder. He spoke of mechanical devices used in his day by workmen to protect themselves from lead fumes.(70) Pliny used the work minium in its present meaning of red lead, and white lead was known to the famous Arabian alchemist, Geber. Early it was the widespread use of lead as material for cooking vessels and other household articles that caused the most notorious outbreaks. In France in the Poitou district lead was added to wine to cause fermentation and there was the subsequent "colic of Poitou". Stockhausen in 1656 published a treatise setting forth that lead was the causative agent in the "colic of Poitou"; he forthwith drew an accurate picture of clinical lead poisoning. The best work on the subject of industrial lead poisoning was done in France in the arly part of the nineteenth century, culminating in and overshadowed by the epoch-making treatise of Tanquerel des Planches, "the Columbus of lead poisoning". Very little has been added since to the original observations of Tanquerel. However, a vast amount of work has been done in Germany, England and France - Germany especially having contributed to the study of the pathological anatomy.

PHYSICAL AND CHEMICAL PROPERTIES OF LEAD COMPOUNDS.

The lead minerals of most importance to metallurgists are galenite (lead sulphide), cerussite (lead carbonate), and anglesite (lead sulphate). Pure lead is a silvery metal of density 11.37, which melts at 327.4° and boils at 1525°. It is the softest of all metals and a good conductor of electricity. It is moderately active chemically, but its true activity is often masked by the formation of insoluble salts around it which act as a protective coating. It quickly tarnishes in air owing to the formation of bluish gray oxide of lead. Fluorine and the other halides act vigorously on it. Excepting hydrochloric and sulphuric acids, most acids act on lead to form soluble salts. In compounds, lead is either bivalent or quadrivalent. The bivalent hydroxide of lead is basic and gives rise to numerous well defined salts, most of which are colorless. The quadrivalent lead hydroxide is an acid and has but few well defined derivatives. Of the oxides there are three which are important; lead suboxide is the compound usually formed on lead exposed to air. Lead monoxide or litharge exists in a number of modifications, the colors ranging from yellow through brown and to red. Lead dioxide is chocolate brown and is important in storage battery construction. Lead nitrate is a common form. Lead acetate or sugar of lead has a sweetish taste. White lead, lead carbonate is a valuable constituent of paint. There are other lead salts too numerous to mention.

TOXICITY.

Rambousek (71) states that the toxicity of a lead compound is in direct proportion to its solubility in weak hydrochloric acid. The nitrate, acetate and chloride are soluble even in water. Easily soluble in weak acid (0.1 normal hydrochloric acid) are the oxides, carbonate, basic carbonate and monosilicate. The sulphide, sulphate, chromate and disilicate are

all slight coluble. According to Rambousek the acetate and the basic carbonate are the most poisonous. The iodide, oxides and sulphate work more slowly. Other workers do not always agree concerning which are the most toxic, but Hamilton states that in the United State the statistics show white lead to produce more poisoning than red lead. About twenty five years ago lead sulphate came into prominence in many industries, it being said by its producers that this particular form of lead was insoluble in body fluids. Physicians for a time gave sulphuric acid lemonade thinking to change all lead in the body to the sulphate and make it inocuous. (70) Goadby, however, found the sulphate even more soluble than the carbonate. Carlson and others did not agree and there are many startling evidences that the sulphate is at least not so poisonous as the carbonate.

Practical experiments with lead compounds in industry show that the danger of a given compound depends quite as much on the physical properties as on the chemical, for if a given compound is light and fluffy it will do more harm than one which is far more toxic but not dusty. Thus lead acetate gives no trouble though soluble even in water. It is sticky, so that it does not contaminate the air, and it has a sour taste so that a man is conscious of it at once if any gets in his mouth. Litharge which is not so soluble is tasteless and is also very light and fluffy; it is extremely difficult to handle and is productive of much lead poisoning.

(73) It is stated that somewhere about 2 milligrams (0.002 gm.) of lead is the lowest daily dose which, inhaled as fume or dust, may in the course of years set up a chronic plumbism. Probably if the air breathed contains less than 5 milligrams per 10 cubic metres of air, cases of encephalopathy will never, and cases of colic very rarely occur. This is a quite

practical figure to keep the dust down in any process amenable to exhaust ventilation.

PATHOLOGY.

According to most authorities, the underlying pathology of chronic lead poisoning is a structural change in the blood vessels. It is claimed that all the typical changes such as contracted kidney, atrophy of the optic disc, apoplexy and progressive paralysis of the insane are to be attributed to changes in the vessel walls. Maier in the eighties held that the changes were chiefly an end-arteritis and a peri-arteritis. However as to the exact nature of the vascular change there has been much controversy. Some believed there was a vascular hypertrophy due to the stimulation of the smooth muscle cells directly. Some of the French workers thought the primary effect was on the adrenal cortex and there was a stimulation of blood pressure accounting for the vascular hypertrophy. Siccardi, however, got this effect just by bathing the vessels in a lead solution. Thoma stated that the changes are probably due to vacillations of the blood pressure from whatever the cause. However, there does exist change in the arteries. There is a proliferative endarteritis which is probably reparative and compensatory to the damage done to the muscular coat, but as is common in such repair processes, the changes may be out of all proportion to the damage in the media. The subendothelial connective tissue proliferates and then under goes fatty, hyalin and calcareous degeneration, resulting sometimes in complete occlusion of the vessel.

The pathology found in the brain was first studied microscopically by Von Monakow (70), who reported changes typical of progressive paralysis of the insane, especially in the frontal and parietal regions. This consisted of atrophied areas, an increase in the adventia of the vessels, with

cell proliferation and infiltration, fat droplets and pigment. There was atrophy of the hypoglossal and trigeminal nucleus. Seiffert (70) found atheromatous plaques in the basilar arteries, with thickening of the pia and enlargement of the lateral ventricles. Obliterative endarteritis of the vessels of the retina, choroid and optic nerve have been described. Westphal, reported by Hamilton (70), believes there are at least four ways in which lead may act on the brain. There is the direct action, the action of lead on the vessels, the action of lead on the kidneys with production of uraemia and, fourth, the combined action of all or some of these. Occasionally there are cerebral symptoms with no anatomical change. This is thought to be due to hypertension.

While some of the older workers held to the theory that lead palsies were of central origin, it is rather conceded at present that the peripheral nerve lesions may be primary and need not be a secondary neuritis. Gombault and Charcot say lead palsy is a special form of peripheral neuritis, segmentary and periaxial, the axis cylinder escaping damage and normal segments of nerve trunk being found above and below the damaged ones. Thus, in contra-distinction to Wallerian degeneration with involvement of the axis cylinder, the neuritis of plumbism is curable. Van Gieson (70) examined the nerves of a man who had died of lead poisoning. He found in the ulnar nerve about one fibre in ten moderately degenerated; in the external peroneal, one in four; in the sciatic, one in ten; in the left external cutaneous, three in ten; in the right radial, one in twenty, in the left plantar, one in twelve. There were degenerative changes in about one-third of the ganglion cells, such as vacuoles and breaking up of chromophilous granules.

Much evidence indicative that lead poisoning is primarily a disease

of the vessels is produced in a study of the anatomical structure of the kidneys in lead poisoning. No poison has so characteristic an effect on the kidney. The excretion of even small amounts injures the cells of the parenchyma , destroys them and eventually sets up a true cirrhosis, which according to Leyden is identical with Virchow's atrophic granular kidney. The first stage is one of typical glomerular ischemia, with very marked secondary changes in the parenchyma, and as it goes on there is an end-arteritis obliterans, involing especially the smaller vessels. There is sometimes a subacute form of renal plumbism, with marked edema, and here the pathological changes are mixed; for there is not only thickening of the vessels with occlusion of the lumen, but a marked degeneration of the convoluted tubules. The enothelium of the glomerular loops thickens and hard shining masses result. The later stages of the lead kidney conform absolutely to the type of secondarily contracted kidney.

Gastro-enteric symptoms are among the most prominent in lead poisoning, but the pathology is still rather much debated. Constipation of the most obstinate sort is common; the colic is classical of the disease. However, whether the action of the lead is direct on the smooth muscle or whether through a nervous mechanism is subject of controversy. Since both the colic and the hypertension are relieved by amyl nitrite, it would seem that the action is by way of sympathetic irritation. Atropin and scopolamin act like magic to stop the colic; their action is to paralyze the vagal endings. Walko claims to have seen colic with hypotension and so rather discredits the theory of nervous irritation of sympathetic origin. He thinks it is a neuralgia of the mesenteric plexus. Tanquerel years ago found enlargement of the abdominal ganglia of the sympathetic. Maier found connective tissue proliferation and contraction in the ganglia. He also produced experi-

mentally a cloudy swelling of the glands of the stomach. Disappearance of the glands of the stomach with thickened stomach walls have been described.

Lead causes a secondary anaemia, not very pronounced, with the red cells usually not under four million and the hemoglobin around eighty. According to Aub, lead is carried mostly in the blood plasma as an insoluble triple phosphate, but it is picked up by the cell membrane to form an insoluble lead phosphate surface to the cells, making them hard and brittle and easily broken. This explains the ease with which peripheral destruction takes place and also accounts for the anaemia. The anaemia calls forth young cells, reticulated corpuscles, but these under the attack of lead in the plasma undergo degeneration and this degeneration is shown by basophilic clumping of the reticulum. The so-called stippled red cells are therefore degenerating recitulated corpuscles and they are the result of the response of the blood building tissues to the anaemia caused by the lead and the destructive action of it upon the newly formed cells. The effect on the white cells is less marked. Frequently there is a leucocytosis and there are likely to be numerous atypical forms, giving the blood an appearance like leukaemia.

In the bone marrow there is a loss of fat, slight pigmentation and increase in the cellular elements. The nucleated reds may form compact masses. In the centre of such a mass the cells are closely packed and the nuclei show irregular figures, but at the outer edges they are looser and look like normoblasts. Between these areas are white cells, granular myelocytes, transitionals, eosinophiles, polymorphonuclears and a moderate amount of large and small lymphocytes. Much of the lead is stored in the bones and it was thought that this lead may have had a deleterious effect on

the forming cells and caused the anaemia; however, this lead is stored in the solid shaft and not in the marrow. The spleen has been found to show changes of a myeloid nature - - - nucleated reds being found there, which were absent in the bone marrow.

SIGNS AND SYMPTOMS.

An early sign is the so-called blue line appearing on the gums close to the tooth margin. This is to be distinguished from a second line that appears on the teeth themselves and can be rubbed off. The true lead line is not invariably present, but when it is it is formed by the action of the sulphuretted hydrogen in the tartar on the teeth with the lead in the tissues, forming an insoluble lead sulphide. Of course, one who keeps his teeth free from tartar is less apt to have the line. Pallor may appear early and there may be a mild anaemia. Sternberg (72) believes that a diagnosis of lead poisoning may be made with no more than a lead line, pallor and slight anaemia for a basis. The pallor often is due not so much to true anaemia ss it is to a constriction of the vessels. It is stated in Nelson (73) that the first action of lead when absorbed into the system is on the blood and circulatory system, diminishing the number of red cells and the amount of hemoglobin. A description of what these changes are is given in the section on "Pathology".

Gastro-enteric symptoms are the commonest. Early there is a chronic loss of appetite, coated tongue, a disagreeable sweetish taste, foul breath, thirst, eructation of gas, nausea, oppressive feeling in the stomach, general fatigue, loss of weight; constipation is chronic and obstinate. Characteristic is lead colic. Beginning in extreme obstipation, the attack culminates in an attack of intense, agonizing pain. This is spasmodic, and exploratory finger in the rectum can palpate the alterations of violent

contractions and slight relaxations in the bowel. The pain may be intense enough to cause collapse, even delirium with evidence of great suffering. At times the attack is so sudden as to cause the patient to think he has been struck a blow. Lead workers have been picked up on the street, helpless with lead colic. The pain is referred to the umbilical region, and the patient falls down, doubles up and presses both hands into his abdomen. In bed he is likely to lie on his face, the pressure seeming to give some relief. Certain cases claim to have exquisite tenderness over the abdomen; often a diagnosis of abdominal inflammation is hard to discredit. Many lead workers are neurasthenic. The pulse, during oneof these attacks, is decidedly slowed, small and with increased tension. The blood pressure is raised during the attack but drops as the pain lessens. There may be complete suppression of urine during the attack and the first urine passed after it may contain urobilin, hematoporphyrin and even albumin and casts. The respirations are rapid and labored. A peculiarly characteristic observation is that during the most acute pain and collapse, there is an absence of perspiration. There may be lancinating pains in the limbs. The duration of the acute stage is usually twenty four hours.

Common also is arthralgia. Men susceptible to colic usually (70) also have arthralgia. Prodromata of arthralgia are usually numbness and lassitude in the limbs. The attack is very likely to come on at night, is most often localized in the legs, then in the arms and shoulders, in chest walls, back and head. The pain is described as being like a painful electric shock, boring or stabbing. Paresthesias, formication, numbness, and cold or heat may be accompanying. It comes on in paroxysms that may be started by cold or by motion. Slow gentle pressure relieves the pain, deep pressure increases it. The muscles cramp and may be felt or even

seen as hard balls. There may be no heat or swelling, and the pain does not follow the whole course of a nerve trunk. As a differential point, the pain on motion is less severe than in articular rheumatism; neuralgia is ruled out by the fact that the pain is not along a whole nerve trunk. Lead has a marked influence on the production of gout. Distinguishing features of this type of gout are the youth of the victims, the rapid spread of the disease, involvement of joints usually spared in ordinary gout, and in the great tendency for the formation of tophi. Estimates that consider the part of lead in the production of gout state from half to a quarter of all gout cases have lead as a background.

A rarely primary but fairly common manifestation of lead poisoning is paralysis. This paralysis is a progressive muscular atrophy, toxic amytrophy, which may be of the pure atrophic type, usually localized and of slow development, rarely generalized, and rapidly progressive; or it may (70) belong to the spastic, atrophic type of Charcot's amytrophic lateral sclerosis. There are five types generally recognized: first, is the antibrachial type which involves the extensors of the wrist and fingers with the supinators escaping; second is the brachial type which involves the deltoid, bicops, brachialis anticus and the long supinators, sometimes called the scapulo-humerus type and may be primary or may follow the antibrachial; third is the Aran-Duchenne type of amytrophy, --- a more or less rapid atrophy of the small muscles of the hand which begins in the thenar eminence, then involves the interosseous and hypothenar muscles with flattening of the hand, and then, as the atrophy progresses and the middle and nail fingers flex the "main en griffe" results; the fourth type is the peroneal which attacks the extensors of the toes, the peroneals, and sometimes the tibialis anterior and which usually is bilateral and attended with a loss of tendon reflexes;

the fifth type is the very rare laryngeal type. By far the most common is the first type; Tanquerel says there are but 13 of the lower extremity cases to a hundred of the first type. In this first type the first thing noticed is that the middle and fourth fingers stay flexed when the others are extended, the middle and fourth fingers not having extensors of their own; the common extensor is paralyzed. Also one affected cannot with extended fingers flex the hand dorsally, and if he tries to do it the first phalanges of the fingers bend. In this type the lesion is always symmetrical, generally with the most used hand effected most. Injury to the other muscles follows more or less rapidly. Characteristic is the escape of the thenar and interossei. The curious localization of the palsies seems to be in some way related to function, for those muscles that are used most are most attacked, this being especially true where some form of action is over-used, particularly if the muscles used are not those that have had evolutional development. As an example, painters who in their work use a wrist movement that is rather monotonous and which is not one that is so common as to have built up through heredity rugged muscles to perform it, most commonly have wrist drop.

Lead encephalopathy is yet another manifestation. Tanquerel says that characteristic of lead encephalopathy is the great variety of its manifestations. It is the least common of the various phases of lead poisoning. The warning symptoms usually are severe headache, dizziness, sleeplessness, bad dreams, hallucinations or disturbances of vision. The delirious form is characterized by confusion, incoherence, sensory hallucinations, slight tremors of arms and face, difficulty in walking, embarassment of speech and often amaurosis. The comatose form occurs suddenly, often in the midst of apparently good health. There are several forms of the con-

vulsive, partial preservation of consciousness being a distinct feature of lead epilepsy. Westphal adds to the types described by Tanquerel an apoplectic form, but believes that even with this the field is incomplete, because into the picture of lead encephalopathycome features of progressive general paralysis, of bulbar paralysis, of disseminated sclerosis and laryngeal paralysis, of choreic symptoms and hysterical functional disorders. Women are more susceptible to lead encephalopathy than men,and young girls are especially susceptible. An attack is usually preceded by pallor, headache, perhaps hysterical excitement, which is followed by a convulsion in which the young woman may die or from which she may pass into coma, terminated by death, or by return to consciousness with severe headache, mental clouding, partial or total blindness. From this stage she may pass into mania, transient or ending in permanent dementia; or she may recover with impairment of vision, or she may recover completely.

Lead workers are notoriously subject to arteriosclerosis with contracted kidneys and hypertrophy of the heart. With these are the usual symptoms of arteriosclerosis, nephritis, hypertension and such.

Diagnosis of acute plumbism is not difficult; the chronic form presents more trouble. Roth (72) in Germany and others elsewhere feel that lead is excreted in the urine so constantly and uniformly in chronic poisoning that urine examination for lead is a great aid. On the other hand, Rambousek (71) thinks the kidney elimination of no consequence. Lead in the feces is of no consequence since it does not prove that any of it has been absorbed. Stippling of the red cells was hailed as a sure diagnostic aid in 1906, but four years later Biondi (72) claimed that stippling was a good positive sign but no good as a negative one and that the presence of stippled cells simply means young corpuscles and depends on the activity of the

hemopoietic system. The diagnosis probably should rest on several elements, among which history of exposure is important. With loss of weight, loss of appetite, foul breath, weakness and other gastro-enteric symptoms and with a lead line present the diagnosis is made. Sternberg (72) believes that a diagnosis may be made simply on the basis of a lead line, pallor and the general appearance in a lead worker.

INDUSTRIES INVOLVED IN LEAD POISONING.

There are countless industries which have to do with lead in some form or another. Lead, as has been said before, is the one toxic metal a contact with which few escape in a lifetime. Among the important industries in which the lead hazard exists is lead mining. Lead mining every year claims victims of lead poisoning, the number depending largely on the mine and the type of ore that is found. In lead smelting, the danger also exists, especially in the dusty processes. Metallic lead is used in a wide variety of industries where it is cast or moulded into various shapes for various uses. Makers of lead wire, sheet lead, pipe, machine parts, plumbers' goods, bullets and shrapnel, picture frames, coffin ornaments, grids for storage batteries, car and can seals, stoppers for bottles and for basins, tin foil, lead foil, printers' type - - - all of these are exposed to molten lead and instances are on record of poisoning from the making of each of these. Other industries involving a large use of metallic lead are the making and the use of solder and bearing metal, lead burning with the oxyhydrogen flame, and lead tempering of machine parts, piano wire, magnetoes, etc. The plumbers' trade, while not so much concerned with lead as in years gone by, still has repair work with joint wiping and exposure to lead. The dangers in these trades are easily controlled, however. In the printing trade there are many factors

to lead to easy lead poisoning. The workers are of a character that get little exercise, the working quarters are generally poorly heated. The sources of lead dust are: in the composing room, the dust from type cases; in the linotype room, the scraps of lead from the machine which fall to the floor and are ground to dust by the feet of passers by, and the dust from the cleaner machine and plunger; in stereotyping and electrotyping, the scraps from trimmers and routers and saws, and the dross from the kettles. In addition, most shops melt and recast old type and scrap, and this is another source of lead dust. Lead poisoning may also be acquired by exposure to the fumes from molten lead in stereotyping, electrotyping and remelting and casting type. The making of white and red lead is potent with danger of poisoning. Manufacturing storage batteries is an industry of considerable importance in this country. The casting and especially the "pasting" processes produce considerable liability to poisoning. The assembling process where there is necessity for filing, straightening and trimming the plates is always productive of lead dust. Another kind of industry in which lead is involved is that in which enamels, glazes and porcelain enameled sanitary ware is made. The making of pottery involves the same sort of process.

It is impossible in the United States to discover even approximately the proportion of painters who suffer injury from the use of lead paint, for it is not even known how many painters there are in the country or how many are exposed to lead. It is, of course, the most widespread of the lead using trades, even more general in its distribution than printing or plumbing, for no community is too small to employ a painter. Not all painters' poisoning comes from lead; often the vehicle may be at fault. Hamilton (72) cites experiments carried out at the Pasteur Institute showing

that the toxicity of white lead depends to some extent upon the vehicle in which it is carried. Among the paint pigments, there is no harmful pigment now used except lead. Methods of applying paint vary and with this variance there is also a varying toxicity. Spraying of paint without proper ventilation develops the greatest hazard; often this method of painting is used in quarters too small to provide sufficient ventilation. Mixing of dry white lead with the oils is a danger not so often met with. Sandpapering surfaces to smooth them following application of a coat of paint is pregnant of great danger especially where it is done in close confines. The removal of old paint whether by sanding, by scraping or by use of a pneumatic hammer generally produces dust containing lead. There is controversy concerning the danger of skin absorption in those who get paint smeared over their hands in their work. The type of painting done by commercial artists is not free from danger of lead poisoning, and the fact of this is hardly appreciated by those who are doing this type of work.

PREVENTION.

The means for prevention as in the other industrial anaemias resolve themselves to a few general considerations, all of which are but the obvious. Foremost is the need for substitution of less noxious substances where such substitution is possible. This particularly refers to lead compounds used as pigments in paints where zinc could be used. In the dusty trades, meticulous attention to detail is needed in securing as perfect a locally applied system of exhaust ventilation as possible for the removal of the fumes and dust. Important also is close medical supervision with periodic examinations, looking for the early

signs of plumbism. Women and girls, and especially pregnant women, should never be allowed to come in contact with lead or work where there is a possibility of lead poisoning. Likewise lead has a deadly influence on young boys; print shop apprentices should be restricted in their activities as should young people in other lead industries. Personal cleanliness, hygienic living, exercise, fresh air, maintenance of a high standard of health are prime essentials in lead workers.

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