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INDUSTRIAL ACCIDENTS AND HYGIENE SERIES

INDUSTRIAL POISONING IN MAKING COAL-TAR DYES AND DYE INTERMEDIATES

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INDUSTRIAL POISONING IN MAKING COAL-TAR DYES AND DYE INTERMEDIATES.[a]

INTRODUCTION.

The making of coal-tar dyes and dye intermediates in the United States has grown enormously since 1914, and during this time the industry has passed through many phases. The author's first acquaintance with it was in 1916–17, when, in the course of an investigation of plants manufacturing and loading explosives, a number that were also manufacturing dye intermediates were visited. Moreover, some compounds are used for both purposes; for instance, dinitrotoluene, dinitrobenzene, diphenylamine, and anilin. At that time the methods used were sometimes crude and decidedly dangerous, because it was only in a few old plants that the nature of these compounds was well understood, the risks known, and the proper precautions taken. It was generally believed that vapors were the greatest danger; that men became poisoned by breathing fumes of volatile liquids, and when preventive measures were undertaken they were based on this idea. It was only later that, as a result of sad experience, certain solids, such as dinitrobenzene and paranitranilin, were discovered to be quite as troublesome as a volatile liquid like anilin, or even more so. It was also found that one could not revive a man with anilin poisoning by taking him out in the fresh air; one must also get rid of the anilin on his skin by stripping and bathing.

Gradually the results of experience became known and conditions improved more or less. The improvement was hastened by the closing of the smaller works and by the concentration of dye intermediate manufacture in a few large plants. While in 1916 anilin and nitrobenzene were made in dozens of places, they are now made in only a few, and there has been a very decided falling off in the cases of

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[a] This report is based on 36 inspections of American plants producing crudes, intermediates, and colors, made during the years 1916 to 1919, and on visits to the following foreign works during the summer of 1919: British Dyes (Ltd.), Huddersfield; Levinstein (Ltd.), Manchester; Claus & Co. (Ltd.), Clayton, Manchester; Clayton Aniline Co. (Ltd.), Clayton, Manchester; Mersey Chemical Co., near Liverpool; Poiret & Cie., St. Denis, near Paris; Allgemeine Chemische Gesellschaft, Basel; Leopold Casella, Mainkur, near Frankfort-on-the-Main.

intoxication from these compounds. There has also been a great improvement in the care given to the employees. The larger plants have safety or welfare superintendents, whose duty is to provide against accidents and accidental poisoning. Physicians are employed to attend such cases, and these physicians acquire skill in diagnosis and treatment which can not be obtained by the ordinary practitioner. In the best American plants the physicians also do very valuable preventive work. The competent physician is familiar with the different processes and the dangers inherent in them, and keeps watch for the earliest symptoms of occupational intoxication among the men. The manufacture of dyes and intermediates in the United States has undergone great improvement and is improving from day to day, but it can not be said that this improvement is at all uniform or that there are not still some unnecessarily dangerous departments even in the best plants, and a few are still far from what they should be, both in the matter of construction and operation and in the personal care of the force. It is because of this great variation, this lack of standardization of the safety work in the industry, that it seems useful to present the results of an investigation carried on at intervals during the last three years, so that the different manufacturers may learn of the methods used in places other than their own and the experience gathered in one place may be made available for all places doing similar work.

It seems valuable also to publish in convenient form the information that can be gathered from the literature, especially of Germany, concerning the action on the human body of the great variety of compounds used in this complicated industry. Germany has for years conducted elaborate animal experiments with these compounds, and in addition an enormous human experiment has gone on in her dye works. It seems a pity not to avail ourselves of the results rather than to go on and repeat such human experiments ourselves. Of late, American observers have added their contribution to this branch of industrial toxicology, and wherever possible the American publications have been used. The compounds that are dealt with in this report are not by any means all that the color worker comes in contact with. Others, whose chemical composition leads one to suspect that they possess toxic properties, may later on prove to be quite as dangerous as those about which we already have sufficient data to indicate their poisonous character. The only ones taken up in this report are those which have been found to cause actual poisoning in human beings.

One advantage the American industry possesses when compared with the European is the absence of women in the working force. During 1918 plans were under way to substitute women for men in a few plants, and some women were actually employed, but as soon as the armistice was signed the women were discharged and there is no intention now of employing them in any plant. This is a matter for congratulation because it is believed by all authorities that the employment of women in work exposing them to any poison should be discouraged as much as possible, not because they are necessarily more susceptible to poison than men, but because if they do suffer from the effects they may pass the injury on to their offspring.

The report is not presented as a complete one in any sense, certainly not as a complete description of the processes used in dye and dye intermediate manufacture. Only the barest outline of these processes is attempted, and this merely because the dangers of the work can not be described without some such slight outline of the chief reactions and their resulting compounds.

The making of dyes has necessitated the production and use not only of benzene, nitrobenzene, and anilin, but also of an enormous number of derivatives, many of which have a toxic action on the skin, on the central nervous system, on the blood, or on all three. The crude compounds of the coal-tar series that serve as starting points for the production of dyes are benzene, toluene, xylene, naphthalene, anthracene, and phenanthrene, the first three of which are decidedly toxic. Naphthalene was tested by Eulenberg[1] who says that it causes in animals nothing worse than an irritation of the mouth, nose, and eyes, with salivation and lachrymation. Men employed with hot naphthalene may suffer from headache and confusion caused by the fumes. Eulenberg found the same effect from hot anthracene, and also occasionally an eczema.

BENZENE (C_6H_6), TOLUENE ($C_6H_5CH_3$), AND XYLENE ($C_6H_4(CH_3)_2$).

Benzene is obtained in this country in the manufacture of coke and of illuminating gas. In coke works the coal is roasted and the lighter vapors, benzene, toluene, and xylene, are absorbed in heavier oils with a higher boiling point, and are then subjected to fractional distillation. Benzene and its homologues are also recovered from coal-gas residuals in gas works. In making gas the tar left in the mains and scrubbers is allowed to stand till the gas liquor separates out, a source for the obtaining of ammonia, then the tar is distilled. The first bodies to pass over are benzene, toluene, and xylene; next come crude carbolic acid and naphthalene "dead oil," then anthracene, leaving a residue of coal-tar pitch.

In well-constructed and well-managed plants for the production of these bodies there is practically no danger of fumes or contact with the volatile poisonous substances except when it is necessary to repair or clean the apparatus. When this is done extraordinary precautions must be taken to protect the men, and sometimes in spite of these precautions very serious accidents occur. The same thing is true of the use of the light coal-tar distillates in making dye intermediates; the cases of industrial poisoning follow almost always some accident or an unusual exposure in the course of a job of cleaning or repairing.

Benzene is a fairly new industrial poison in the United States, for its use before the war was decidedly restricted, since it was imported from Germany and therefore expensive. The petroleum products, naphtha, benzine, and gasoline, were used as solvents for fats, gums, and rubber, because they were obtainable in large quantities in this country. After the outbreak of the war there was a sudden demand for toluene for the manufacture of trinitrotoluene and of benzene for the manufacture of picric acid and tetryl, and at the same time the coal-tar dye industry, which was growing with great rapidity, added

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[1] Quoted by Koelsch in Münchener medizinische Wochenschrift, July 24, 1917.

its demand for these two compounds, and the rubber industry, which had become dependent upon German anilin, was obliged to procure benzene and manufacture anilin. At present large quantities of tar distillates are produced in the United States and used, not only in the manufacture of dyes, drugs, and perfumes, but also, because of their powerful solvent properties, in rubber manufacture and in the making of shellacs, varnishes, varnish and paint removers, and dope for airplanes. They are also coming into increasing use as fuel for motor cars. In consequence of this large production and use we have had during the last five years a much larger number of cases of industrial poisoning from benzene and toluene than were reported in the whole of American medical literature up to 1914.

In describing the effects of these bodies the three—benzene, toluene, and xylene—may be treated together, since they differ only in degree. Toluene is benzene with one methyl[2], CH_3, group taking the place of one H atom in the benzene ring, and xylene has two such groups. The entrance of the methyl group lessens toxicity and xylene is said to be distinctly less poisonous than benzene, but the difference between benzene and toluene is not great; in fact, there are experimenters who claim to have found toluene the more toxic of the two. These bodies are poisonous to the central nervous system, producing loss of consciousness, lowered temperature, and disturbance of respiration and pulse rate. In mild cases there is a condition resembling early alcoholic intoxication, with excitement, pleasurable or combative, headache, and dizziness. This is followed by depression, a feeling of general illness, loss of appetite, and nausea, sometimes vomiting. If the exposure is greater, if the fumes are heavier, the effect is very rapid and the stage of excitement may take the form of acute delirium; the man shouts and sings and may be so unmanageable that his would-be rescuers find it impossible to get him out of his dangerous situation before it is too late. Loss of consciousness succeeds the delirium. The respiration is rapid and shallow, the pulse weak and rapid, and convulsions may precede death. A more excessive exposure may cause immediate collapse and death within a few minutes, from paralysis of the nerve center controlling respiration.

In the manufacture of explosives, chiefly of picric acid from carbolic acid, which in its turn was made from benzene, there were during a year's time, 1915–16, 14 serious cases of industrial benzene poisoning officially reported, seven of which were fatal. All of these but two were men who were employed in some unusual piece of work—pipe fitting, repairing stopcocks, cleaning stills and tanks. Germany has had a similar experience. The German factory inspection reports for almost every year mention cases of severe or fatal poisoning from benzene in men who were repairing or cleaning benzene receptacles. These cases, however, are rare, and so are the British cases. We have still in the United States an excessively large number of deaths from benzene poisoning, and a study of the records shows that in some instances the necessary precautions are still slighted in spite of the growing number of casualties.

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[2] For those unfamiliar with these chemical terms a short description is given in the appendix of the structure of the benzene ring and the principal derivatives of the ring, an explanation of isomeric forms, etc. The author is much indebted to Dr. W. Kritchewsky, of the Sunbeam Chemical Co., Chicago, for his assistance in preparing the chemical parts of this report.

If the poisoning takes place, not through a single exposure but through repeated exposures, the action of benzene is characteristic and easily recognized. It acts on the blood-forming organs, especially the marrow of the bone, and as a result there is a fall in the number of both red cells and white cells. In one of the cases described by Selling,[3] of Baltimore, the red cells, just before death, numbered only 640,000 and the white cells 600. This was in a girl of 14 who had been using a cement of rubber and benzene to seal cans. Harrington,[4] of Massachusetts, reported five cases of chronic benzene poisoning in rubber-boot makers. One of these, a man who had worked for 11 months, died in coma with convulsions. Before death the red cells had fallen to 1,616,000 and the whites to 850. The second striking effect of benzene is on the capillary blood vessels, which rupture, allowing blood to escape under the skin and from the mucous membranes. The skin is covered with purplish spots like bruises, there is bleeding from the gums, sometimes severe nosebleed or hemorrhage from stomach or intestines, and in girls menstrual hemorrhage.

The tissues attacked by benzene are those which must be depended upon for the production of the so-called antibodies which defend the body against infection by the germs of disease. As a consequence, poisoning by benzene, and to a less extent by toluene, lowers the resistance to infections. In animals injection of benzene has been shown to favor the development of an acute infection and also the lighting up of a latent infection. This fact is of great importance in connection with industrial poisoning from benzene.

The susceptibility to benzene poisoning varies very much, a fact which must be borne in mind in connection with industrial cases. Not long ago a report was made on the death of a pipe fitter from benzene fumes. The man was changing coils in a benzene tank which had been thoroughly blown out with steam before he entered. There was another man in the tank with him who was not affected, and the company doctor therefore insisted that it was the physical condition of the former that really caused his death. In a way that was true; oversusceptibility to poison is certainly a physical condition, yet no one would think of giving such an explanation for the deaths from typhoid fever, which occur as a result of drinking infected water, although there are always a large number of people who have drunk the same water and yet escaped an attack of typhoid fever. Individual susceptibility plays just as large a part in epidemics of infectious disease as in poisoning from compounds used in industry. An instance of the varying resistance to benzene is related by the manager of a coke by-products plant. There was an overflow of benzene through some accident, and two men who were working in the room collapsed and fell in a faint. Two others who went in to rescue them were also overcome, and so were two more. After the six men had collapsed, there was a panic among the other workmen, but finally an Italian offered to go in, saying that he never minded the fumes. He did go in, not even protected by a helmet, and dragged out the six men, one after the other, himself apparently quite unaffected by the benzene. Plainly it would be unfair to take the Italian

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[3] Selling, L. Johns-Hopkins Hospital Bulletin. 1910, XXI, 33.
[4] Harrington, T. F. Boston Medical and Surgical Journal. 1917, CLXXVII, 203.

as the normal type; indeed, his lack of susceptibility was a deviation from the normal.

In the manufacture of dyes the only cases of benzene poisoning so far reported have been of the acute type, resulting from a single exposure to more or less heavy fumes. One instance will be sufficient to illustrate this sort of accident, for all the reports read very much alike. A man was sent to the top of the benzene washer to change the piping on the spray nozzle. He was told not to go into the washer, which was empty but had not been cleaned. He ignored this order, took off the manhole cover, placed a ladder down into the washer and went in, one of his helpers following him. The moment he got to the bottom of the ladder he felt that he was going to faint, started to climb up, but would have fallen if two helpers above had not caught him and dragged him out. As they did so they saw the other man fall on the bottom of the washer, but they were obliged to help the pipe fitter down from the washer before they could return for the helper, and by the time they got him out he was dying.

In this case no attempt had been made to render the washer safe because the man was not supposed to go in, but there are repeated instances recorded of severe and even fatal poisoning in men who have not been allowed to enter the tank or still until it has been emptied and steamed out repeatedly. Even a helmet of the Draeger type is not always sufficient for protection. Not long ago a man who wore one of these helmets fainted inside the tank and died soon after he was removed. The only explanation that could be offered was that the helmet had not entirely prevented him from breathing through his nose.

Several cases on record in Germany show how dangerous may be the work of cleaning and repairing receptacles that have held benzene. Lewin[5] in 1907 reported a case of fatal poisoning in a workman who had tried to rescue a man overcome with benzene fumes. A benzene kettle had stood empty for 22 hours, then it was washed out three times with cold water and twice with steam and was allowed to stand all night filled with cold water. The man who was sent in to make repairs took with him a pipe through which was blowing a strong current of compressed air. Nevertheless, he fainted and fell to the bottom of the kettle. Several men tried to get him out, but all grew dizzy and confused and had to give up, when an engineer, with a diver's helmet succeeded in dragging him out. He was revived, but one of the men who had tried to rescue him died 10 minutes after climbing out of the kettle.

The German factory inspection report for 1913 contains an account of a similar case. Here, also, the tank was supposedly thoroughly cleaned, for it was boiled out three times, but the workman who went in lost consciousness; and although the two men who had been set to watch him dragged him out promptly he never came to.

There is far less fatal benzene poisoning in Great Britain than in the United States, and one explanation for this fact was given by the manager of a dye works. He said that it was not safe to send a man into a benzene tank or still, no matter how carefully it had been cleansed, till it had aired out for fully two days, for accidents were very likely to occur if the men were allowed to enter at once.

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[5] Lewin. Münchener medizinische Wochenschrift. 1907, LIV, 2377.

He believed that the metal absorbs benzene and this must first be allowed to evaporate.

The use of solvent naphtha, which is really an impure mixture of toluene and xylene, in making naphthionic acid and in making benzidin, provides another source of poisoning from these coal-tar distillates. Naphthalene is nitrated with Chili saltpeter and sulphuric acid, then the nitronaphthalene is reduced with iron fillings and hydrochloric acid and the resulting alphanaphthylamine is removed from the iron sludge with the aid of solvent naphtha heated with steam. The naphtha is later recovered for further use by distillation. In one method of benzidin, and tolidin production, reduction is brought about by zinc dust and solvent naphtha.

BENZENE DERIVATIVES.

The most important compounds used in the manufacture of dyes are derivatives of benzene. The number and complexity of these compounds is very bewildering to the ordinary investigator, but it is not necessary that he should be familiar with all of them in detail, because their action on the human body is much the same, although it is modified somewhat by differences in chemical structure. The following is a brief statement of what is known as to the relation of chemical constitution to physiological action in the coal tar or aromatic series.[6]

The phenols are hydroxy (HO) derivatives; for instance, carbolic acid is hydroxy-benzene; cresol is hydroxy-toluene; naphthol, hydroxy-naphthalene. The entrance of this hydroxy nucleus renders the naphthols, alpha and beta, more irritating in their effect than is naphthalene. An increase in the number of hydroxy groups increases toxicity, thus pyrogallol, trihydroxybenzene, is stronger than phenol, commonly called carbolic acid, which is monohydroxy benzene. But phenol is not nearly so dangerous an industrial poison as benzene, for it is far less volatile. Severe burns may be caused by phenol, although even this is not common, but systemic poisoning is practically unknown in industry.

Pyrogallol, commonly called pyrogallic acid, is used in at least one plant in the United States to produce gallocyanine. German reports tell of poisoning by this compound, but no such case has as yet come to light in this country.

The entrance of the sulphonic group (SO_2HO) into a benzene derivative removes toxicity, thus anilin is rendered harmless by sulphonation, so is phenol. The entrance of COOH often has the same effect; nitrobenzoic acid is harmless, although nitrobenzene is very poisonous. The acetyl group ($COCH_3$) lessens toxicity; acetanilid is less poisonous than anilin. The introduction of an alkyl group, methyl (CH_3) or ethyl (C_2H_4) lessens toxicity, dimethylanilin being less poisonous than anilin. This is, however, only when the replacement is in the side chain,[7] taking the place of H in the NH_2 group. If the replacement takes place within the ring, toluidin is formed, which is quite as toxic as anilin. The toxicity of the

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[6] Fraenkel, Sigmund. Die Arzneimittel Synthese auf Grundlage der Beziehung zwischen chemischer Aufbau und Wirkung, Berlin, 1912.

[7] See Appendix for an explanation.

diamines is greater than that of compounds with a single amine (NH_2); phenylendiamine is more toxic than anilin.

Chlorine entering an aromatic compound changes it very little, certainly does not increase its toxicity, in fact, chlorbenzene seems to be less toxic than benzene. The nitroso group (NO) and the nitro group (NO_2) increase toxicity always whether they enter the ring or a side chain. All aromatic compounds with nitrogen are more toxic than those without, but there is no rule as to increasing toxicity with an increasing number of NO_2 groups. For instance, the 1–2–4 isomer [7] of dinitrophenol is much more poisonous than trinitrophenol (picric acid). Mononitrobenzene is more poisonous to the central nervous system than dinitrobenzene, but the latter has a more destructive action on the blood.

There is no rule as to the toxicity of the polymerides, but usually, according to Fraenkel,[6] the para position is more toxic than the ortho. This is the general opinion of practical men with regard to ortho and para toluidin, the latter of which is generally regarded as much more troublesome. Usually, paranitranilin is considered more dangerous than meta, and ortho less dangerous, but animal experiments carried on by Lewis, of the Sprague Memorial Laboratory in Chicago, showed that for rabbits meta was more toxic than para. In the case of the nitrochlorbenzenes the ortho isomer stands at the head, then the para, and last the meta. As to the phenylendiamines, there is a great difference of opinion among the men in the dye industry, some holding that the para position is the worst, others the meta.

Substitution products formed by replacement of the hydrogen of the ring are decidedly more toxic than substitution products formed by replacement of the hydrogen of a side chain. The toluidins are very toxic; benzylamine is harmless.

The physiological effect of 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 Curschmann [8] there is an important difference between the nitro and amido compounds in that the latter are simply blood poisons and all of 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 with regard to the nitro compounds is undeniable, but according to Heubner [9] it is true of all the benzene derivatives, the amido as well as the nitro. Heubner succeeded in his experiments on rabbits in producing a narcotic effect with collapse and paralysis before blood changes had had time to take place, and he holds that not only nitrobenzene but phenol and anilin affect the lower centers, those of respiration, vasomotor control, and heat regulation.

In a light case of poisoning from one of these aromatic compounds the face is flushed, there is a sense of fullness and throbbing in the head, burning in the throat, tightness in the chest, then a violent throbbing headache comes on, with dizziness, roaring in the ears,

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[6] Fraenkel, Sigmund. Die Arzneimittel Synthese auf Grundlage der Beziehung zwischen chemischer Aufbau und Wirkung, Berlin, 1912.

[7] See Appendix for an explanation.

[8] Curschmann, F. Deutsche Vierteljahrsschrift für öffentliche Gesundheitspflege, 1911. XLIII, 225.

[9] Heubner. Zentralblatt für Gewerbehygiene, 1914. II, 409.

and some disturbance of sight. The flushing of the face subsides and the color becomes livid, with bluish lips and tongue, while the whites of the eyes are often tinged with yellow. If prompt treatment is given, which means removal from all contact with the poison, the attack may last only a few hours, and the man is able to return to work on the following day. But even in so mild a case as this the bluish color of the lips and tongue may persist for several days. In severer cases, the color of the face is gray-blue, the lips and tongue 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 complain of cramps in the abdomen and extreme weakness. Sometimes, usually a few hours after the onset of the attack, consciousness is lost. The respiration is shallow and quick; the pulse is small, fluttering, irregular, and enormously accelerated; the skin is cold and the blood pressure is usually low. If coma persists the respiration and pulse grow slower and slower, there is involuntary defecation and urination, and convulsions usually occur just before death. It is a characteristic feature of all these poisons that the attack seldom takes place while the man is at work, almost always while he is on his way home, or even some hours later.

Blood.—Many studies have been made of the blood in poisoning from benzene derivatives, and the changes in acute intoxication seem to occur in the following order. Methemoglobin is formed early in the course of intoxication, and probably coincidently with it is a destruction of red blood cells. (Curschmann,[8] Lehmann,[10] Mohr.[11]) 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, there is some fragmentation and polychromatophilia (abnormal reaction to staining fluid). Early in the attack the blood becomes chocolate colored and thicker than normal, and spectroscopic examination may reveal lines which are said to be those of methemoglobin (Mohr[11]), or rather, lines situated between the methemoglobin and the oxyhemoglobin, and therefore not quite typical (Price-Jones and Boycott,[12] Brat[13]). If, however, the spectroscopic test is not made till later in the attack, it is usually impossible to detect these lines. Indeed Curschmann says that by the time cyanosis is fully developed methemoglobin can no longer be demonstrated.

The evidence of the destruction of red corpuscles is succeeded in a few days, from the second to the fifth, by evidence of active regeneration, and the blood picture then may be very much like that of pernicious anemia, with variations in staining and in size and with the appearance of stippled cells and nucleated cells. The changes in the white cells are not so characteristic, but during an acute attack there is usually a polymorphonuclear leucocytosis. Later, as also in chronic poisoning, there is a lessened number of these cells and a relative increase of lymphocytes (Hudson[14]). In

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[8] Curschmann, F. Deutsche Vierteljahrsschrift für öffentliche Gesundheitspflege. 1911. XLIII, 225.

[10] Lehmann, K. B. Archiv für Hygiene. 1912. LXXV, 1.

[11] Mohr. Deutsche medizinische Wochenschrift. 1902. XXVIII, 73.

[12] Price-Jones and Boycott. Guy's Hospital Reports. 1901. LXIII, 309.

[13] Brat. Deutsche medizinische Wochenschrift. 1901. Nrs. 19 and 20.

[14] Hudson, W. G. Medical Record. 1917. XCI, 89.

the slower forms of poisoning the destruction of red cells acts as a stimulus to further cell production on the part of the bone marrow, and an increased red cell count may be found. Malden[15] examined the blood of 13 men employed in an English factory where anilin and nitrobenzene were made. Six of the 13 had a high red cell count with a low hemoglobin, and many imperfectly developed red cells. Loss of hemoglobin ran from 5 to 50 per cent. The cells showed great variations in size, the large predominating, but more noteworthy was the appearance of stippled cells, which Malden considers quite as characteristic of the early stages of anilin poisoning as it is of lead poisoning. Malden summarizes the changes in the blood caused by small repeated doses of anilin thus: Red cells increased in number with loss of hemoglobin; low color index; degeneration and imperfect regeneration of red cells, increase of lymphocytes, decrease of polymorphonuclear leucocytes.

Urine.—Very varying results are reported from the analysis of the urine in cases of acute poisoning. Hay[b] produced symptoms in himself of intoxication with marked cyanosis by rubbing dinitrobenzene on his skin, but his urine showed no abnormality. Sugar and casts are commonly absent in the urine, although there are occasional instances of reduction of Fehling's solution. Albumen is usually not found, except perhaps for a trace, in acute intoxication of moderate degree, even when the urine is a dark brown color. This brown color is very common and is often the first warning the workman has that he is beginning to experience the effects of the poison. A chemist who once had had a severe attack of anilin poisoning from drawing a quantity into his mouth while siphoning, told me that always after that if he came in contact with anilin he would notice this change in the color of the urine, although he might feel no subjective symptoms at all.

In severe poisoning the urine may be a dark brown or the color of port wine, or a smoky red, and in such cases methemoglobin or unchanged hemoglobin or blood pigment, bile pigment, hematoporphyrin, may be detected. Albumen can sometimes be demonstrated, but not always, even in severe cases (Mohr[11]). Some observers insist that bile pigment is never found in the urine; others that bilirubin can be detected in the majority of cases. Mohr found hydrobilirubin frequently after dinitrobenzene and chlorbenzene poisoning. No thorough study has as yet been made of the reduction of Fehling's solution, although the occurrence of this phenomenon is reported fairly frequently. Six such cases were described in a personal communication by Dr. Kessler, of Marcus Hook, in men who had been working with dinitrobenzene and anilin. Their urine was dark brown, contained bile pigment, and had reducing properties. A seventh case was one of fairly severe poisoning from mononitrobenzene.

Dr. Sutherland, of the du Pont Co., who has some 1,200 men under his care, says that he finds not infrequently urines reducing Fehling's in men who show signs of poisoning from nitro or amido compounds.

Müller reported a case of anilin poisoning, in which the urine contained no sugar, no blood, nor albumen, but had strongly reducing

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[b] White and Hay. Lancet. 1901. II, 582.
[11] Mohr. Deutsche medizinische Wochenschrift. 1902. XVIII, 73.
[15] Malden. Journal of Hygiene. 1907. VII, 672.

properties. According to von Jaksch,[16] a substance which reduces copper sulphate and is also lævorotatory was found in the urine of a man suffering from nitrobenzene poisoning. This urine smelt strongly of oil of mirbane, contained a trace of sugar and an increase of ammonia and acetone.

Neubauer[17] says that in severe anilin poisoning anilin may be found unchanged in the urine, but this is rare. Usually it is changed by oxidation and conjugation to paraamidophenol—sulphuric ester. Nitrobenzene and the nitranilins are also excreted as paraamidophenol, while the reduction product of dinitrophenol, which appears in the urine after poisoning from this substance, is amido 2 nitro 4 phenol.

Bladder tumors.—In the early years of the present century the physicians attached to the great color works at Hoechst noticed that workmen in this plant were to an unusual degree victims of tumors of the bladder, sometimes cancerous, sometimes benign. In 1904 they began to ask information from 18 other German dye works concerning the occurrence of bladder tumors and of inflammation of the bladder, cystitis, and the responses to these inquiries brought to light 38 cases, 18 of which were fatal. This report attracted great attention and was followed by others from time to time until, in 1920, the number of known instances of bladder tumor in German dye works reached 177.

At a meeting of industrial physicians in Germany in 1913 Leuenberger spoke on this subject, pointed out the fact that it was undoubtedly an amido, not a nitro body, which must be held responsible for bladder tumor formation and urged the physicians attached to dye works to tabulate their cases and discover which were the dangerous departments and what was the compound eliminated in the urine that acted as an irritant to the bladder. The answers to these questions are now appearing in the Zentralblatt für Gewerbehygiene.

Schwerin, of the Hoechst factory, studied the histories of 99 of the 177 cases and found that they were distributed in the following departments:

	Cases.
Fuchsin and rubin	21
Benzidin and naphthionic acid	28
Naphthylamins	30
Anilin	8
Other bases, not specified	8
Palatine black	1
Blue	1
Patent blue	1

A later report by Curschmann discusses 28 recent cases—included among the 177—of which 15 were malignant, 12 benign, and one mixed. These cases were distributed as follows:

	Cases.
Fuchsin and rubin	3
Benzidin and naphthionic acid	3
Betanaphthylamin and naphthol	10
Anilin	5
Other bases	3
Blue	4

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[16] v. Jaksch. R. Klin. Diagnostik innerer Krankheiten. 6th ed. Berlin-Vienna. 1907.

[17] Neubauer. Analyse des Harns. 11th ed. Hupperts's Lehrbuch. Wiesbaden. 1913. Vol. 2, 1479.

The age at which the growth made its appearance was over 50 years for 14 of the 28, between 40 and 50 years for 8, and between 30 and 40 for 6. The 12 men who had only benign tumors had worked for a shorter time in the industry than had those with cancerous growths. Five had been employed in dye works for 10 to 15 years, 5 more for 15 to 30 years, and 2 for more than 30 years, but of the 15 with cancer, only 2 had worked less than 15 years. The histories of many of these cases show that a tumor which is at first only a papilloma may later undergo cancerous degeneration.

Curschmann says that although anilin may give rise to these tumors yet there is no apparent connection between ordinary anilin poisoning and bladder tumors.

Leuenberger, at the conference of industrial physicians in 1913, expressed the view that the amido compounds which seem to be responsible for tumor growth in the bladder undergo hydrolysis (introduction of HO into the ring) in the body and suggested that it might be possible to ascertain which of the amido bodies are eliminated in this particular form, as paraamidophenol, and then see whether they are actually the ones which are associated with the tumor cases. It is true, as Schmiedeberg found years ago, that anilin and several other aromatic amido compounds are changed in the body to paraamidophenol and excreted in the urine as paraamidophenol-sulphuric-ester. But this is not true of some compounds which are apparently very important sources of tumor cases. Paratoluidin is one; others are alpha and beta naphthylamin, both of which latter are excreted in the urine unchanged.

Kuchenbäcker, arguing that such a body as paraamidophenol, having a free amido group, should be capable of diazotizing in acid solution with nitrate and produce an azo color, tested the urines of men in a benzidin-naphthionic department and found that those especially of men who were exposed to dusts produced a reddish azo dye, varying in intensity according to the degree of dust exposure. He could also obtain an azo color from the urine of dogs fed with anilin, and with orthotoluidin, but not after feeding with paratoluidin nor with benzidin, nor tolidin, nor alpha nor beta naphthylamin.

It seems, therefore, that paraamidophenol is not the only compound responsible for the cystitis and the later papillomatous tumors which occur in these dye makers, and for the present the matter rests here. The work of determining just what does take place in the elimination of these various aromatic bodies and what resulting compound sets up the cystitis which precedes tumor formation is going forward in the German laboratories with the hope that it will be possible some day by means of urinary tests to discover when such a condition is threatened. Meantime they have at least ascertained which are the departments in which bladder difficulties are to be looked for and are in a much better position to guard against this form of occupational poisoning than hitherto.

In England the dye industry is not yet old enough to have produced more than a very small number of bladder tumors. The physician connected with the oldest of the English plants has known of two cases, although he believes that there may have been more which escaped detection. Since only exceptional cases in Germany have developed after less than 10 years' exposure, it is highly improbable that American dye works have as yet been responsible for any cases, and our great labor turnover will probably serve to protect the greater number of dye workers from it. However, skilled workmen and foremen and chemists are not shifting, and it will be well for American dye makers and industrial physicians to bear in mind the German experience and be on their guard against similar occurrences in their plants.

Industrial poisoning from these compounds, especially from the amido compounds, is rarely fatal. If death occurs it is preceded by coma, increasing paralysis of heart and respiration, convulsions, and sometimes edema of the lungs. These compounds do not usually produce any very characteristic changes in the organs with the exception of a few, such as, for instance, trinitrotoluene, which causes a very characteristic degeneration of the liver. The usual findings consist in slight degenerative changes in liver, heart, and kidneys and sometimes pneumonia or edema of the lungs, or hemorrhages into the lungs and stomach and intestines.

Mode of entrance.—The volatile compounds of this group may be inhaled, but even with the volatile compounds absorption through the skin is more important, and it is probably the only mode of poisoning for the solid compounds.

The more volatile a compound the more rapid the poisoning. Cyanosis is greater in poisoning by amido derivatives; the effect on the central nervous system is more pronounced in poisoning by nitro derivatives. In Hay's[b] experiment on himself, a few hours after a second application of 0.1 gram of dinitrobenzene in ointment his lips became a vivid blue color, his skin leaden, his pulse was 120, with high tension, and there was a sense of fullness and throbbing in his head. Curschmann[8] produced fatal poisoning from paranitranilin in cats by rubbing a few grams on the skin, and the same result was obtained with phenylene diamine. Skin absorption is favored by intimacy of contact, pressure, or rubbing, a hot atmosphere which flushes the surface blood vessels and causes sweating, by personal idiosyncracy (probably dependent on the character of the sweat), and finally by the ability of the compound to dissolve fatty acids and pass rapidly through the skin.

Although there is no doubt that skin absorption is very much the most important factor in industrial poisoning, symptoms may also be produced by the inhalation of fumes and dust, as was shown, for instance in the British studies in trinitrotoluene poisoning during the war. Most of the TNT poisoning in the ammunition works followed direct contact with the substance, but there was also evidence that fumes and dust were not negligible. The same thing was found to be true in American TNT manufacture and loading, where the greater part of the trouble came from contact, but fumes, especially when mixed with steam, gave rise to unmistakable absorption of the poison.[18] Several instances have been reported of uncomplicated fume poisoning from anilin and other compounds in

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[b] White and Hay. Lancet. 1901. II, 582.

[8] Curschmann, F. Deutsche Vierteljahresschrift für öffentliche Gesundheitspflege. 1911. XLIII, 225.

[18] Practical points in the prevention of TNT poisoning. MONTHLY LABOR REVIEW, United States Bureau of Labor Statistics. January, 1919, p. 248.

dye works. For instance, a poisoning occurred on the second story of a reduction building from anilin fumes which passed through the cracks in the wooden floor from the story below. The apparatus was very poor in this reduction department, and it was often necessary to open up the reducers and dig out the caked iron filings, so that the fumes of anilin were often quite heavy. In another case, a man was working a machine like a cream separator for separating anilin from water. He did not come in contact with the anilin at all, but he was taken ill and was under treatment for eight days. The installation of a suction fan to draw away the fumes made it possible for him to go back to his work with no further trouble.

From another plant comes the history of a man who was set to make repairs above a reducer where monochloranilin was being made from nitrochlorbenzene. Reduction was over and fumes were coming off from the hot open reducer. The man was working at the ceiling just over it, and after 45 minutes he had to be carried down, overcome by the fumes. He was dangerously ill for several days, and could not return to work for some weeks. Cases of fume poisoning also occur among men engaged in centrifuging (called "wringing" or "spinning") the mixed toluidins to separate para crystals from the oily ortho. Even when the centrifuges are out of doors very heavy fumes are given off during the process and apparently severe poisoning may occur without any contact at all.

The above is a description of typical poisoning from most of the nitro and amido derivatives of benzene. It is necessary, however, to take up the more important compounds in greater detail, because they differ from one another more or less with regard to the prominence of one or the other symptom and they differ in degree of toxicity, and in at least one instance (dinitrophenol 1-2-4) there is a decided divergence from the usual type.

THE NITRO COMPOUNDS.

Mononitrobenzene ($C_6H_5NO_2$) and *metadinitrobenzene* ($C_6H_4(NO_2)_2$) are very important in the dye industry. Mononitrobenzene is a yellow oily fluid, smelling like oil of bitter almonds, insoluble in water but readily soluble in fats. It therefore passes easily through the skin and may cause poisoning in this way or through the inhalation of fumes. In animals death is brought about more quickly by the liquid mononitrobenzene than by the solid dinitro, and this is also probably true in human beings. Occasionally mononitrobenzene is spilled or splashed on the skin and then the symptoms of poisoning come on very quickly. The blood may turn chocolate color and the urine dark within a few hours after a slight accident of this sort. If the clothing is soaked with nitrobenzene the resulting collapse may be very sudden and severe.

An account of a fatal case of nitrobenzene intoxication may be found in the records of the Massachusetts General Hospital for July, 1916. The patient, an elderly man, was at work in a soap factory, carrying a 5-gallon can of oil of mirbane. He seems to have spilled some of the fluid on his trousers, and was seen to grow rather shaky and then suddenly collapsed, spilling more of the fluid on himself. It is evident from the record that his mirbane-soaked clothing was not removed but that he was sent to the hosptal as he was, so that it is no wonder that by the time he reached there his condition was serious. He was unconscious, breathing slowly and irregularly, but the heart was regular with good action. His pupils were small, irregular, and did not react. The skin was of a dark gray-blue color. Some blood was withdrawn from the arm vein and it was chocolate colored. Respiration failed, becoming more irregular and shallow, but the heart action was good till just before death, which occurred one hour after he reached the hospital.

Dinitrobenzene (meta) is a solid, which, however, volatilizes slightly at room temperature. By universal agreement it is pronounced the most troublesome compound that is used in anilin-dye manufacture. This does not mean that it is more poisonous than mononitrobenzene, but that the requirements of manufacture are such that men are necessarily brought in contact with it far more, and therefore industrial poisoning is much harder to control. The symptoms of acute poisoning are the same as those of nitrobenzene poisoning, but in addition to acute intoxication there is a more chronic form, which has been described by the British and the Germans, both of whom have had ample opportunity to observe it among the workers in factories making roburite, an explosive much used before the war, consisting of dinitrobenzene and ammonium nitrate. Prosser White[19] describes a severe form of anemia in dinitrobenzene workers, with a dusky yellow skin, jaundiced sclera, an appearance of partial asphyxia, wasted muscles, dulled sensibility, partial paralysis of the hand, defects of vision. Dr. Roxburgh, of Manchester, England, told of a symptom he had observed as an aftereffect of dinitrobenzene poisoning in two men, which consisted in ataxic gait, the men staggering as if from drunkenness. This came on intermittently during more than a week's time.

Röhl[20] saw 60 cases of dinitrobenzene poisoning in a roburite factory at Witten. The men were emaciated and weak, the skin was dirty yellow, the pulse weak, the spleen enlarged, there was dizziness, narrowing of the field of vision, and disturbances of sensation, especially a feeling of cold and weight in the legs. In the worst cases the blood was chocolate colored.

In American dye works DNB, as it is called, is much dreaded. Often it is the only substance that causes real alarm. There is much more exhaustion, more weakening of the heart, than in poisoning from anilin, and the effects of an acute attack last much longer, dragging on sometimes for days or weeks. The anemia may be extreme and persistent. Acute poisoning from a single large dose is exceptional and is usually the result of an accident. In one plant 16 men were poisoned, several of them being unconscious for 6 to 8 hours, and one had convulsions at intervals for 12 hours. They were tearing out bricks and rafters in an old room which had been used for the production of DNB.

It is not only in the production of DNB but in its use as an intermediate, especially for reduction to metaphenylendiamine and for reduction to metanitranilin, that the danger arises. Formerly DNB

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[19] Prosser White. In Oliver's Dangerous Trades. London, 1902, p. 475.

[20] Röhl. Ueber akute und chronische Intoxikationen durch Nitrokörper der Benzolreihe. Inaugurations Dissertation Rostock, 1890.

used to be run out into open pans, where it caked, and men were sent to chop up the cake and shovel the fragments into trucks, in the course of which work a great deal of poisoning occurred. One man was interviewed in a hospital, where at the end of a week he was still somewhat cyanotic. He had worked for nine days in an open shed breaking up and shoveling solid DNB. On the ninth day he had a severe one-sided headache and was so dizzy that he was obliged to go home. The next day he came back to work, but after a little while he became very ill and deeply cyanosed. He was sent home, but the cyanosis persisted, and the company sent him to the hospital for a week. Another man from the same department had to be sent to the hospital after only one day's work. Later on this method of handling DNB was generally abandoned because of the effect on the men, and the molten DNB is now usually run out to meet a stream of cold water, which granulates it. However, even the shoveling and dumping of the granulated material may expose a man to sufficient fumes to poison him. Before the introduction of the pelleting method it was found in one plant that 50 per cent of all the sickness was among the DNB men, although they numbered only 24 in a force of 1,500. A history of 27 cases of acute poisoning in men breaking, screening, and washing DNB shows the duration of incapacity was from 1 to 12 days.

Nitrotoluenes.—Ortho and paramononitrotoluene ($C_6H_4CH_3NO_2$) are used to produce by reduction the important intermediates ortho and paratoluidin. During the war dinitrotoluene ($C_6H_3CH_3(NO_2)_2$) was produced as a stage in the manufacture of TNT. In the dye industry it is used for the production of toluylendiamine. According to Dambleff[21] and Jaffé[22] the ortho is the more poisonous of the mononitrotoluenes, at least for animals, but neither ortho nor para is as toxic as mononitrobenzene. They act more slowly and apparently only upon susceptible subjects, for many men can handle them with seeming impunity. They are absorbed through the unbroken skin and in susceptible persons they produce symptoms resembling those of nitrobenzene poisoning. Zieger[23] says that the pathology and symptoms of mono and dinitrotoluene are the same, enlargement and tenderness of the liver, cyanosis, gastric disturbance, painful, scanty urination, destruction of red blood cells, methemoglobin, and the symptoms pointing to oxygen starvation. There is a record of a typical case, with cyanosis, shortness of breath, and headache, in a man who was sent into a tank which had contained mononitrotoluene, but which was supposed to be quite clean.

The French committee on munition poisons found DNT toxic to animals, the deadly dose being 0.5 gram per kilogram of weight. A marked effect on kidneys and liver was noted. DNT seems to differ in its action from TNT in several ways. Dambleff quotes Zieger as emphasizing the eye symptoms in DNT workers, a venous congestion of the retina and disk. Cases of multiple neuritis have been described in DNT workers differing from anything observed as a result of the

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[21] Dambleff. Beiträge zur Kenntniss der giftigen Wirkung nitrierter Benzole, Toluole, etc. Inaugurations Dissertation Würzburg, 1908.

[22] Jaffé. Quoted by Kobert. Lehrbuch der Intoxikationen. Stuttgart, 1911, p. 804.

[23] Zieger. Inaugurations Dissertation Würzburg, 1913.

action of TNT. For instance, Hamilton and Nixon[24] give the following history of an interesting case: The man was a foreman, 39 years old, whose health had always been good, with no history of family idiosyncrasy or of alcoholism or venereal disease. He had worked for two years in contact with DNT. At the end of the first year he had numbness and prickling in the feet which, after five months, spread to the knees. There was no pain, but a sensation like the prickling of an electrical current. He was changed to outside work and improved, but when he went back to the old work the numbness increased in feet and legs. Then his sight began to fail, and examination showed 20/40ths in the right eye, and 20/70ths in the left. There was slight cyanosis, anemia, and numbness in the tips of the fingers. Four months later his sight failed so that he was obliged to quit work. Some time after that, the authors found the sight to be 6/200ths in each eye. The man could find his way about, but could not recognize faces. His physical condition was practically normal except for the loss of 8 pounds and he complained of loss of strength. Examination of the fundus showed well-developed atrophy, with pale disk, some swelling of the veins, and contraction of the arteries. Vibration sense and joint sensibility were lost in the toes; touch was impaired but not pain; there was impairment of touch sense in the fingers. Coordination was impaired in the legs; not in the hands. He complained of a pulling up or jerking of the muscles of the legs like an electric shock. The only reflex affected was the patella, which was diminished. He was anemic, the red cells numbering 4,900,000, hemoglobin 80 per cent, whites 8,000, with a normal differential count. He improved under rest with sweating, and 10 months later had 20/40ths vision in his right eye, 20/60ths in his left. Another man in the same plant quit work at the end of six months because of numbness in his feet and swelling so that he could not put on his shoes. Two other men complained of numbness in the feet, with tingling, difficulty in walking, and headache.

Koelsch[25], in Germany, and the experts of the French committee on munition poisons hold that the poisoning experienced in connection with DNT manufacture is due not to the DNT itself but to tetranitromethane and perhaps to certain isomers of DNT and TNT. The pure substances they hold to be very slightly toxic. Certainly it is true that the worst place in a nitrating department for DNT is the centrifuge for the separation of DNT from other products of nitration, and the men engaged in such work believe that the oily liquid which separates off and is rejected is the source of the trouble.

The effects of trinitrotoluene were closely studied during the war. It is a slowly acting poison and affects about one-third of the people who are exposed to it. Injury to the bone marrow causes a great destruction of red blood cells and as a result a hematogenous jaundice develops. Among the British munition workers there were 360 known cases of toxic jaundice from TNT poisoning, with 96 deaths. Much more rarely an aplastic anemia of extreme type developed without the typical degeneration of the liver. Both forms were found also in American munition works. Trinitrotoluene is not

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[24] Hamilton, Arthur S., and Nixon, C. E. Journal of American Medical Association, 1918, LXX, 2004.

[25] Koelsch. Münchener medizinische Wochenschrift. July 24, 1917.

used in dye manufacture and it is important in this connection only because its method of action has been so thoroughly studied that the literature of TNT poisoning may serve as a guide to us in the understanding of similar compounds that are used in dye manufacture.

Nitronaphthalenes ($C_{10}H_7NO_2$, $C_{10}H_6(NO_2)_2$, etc.).—The nitronaphthalenes have been found by German observers, Silex[26] and others, to have an effect upon the eye. It is very gradual and not painful, consisting in very small transparent vesicles on the cornea which cloud it and diminish vision. Industrially these bodies are practically harmless because they have a low volatility and slight solubility. In animals, Röhl[20] found that he could produce methemoglobin with nitronaphthalenes.

Anisol ($C_6H_5CH_3O$).—Anisol is phenol with one methyl group displacing the H of the hydroxyl group. Orthonitranisol is a dark brown liquid of strong penetrating odor. Dambleff[21] found that he could produce death in a rabbit, with hemorrhage into the lungs, by rubbing into the skin a quantity representing 0.5 gram per kilogram. Trinitranisol was apparently used by the Germans during the war as an explosive; at least it is mentioned among the compounds studied by Koelsch in his inquiry into munition poisons. He found that it seemed to cause no general symptoms but an affection of the skin to which practically all workmen were susceptible. An eruption came on very quickly after only a few hours' exposure, spread all over the body, with very painful swelling of the eyes, swelling of the lymph glands, edema of the skin, superficial abscesses and secondary symptoms from the acute inflammation.

The French committee on munition poisons found dinitranisol to be one of the two worst toxic compounds among those that were tested on animals.

Dinitrophenol ($C_6H_3HO(NO_2)_2$).—Before leaving the nitro compounds it is important to mention one which is used in dye manufacture to a limited extent, and is not in itself important, but its physiological action should be studied in detail because it differs so radically from the action of all the other known nitro derivatives of the benzene ring which have thus far been studied. Before the war this compound was not known to differ in any way from the others, but during the war it was manufactured on a large scale in France and entered into the composition of the mixture used by them for loading high explosive shells. The enormous human experiment carried on in the French munition plants showed this compound to be possessed of striking peculiarities, and it is important to call attention to these because obviously it is possible that other nitro bodies may, as they come into more extended use, prove to have similar characteristics.

The compound in question is dinitrophenol, but only one isomer, the one having the HO group, which changes benzene to phenol, occupying position 1 in the ring, while the two nitro groups occupy

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[20] Röhl. Ueber akute und chronische Intoxikationen durch Nitrokörper der Benzolreihe. Inaugurations Dissertation Rostock. 1890.

[21] Dambleff. Beiträge zur Kenntniss der giftigen Wirkung nitrierter Benzole, Toluole, etc. Inaugurations Dissertation Würzburg, 1908.

[26] Silex. Berliner klinische Wochenschrift, 1900, p. 1191.

positions 2 and 4.[27] It is therefore known as dinitrophenol 1–2–4. The method of manufacture used by the French and in two American plants which were manufacturing for the French starts with monochlorbenzene, which is nitrated to dinitrochlorbenzene. The hydroxide of calcium or sodium displaces the chlorine and then is removed as a soluble chloride by hydrochloric acid, leaving dinitrophenol. This was used together with trinitrophenol, picric acid, usually in the proportion of 40 DNP to 60 TNP. The French did not expect any serious trouble from occupational poisoning in this work because they had long been familiar with picric acid and assumed that dinitrophenol would resemble it very closely. So much illness, however, developed in connection with the handling of dinitrophenol and exposure to fumes and dust that the Government ordered a thorough inquiry into the action of this compound, and the result of the inquiry, together with the clinical reports of actual cases of poisoning, have been abstracted for American readers by Roger G. Perkins,[28] of Western Reserve University, consultant in hygiene of the United States Public Health Service.

Briefly stated, the essential facts are these: Three varieties of intoxication are described: First, mild, subacute, which serves as a warning to the physician to remove the workman from danger in time. The man complains of loss of appetite, nausea, sometimes vomiting, colic, and diarrhea. There is general weakness, with headache and dizziness and moderate sweating, especially at night. The tongue is white and furred, and there is decided loss of weight. The urine shows the presence of a reduction product, amido–2–nitro–4–phenol, which test is depended upon to indicate absorption of dinitrophenol. The second form is an acute intoxication which usually is preceded by the type just described. The onset is sudden, a complaint of extreme weariness in the limbs, painful constriction at the base of the chest, and a burning thirst. The face is pale, with slight cyanosis of the lips. The man sweats abundantly and shows an agitation and anxiety which is quite characteristic. Another very characteristic sign is short, difficult respiration, the difficulty being greater on inspiration, while in an asthmatic attack it is expiration which is hardest. There is only a slight rise of temperature, the pulse is regular and the lungs usually clear. There is a decided diminution in the quantity of urine, and the reaction for the detection of the reduction product, known as the Derrien reaction, increases in intensity. Removal from work, with a rest cure, is usually followed by an increase in the amount of urine passed and a rapid recovery, but no immunity follows the attack, and these men require special watching. The third form is fulminating intoxication. This is especially noted among alcoholics or persons with renal or hepatic troubles; death may take place in a few hours. The onset is sudden, with an attack of weakness or, less often, violent colics and diarrhea. A few hours later there is fever up to or over

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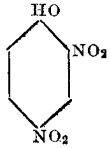

[28] Perkins, R. G. U. S. Public Health Reports, 1919. Vol. 344, p. 2335.

40° C. (104° Fahrenheit), abundant sweats which stain the skin yellow, even over the parts where there has been no exposure to the chemicals. There is intense thirst, the pupils are contracted, the patient is frightened and excited, and there may be partial or general convulsions. This is followed by unconsciousness, coma, and death in a few hours. It is the clinical picture of a fatal case of uremia. The symptoms in the severe cases which get well are much the same at first, but the second or third day shows marked improvement, with rapid recovery. Some very rapid cases are described, developing while the workman was on his way home. He is found somewhere along the road breathing with difficulty, covered with sweat, with a temperature of 41° C. or even 43° C. (105.8° or 109.4° Fahrenheit), and he dies before anything can be done. Sometimes there is a rise of several degrees of temperature after death. Urine obtained by catheter shows an intense Derrien.

Perhaps the most interesting feature of the post-mortem examination is that no characteristic lesions are found. There may be edema of the lungs, at times a fatty infiltration of the liver, but the microscopic lesions in the liver and kidney cells are inconstant. The blood and organs always contain DNP, or its derivatives, but this is also true of the organs of workmen who die from accidental causes while employed on DNP.

The French experimenters found that the action of dinitrophenol 1–2–4 is highly specific. None of the above symptoms are produced by ortho or meta mononitrophenol while paramononitrophenol, which produces similar results, does so only in heavy doses and transiently. The same thing is true of the 1–3–4 isomer of dinitrophenol. The other isomers have a different effect, causing the formation of methemoglobin. Dinitrophenol 1–2–4 is a specific poison, causing in all warm-blooded animals an exaggeration of the heat radiation activities with progressive elevation of the temperature which may rise to 45° C. (113° F.) at death. The basis of these phenomena is an increase of cellular combustion, oxidation, which has no relation to muscular work, nor to any action on any special organ, nor to a stimulation of the nervous system, for it occurs even in cold-blooded animals.

The compounds tested by the French committee included the nitrotoluenes, the nitroxylenes, nitranisols, nitrophenols, and chlorbenzenes, and they found that the most toxic compound of all was dinitrophenol 1–2–4, with the corresponding isomer of dinitranisol coming next and chlorbenzene last.

There were four deaths from dinitrophenol 1–2–4 in the two American factories which manufactured mélénite for the French. Three of these, who were handling the compound dry, developed symptoms very suddenly and died within 24 hours. From the meager report obtainable it seems that these cases were like those described by the French. The fourth case, which occurred in another factory, was not typical. The man died after an illness lasting several days, and autopsy showed that he was suffering from a toxic jaundice such as occurred in men poisoned by trinitrotoluene. It may be that in this instance some other isomer was present, not the 1–2–4. From a statement made by Leymann [29] in 1902, sudden and severe poisoning may

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[29] Leymann. Vierteljahrsschrift für gerichtliche Medizin, 1902. Supplement, p. 311.

develop in dye works from the dinitrophenol used in making sulphur black. Leymann describes three such cases. One man, who had been cleaning some washing tanks, collapsed suddenly with pain in his chest, vomiting, then fever, and convulsions, and died in two hours. The second case had a similar history. The third is not described. The dinitrophenol used in the making of sulphur dyes is, it is said, the 1–2–4 isomer, and certainly the history of Leymann's cases resembles very strongly those reported from the French munition works.

It is not likely, however, that poisoning from this compound should occur in dye works except as the result of some accident, leakage, or something necessitating the interruption of the process and repair work, for the dinitrophenol that is formed is not isolated, it is at once fused with sulphur to form sulphur black, and workmen would not come in contact with it in the ordinary procedure of the reaction.

ANILIN AND OTHER AMIDO COMPOUNDS.

The symptoms of the amido derivatives of the benzene ring are less serious than those caused by the nitro derivatives. While cyanosis is deeper with an amido compound, it is not accompanied with as severe prostration as follows poisoning with a nitro compound. A case of dinitrobenzene poisoning does not present as alarming a color as one of anilin poisoning, but the symptoms of involvement of the central nervous system, changes in pulse, respiration, and body temperature are much more grave. Convalescence is also slower. Typically a case of anilin poisoning does not incapacitate a man for more than a day or two, although it is a question whether he should be allowed to return to work unless a blood examination shows his hemoglobin not much lower than normal. But after dinitrobenzene poisoning a workman is likely to be ill for a fortnight or more.

A typical case of anilin poisoning, selected at random from a large number of similar records, has the following history: An Irish pipe fitter, a fairly heavy drinker, had worked for two weeks in an anilin reduction department, his work bringing him every now and then in direct contact with anilin-smeared apparatus. He would come back from work weak and tired, complaining of the fumes in the plant. His wife said that his face looked dusky and his eyes unnatural. He did not complain of pain, but of feeling sick all over. On the fifteenth night he lost consciousness and was taken to the hospital. The hospital record reads: Skin all over body steel gray color; face, scalp, and hands blue; unconscious; pupils normal; sclera jaundiced; respiration somewhat labored, 30 to 39; temperature 97.2°; pulse 130 to 140, shallow; lungs normal; heart normal in size and sounds; abdomen normal; hemoglobin 75 per cent; urine dark brown; albumen. He vomited twice on the first day, on the second his mind was clear, his pulse of good quality, but still rapid, 112; respirations 29; temperature 98.4°; no albumen in the urine. By the seventh day he could be discharged, but on the tenth day he was still weak and his sclera still jaundiced.

A severer poisoning results in intensification of all these symptoms. A workman engaged in experimental work which involved exposure to contact and fumes was seen July 24, 1915. He was in profound coma, his breathing was stertorous, and his pulse was irregular and of very poor quality. He was so cyanosed that the skin over his whole body was a deep plum color. That morning at 7 he had gone to work feeling perfectly well in every way and, according to the history obtained, he was exposed to fumes of anilin for an hour and forty minutes before he began to notice any sysmptoms of depression. First came throbbing in the head and increasing nausea, which he thought were due to the hot weather and the poorly ventilated room. He next noticed palpitation of the heart, and then a violent headache came on, increasing in intensity and accompanied by vertigo. As he said, "I felt as if I had been standing on my head for a long time and that every ounce of blood in my body had rushed to my brain." The dizziness increased and he lost consciousness completely about 45 minutes after the onset of the first symptoms. He was picked up by the other workmen and hurried to the hospital, where oxygen was administered as well as heart stimulants, but apparently with little effect. The cyanosis persisted, the heart action was very feeble and remainded so for over 16 hours, and he did not regain consciousness till the morning of July 25, a period of about 22 hours.

A catheterized specimen of urine obtained on admission showed nothing of note, but a second examination was made 18 hours later, when the urine was found to be smoky, specific gravity 1.022, there was a trace of albumin, no sugar, and the presence of hemoglobin was detected by the Heller test and by the Schönbein-Almen turpentine-guaiac test. This hemoglobinuria persisted for five days.

A blood examination made on entrance gave normal findings in all respects except for a slight eosinophilia, but four days later there were stippled red cells and some irregularity in the size and shape of the cells. The hemoglobin then was 75 per cent. (Sahli.)

The patient suffered from severe headache for five days and complained of weakness and exhaustion for at least two weeks longer, after which he improved slowly.

Friedländer[30] reported from the municipal insane hospital in Frankfort-on-the-Main a case of acute maniacal delirium in a man who had loosened a rubber pipe leading into an anilin receptacle and had received a splash in the face and mouth, swallowing about a mouthful. He became delirious about four hours later and was brought to the hospital in a strait jacket and deeply cyanosed. His mania lasted until the next day, when he was rational but excited. On the third day he was still irritable and restless, his heart still weak and rapid, but cyanosis had vanished, and by the fourth day he was mentally sound. A similar history comes from an American dye works. The man was a pipe fitter and was working at some pipe in the ceiling over the anilin reducers. Suddenly he became maniacal and ran amuck over the plant, and it was six hours before he came to himself. This case was reported as one of fume poisoning, but it seems possible that the steam from the reducers, which does carry some anilin with it, had gradually soaked the ceiling of the room and that in working there the man's hands had become saturated with it.

Another American case was also attributed to fumes of anilin. A foreman was seriously affected by heavy fumes and was sent to the

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[30] Friedländer. Neurologisches Centralblatt, 1900. XIX, 155 and 294.

plant hospital and given oxygen inhalations, whereupon he became delirious, and did not recover from the attack till the following morning.

It is recognized by American anilin workers that long exposure to this body is likely to make men irritable, hard to deal with, "grouchy," and that they are really not up to a full day's work. Their appetite is likely to be poor and they complain a good deal of headache. A chronic form of anilinism was described by an early German observer, Hirt, as characterized by disturbances of sensibility and of the motor nerves, inertia, headache, digestive disorders, skin eruptions, and roaring in the ears. A few years ago men exposed to anilin were not infrequently treated by their physicians for chronic valvular heart disease because the cyanosis, the altered pulse, and the complaint of weakness, breathlessness on exertion, palpitation of the heart, and indigestion seemed to point to such a diagnosis. A typical case of this sort was reported in 1914, when the importance of cleanliness in anilin work was not generally known. The man had worked with anilin for nine months. He complained especially of muscular weakness and fatigue. Palpitation of the heart came on when he had any unusual exertion or simply at the end of the day's work, and he had frequent headaches while at work, sometimes severe and accompanied by nausea and dizziness. He was never cyanosed and examination showed no physical abnormality except a rapid pulse, 94. While the number of red corpuscles in the blood was increased to 5,400,000, the hemoglobin was only 68 per cent. Curschmann lays great stress on this slowly developing form of poisoning, especially from the solid amïdo compounds, the result of repeated tiny doses, with a cumulative effect. He says that in typical cases the first sign of this form of chronic poisoning is a loss of hemoglobin, and therefore a blood examination is of great practical importance, because any workman who has lost from 15 per cent to 20 per cent hemoglobin is facing the risk of an acute attack, and should be suspended from work. A slight cyanosis is likely to appear at this stage, but no typical microscopic changes in the blood till a later stage. One of his cases had an almost typical neurasthenia, and the only thing that pointed to anilin poisoning was the loss of hemoglobin and a rise in blood pressure. Curschmann found that the average blood pressure by the Riva-Rocci in 100 workmen not exposed to anilin was between 110 and 120, but in men intoxicated with anilin it ran from 135 to 165. In cases of pronounced anemia with cyanosis there may be a rise of 40 in pressure, and with it there is always a slowed pulse, down to 48. In these cases there is a slight jaundice and the urine is brown.

Older men do not endure exposure to these compounds so well as younger men. Dr. Raymond Bugbee, of Providence, has given the histories of two men, one between 50 and 60, the other 66 years old, both of whom were severely poisoned with anilin after no great exposure, and in addition suffered from pain in the precordium, which persisted longer than any other symptom. According to Dr. Sutherland of the du Pont Co. negroes have no immunity as compared with whites, but suffer just as intensely from just the same symptoms. The fact that in anilin workers cuts are likely to inflame and suppurate and that sores are slow in healing and may go on to abscess formation has been observed by men in charge of anilin works. (See Adamson[31].)

Several instances are on record of an intercurrent attack of influenza affecting the course of a case of poisoning. For instance, a chemist who was working with metanitranilin went home ill with what proved to be an attack of influenza. This was on a Saturday. On the following Tuesday he suddenly developed an attack of jaundice with cyanosis. Relapses, without any further exposure to the poison are also related. A workman, 31 years old, had had an attack of anilin poisoning several months before in another factory. He was overcome in the second factory on April 2, went home, and apparently recovered, but on April 5, while he was still at home, he suddenly became violently ill, lost consciousness, and was taken in this condition to the hospital, where for two hours he had attacks of projectile vomiting. When he regained consciousness he suffered from headache and dizziness. He was in the hospital for six days.

In the German literature there are frequent references to disturbances of vision in the course of anilin poisoning, but there is no mention of this complication in American literature, so far as the writer knows. An article by Senn[32] deals with a serious affection of the eye among dyers in a Swiss factory. It consisted in a loosening of the epithelial covering of the cornea, with subsequent inflammation, cloudiness, discoloration, and therefore loss of vision. This was found among men who were working over vats of steaming anilin black, which is essentially a mixture of anilin and hydrochloric acid, and Senn attributed it to the effect of the oxidation products of anilin, the quinones, which cause a painful smarting of the eyes so that the man rubs them vigorously and detaches the surface cells, leaving the cornea exposed to further cauterization.

Toluidins ($C_2H_4CH_3NH_2$).—The toluidins, ortho and para, are considered by some to be more toxic than anilin itself. Posner and Liebreich[33] say that crude anilin is more poisonous than pure because of the presence of toluidins, and von Jaksch[34] makes the same statement. Treitenfeld[35] finds that they work very much as anilin does, having the same effect on the central nervous system, but causing rather less cyanosis, but in a case described by Starck[36] the man was not only comatose for 29 hours, but so deeply cyanosed as to be almost black. Rambousek[37] says that the toluidins act like anilin but have a stronger effect on the urinary system, causing strangury and hematuria more than does anilin, and Dr. Kessler, of the Anilin Products Co., says that his experience confirms this. Strangury (suppression of urine) is also noted by Friedländer[30] in toluidin poisoning.

Gibbs and Hare[38] tested the three isomers, para, ortho, and meta toluidin, on animals, and found that all destroy red blood cells, lower

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[30] Friedländer. Neurologisches Centralblatt, 1900. XIX, 155 and 294.

[31] Adamson, George. Journal of Industrial and Engineering Chemistry. 1916. VIII, 1058.

[32] Correspondenzblatt für Schweizer Aertze, 1897, p. 161.

[33] Posner and Liebreich. Quoted by Kobert, Lehrbuch der Intoxikationen. Stuttgart, 1911. P. 790.

[34] v. Jaksch, R. Die Vergiftungen. Vienna, 1912, p. 325.

[35] Treitenfeld. Quoted by Kobert, Lehrbuch der Intoxikationen. Stuttgart 1911, p. 790.

[36] Starck, M. Therapeutische Monatshefte. 1892. VI, 376.

[37] Rambousek, J. Industrial Poisoning. Translated by T. M. Legge. London, 1913.

[38] Gibbs and Hare. Quoted by Kobert, Lehrbuch der Intoxikationen. Stuttgart, 1911.

the temperature, and lame the spinal cord. The fatal dose per kilogram of weight is: For para, 0.1 gram; for meta, 0.125 gram; and for ortho, 0.208 gram. Meta is not used in dye manufacture, and most of the Americans who have had practical experience with para and ortho confirm the statement of Gibbs and Hare that para is more toxic than ortho, although it is crystalline while ortho is an oily liquid. One industrial physician, however, believes that ortho is distinctly more poisonous than para, because it is more easily absorbed. In several large plants the toluidins are said to give more trouble than the fumes of anilin, not necessarily because they are more poisonous but because there is not any process in anilin manufacture except repairing and cleaning which necessitates as much exposure to fumes and contact as does the centrifuging or "spinning" of the two toluidins. A man with a case of paratoluidin poisoning, chronic, with acute exacerbation, came recently to the occupational disease clinic of the Massachusetts General Hospital. He had been poisoned by fumes from the sulphur fusion of paratoluidin for primuline. He had the symptoms typical of chronic poisoning with unusually distressing breathlessness on exertion. A large plant reported seven cases of poisoning within a short time in the research department in men who were separating ortho from paratoluidin.

Even acute mania may develop as a result of toluidin poisoning. One of the cases reported by Friedländer[30] was in a man who had to repair a toluidin pump and splashed some on his face and chest. He did not change his clothes, and two hours later he was found on the ground outside apparently sleeping. When he was roused he became maniacal and had to be taken to the asylum. He was cyanosed, respiration rapid and labored, pulse very irregular, gait staggering. He was in delirium with convulsions for some 14 hours, and his mind was not entirely clear till the third day after. This case also displayed the characteristic urinary symptoms, very scanty, painful micturition, only 100 cc. of urine passed, with agonizing pain, on the first day. This persisted and the quantity did not reach 1,000 cc. till the ninth day. There was albumen in the urine, but no blood. The man was in the hospital three weeks.

Starck's[36] case is another very striking one. The man got his clothing soaked while dipping mixed toluidins from an open receptacle, and did not receive proper treatment till more than 24 hours later, so that the poison had full opportunity to work. He began to feel the effect at 5 in the morning—he was on the night shift—but finished his shift, working on till 7. At 11 he lost consciousness, at 6 that evening he lay in coma, motionless, eyes half open, mouth tightly closed, a little foam on his lips. He was still in his soaked clothing and was given cognac as a remedy. The next morning he was extremely cyanosed, his lips and mouth almost black, and there was some trismus, but he was conscious, complaining of severe headache. His pulse was small, his respiration slow and labored, his breath smelled strongly of anilin, so did the feces. Very severe strangury developed, the urine was bloody and passed only in drops. This increased until he became delirious with the pain, and it was

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[30] Friedländer. Neurologisches Centralblatt. 1900. XIX, 155 and 294.
[36] Starck, M. Therapeutische Monatshefte. 1892. VI, 376.

not till the fifth day that it lessened, but the urine remained bloody till the tenth day. He had distress in the abdomen, great thirst, but loathing for food. After all symptoms cleared up there remained pronounced weakness and he was not fit for work for five weeks. The case was undoubtedly greatly aggravated by neglect and malpractice.

Xylidin ($C_6H_3(CH_3)_2NH_2$).—Very little is written of the action of the xylidins, but they are undoubtedly less poisonous than anilin and toluidin. Acetyl-para-toluidin was found in use in one plant, and was said to be toxic.

Diamines ($C_6H_3CH_3(NH_2)_2$).—The diamines are notoriously toxic. *Toluylendiamine* has long been regarded as a typical blood poison. Stadelmann[39] experimented with toluylendiamine on dogs and found extensive destruction of red blood corpuscles and severe hematogenous jaundice. Dragendorff[40] found methemoglobin, destruction of liver cells, and a loss of alkalinity of the blood, which was brownish black.

The two *phenylendiamines* ($C_6H_4(NH_2)_2$), para and meta, are very important intermediates in dye manufacture. Para was used as a hair dye until its dangerous nature was discovered. It is still used for dyeing furs, under the name of ursol, and is the cause of very severe eczema with swelling of the eyelids and sometimes ulcers and cellulitis in fur dyers and even in furriers and women who wear furs dyed with this compound. When used as a hair dye and rubbed into the roots of the hair, paraphenylendiamine has been known to set up not only a dermatitis but severe symptoms of nervous disturbance, sleeplessness, dizziness, weakness of the legs, even epileptiform convulsions, loss of consciousness, and death. (Knowles[41].) According to Blaschko[42], however, the irritating effect of hair dyes and fur dyes containing paraphenylendiamine is not caused by this compound but by the presence of a mid product, quinone dichlordiamine, which has a much more irritating effect on the skin. Olson[43] also attributes the skin eruptions to quinone dichlordiamine and says that when oxidation is complete phenylendiamine is not irritating to the skin. This probably explains the contradictory statements about this compound, which are made by the men who handle it, for in one factory it will be said to give a great deal of trouble from skin eruptions and in another it is handled with no difficulty at all. Paraphenyldiamine is also used as an intermediate for sulphur dyes. Criegern[44] has described asthmatic attacks in paraphenylendiamine workers and the files of the New York Labor Department contain the report of a case of eczema, bronchitis, and asthma in a man who mixed ursol for dyeing furs.

Meta is used as an intermediate for Bismarck brown, Manchester brown, and many azo dyes. It causes skin eruptions and the steam from filter presses is said to cause systemic poisoning. It is usually considered more dangerous than para, but since it is made by the

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[39] Stadelmann. Quoted by Malden. Journal of Hygiene, 1907. VII, 672.

[40] Dragendorff. Quoted by Kobert. Lehrbuch der Intoxikationen. Stuttgart, 1911, p. 782.

[41] Knowles, F. C. Medical Record, 1916, p. 217.

[42] Blaschko. Deutsche medizinische Wochenschrift, 1913, II, 2406.

[43] Olson, G. M. Journal of American Medical Association, 1916, LXVI, 864.

[44] Criegern. Quoted by Kobert. Lehrbuch der Intoxikationen. Stuttgart, 1911, p. 653.

reduction of dinitrobenzene it is quite possible that traces of unreduced DNB may be responsible for effects attributed to phenylendiamine.

Diphenylamine ($(C_6H_5)_2NH$).—Diphenylamine, which may be regarded as ammonia (NH_3) with two hydrogen atoms replaced by phenyl (C_6H_5) groups, is said by Harnack[45] to cause in cold-blooded animals a slow paralysis, probably from chronic blood changes. Kobert[46] says that warm-blooded animals can tolerate large doses, but later on they die of marasmas, although he is uncertain how far this is due to the effect on the blood. Large quantities of diphenylamine were manufactured in the United States during the war and dissolved in ether alcohol with nitrocotton and then incorporated with the nitroglycerin powders. There was no evidence of any poisoning among the men manufacturing and packing diphenylamine; and if it had any effect on the workers in smokeless powder and mixed powder manufacture, it was masked by the other toxic substances—ether-alcohol, nitroglycerin, and amyl acetate. In dye manufacture diphenylamine is used for the production of metanil yellow and azo yellow.

Nitranilin ($C_6H_4NH_2NO_2$).—Of the three isomers of nitranilin, two are important, para and meta. Kobert[46] and Rambousek[37] both think that paranitranilin is more toxic than meta. Gibbs and Hare[38] say that both cause formation of methemoglobin and laming of the central nervous system and heart. They find para the most toxic, then ortho, last meta. Lewis, of the Sprague Memorial Institute, experimenting on animals, found meta more toxic than para.

Paranitranilin is distinctly important in dye manufacture not only as an intermediate for sulphur dyes and for azo dyes, but also because of its use, together with beta-naphthol, for the production on the fabric of a bright red dye, "para red." The most conspicuous action of para is on the skin, for it causes a very distressing, burning, itching eruption, and extraordinary precautions are necessary to protect the men employed in grinding and packing it. It is also capable of producing serious and even fatal systemic poisoning. Bachfeld[47] reported nine cases of poisoning, four of which were serious, with frequent scanty micturition, burning pain, but no blood or albumen in the urine. A fatal case was reported by Lewin from the Hochst factory. The man had been working for five hours in paranitranilin dust. At least one fatal case has occurred in the United States. A 27-year-old white man was employed for 12 days in the paranitranilin department of a color works, never having before been brought in contact with any of these compounds. The day of the accident he had been working about an hour in the drying room where paranitranilin is dried on trays. The nature of the accident was not reported, but he was said to have been poisoned by dust, perhaps from tipping over a tray of the powder. He was sent to the bathroom and took a bath, remaining there for about an hour. Then he went to the works doctor, and after he had been in the office about 20

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[45] Harnack. Quoted by Kobert. Lehrbuch der Intoxikationen. Stuttgart. 1911, p. 787.
[46] Kobert. Lehrbuch der Intoxikationen. Stuttgart, 1911.
[37] Rambousek, J. Industrial Poisoning. Translated by T. M. Legge. London, 1913.
[38] Gibbs and Hare. Quoted by Kobert. Lehrbuch der Intoxikationen. Stuttgart, 1911.
[47] Bachfeld. Vierteljahreschrift für gerichtliche Medizin, 1898. XV, 396.

minutes he lost consciousness. He was given stimulants and the lung motor was used, but he died two and a half hours after the accident.

Metanitranilin is made from dinitrobenzene, and reports of industrial poisoning from this department are sometimes dubious, because it is impossible to be sure which compound is the cause. Nevertheless, clear cases of metanitranilin poisoning do occur in work in which no DNB is present. For instance, a workman 22 years old was told to clean out a tub in which metanitranilin had been "processed." Soon after, he complained of acute frontal headache, then he vomited and lost consciousness. He was taken to the hospital and the record reads: Vomiting; fainting attacks; headache; rapid heart; very profound cyanosis; lips and mucous membranes almost black.

A similar case is reported by the New York Department of Labor from another American plant. Here, too, the man was sent to clean out a munjer in which metanitranilin had been made. He worked off and on from 9 in the evening to midnight. At midnight he went off for half an hour for supper and when he returned he told the foreman that he was faint and nauseated, but nevertheless, he was allowed to go back to work. At half past 4 in the morning he was found unconscious and was taken to the hospital, deeply cyanosed, respiration rapid and shallow, pulse rapid and of poor quality. Eight ounces of venous blood were removed, the color was dark and it coagulated slowly. He was given saline infusions, but he did not improve, and in the morning transfusion of blood (500 cc.) was made. Under this treatment and the administration of oxygen and stimulants he gradually improved, but did not regain consciousness till 6.30 that evening. His convalescence was very slow.

In one of the ordnance plants during the war metanitranilin was manufactured on a large scale for use together with DNB as an explosive in high-explosive shells. There was much ill health among the men working in this department, from contact and from the steam in the course of washing. The men in charge said that the poisoning was cumulative, that each attack lasted longer than the previous one. The symptoms were those characteristic of an amido compound, with very irritating effect on the skin.

Methyl and ethyl anilin ($C_6H_5N(CH_3)_2$, $C_6H_5N(C_2H_5)_2$).—The alkyl derivatives of anilin, dimethylanilin and diethylanilin, are distinctly less poisonous than anilin, and when poisoning does occur it is possible that the substance responsible is really unchanged anilin. One case that was reported came from direct contact. A stopcock came off and a mechanic, in trying to screw it on, received a spurt of dimethylanilin in his face. Another case was caused apparently by dimethylanilin fumes in the earlier days of American dye manufacture, in 1916.[48] A man of 22 years had been at work only two weeks on the night shift. At half past 10 he climbed a ladder to inspect a vat of dye which was said to be crude violet made from carbolic acid, dimethylanilin, and other substances. He lifted the lid, breathed the fumes, and lost consciousness, not recovering his senses till eight hours later. The cyanosis in this case was so deep that the doctor summoned to the plant thought he must have fallen into the violet dye. The next day he was taken to the hospital complaining of impaired vision, noise in the ears, and intense pain in the abdomen. He was in the hospital seven days.

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[48] From the records of the New York State Department of Labor.

A second man[48] treated in the same hospital had been told to bail dimethylanilin from one container to another, in the course of which he probably got some of the liquid on his hands. He worked from 8 in the morning to 3 in the afternoon, when he told one of the chemists that he felt twitching in his toes and feet, gradually spreading up his legs, and he was faint and nauseated. The chemist made him sit down in the open air for an hour, but he did not wash his hands nor change his clothes. He was then taken home, where he grew weaker and finally lost consciousness, in which condition he was taken to the hospital, where they found him deeply cyanosed and with a weak and rapid pulse. Two weeks later he was still weak and his mind somewhat confused.

Anilin hydrochloride.—This compound of anilin produces exactly the same symptoms as anilin and there may be a good deal of poisoning in the course of its manufacture unless, as is usual, the work is carried on in an open shed or in a room abundantly supplied with artificial ventilation. In one department the man in charge said that once during a month of hot weather all the men in his department were cyanosed. He said that the worst cases came from letting the hot hydrochloride splash on the skin, for it is quickly absorbed.

The fatal case of anilin poisoning reported by White and Sellers at the Brussels Congress of Industrial Hygiene in 1910 was in a man working with anilin hydrochloride, but it was caused by the anilin itself, which splashed over the man's hands and face and body. He died within 24 hours' time. However, it must be remembered that anilin hydrochloride is capable of producing typical anilin poisoning. Price-Jones and Boycott used it in their experiments instead of anilin and brought about all the blood changes characteristic of anilin.

Less important is *sulfanilic acid*, which is produced in the same way, only by the use of sulphuric instead of hydrochloric acid. The same risks attend its production, but as to the toxicity of the finished product there seems to be no information in the literature.

Benzaldehyde (C_6H_5CHO), or oil of bitter almonds, is an important intermediate which, so far as present evidence goes, has no toxic effect. Kobert[46] found it harmless to animals, and there is no report of its ever having caused any trouble in the color industry.

Paraamidophenol ($C_6H_4OHNH_2$).—Paraamidophenol, which results from the reduction of paranitranilin, is an important intermediate, especially for sulphur dyes. The real danger in connection with this process comes from the paranitranilin, which is distinctly the more poisonous of the two. Indeed, the excretion of both nitro and amido compounds from the body is preceded by their reduction to paraamidophenol, which is found in the urine as an alkaline salt of paraamidophenol-ether-sulphuric acid.

Paraamidophenol is one of the substances that causes troublesome dermatitis. *Nitrosodimethylanilin* ($C_6H_4NON(CH_3)_2$) also causes dermatitis. The *naphthylamines* ($C_{10}H_7NH_2$), *alpha* and *beta*, are capable of producing symptoms characteristic of the amido compounds. Alphanaphthylamine does not, so far as appears from the

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[48] From the records of the New York State Department of Labor.
[46] Kobert. Lehrbuch der Intoxikationen. Stuttgart, 1911.

literature and from the testimony of practical men, set up a serious form of poisoning, but one of the earliest cases recorded in American literature of cyanosis from an amido compound was Apfelbach's[49] second case, a man working in a dry color factory mixing various compounds, one of which was alphanaphthylamine. Betanaphthylamine is apparently distinctly more toxic than alpha and in one large American plant, where the men come in contact with it in the crude naphthionic department, it is said to cause not only cyanosis but frequent micturition, perhaps from over-acidity of the urine. This same plant has no trouble at all with the alpha compound. A case of hematuria from betanaphthylamine is noted in the German Factory Inspection Report for 1912.

There are a few more compounds containing the amido group which should be mentioned: *Anthranilic acid*, used for lake colors and for the pigment scarlet B, the dye used for postage stamps, is benzoic acid with one NH_2 group added to the ring, ortho-amidobenzoic acid ($C_6H_4COOHNH_2$). It is only slightly poisonous to man, although in frogs it causes paralysis. Kleist[46] took 2 grams within two hours' time and noted discomfort in the stomach, salivation, and sweating, but nothing else. The methyl ester of anthranilic acid is perfume of orange blossoms. None of the derivatives of anthranilic acid seem toxic to warm-blooded animals.

Amidoazotoluene.—Amidoazotoluene, called scarlet red, is known to physicians as a stimulant for tissue growth, and therefore useful in severe burns to hasten healing. As a rule its use for this purpose has not been followed by any untoward symptoms, but two cases are recorded of severe poisoning after the application of scarlet red ointment to deep burns. Cyanosis, dizziness, headache, pain, slight rise of temperature, rapid pulse, and albuminuria came on after the application of scarlet red. The symtoms disappeared when the dressing was removed and recurred when a second application was made. Amidoazotoluene is derived from orthotoluidin and is used for alizarin color manufacture.

Phenylhydroxylamine is said to be formed in making benzidin, and when this occurs a bad case of blistering may result from contact with it.

CHLOR COMPOUNDS.

Chlorbenzene, etc. (C_6H_5Cl).—The chlorine compounds of the benzene ring are considered less toxic than those which do not contain chlorine. Experiments made by Mayer and his colleagues for the French Government[28] showed that chlorbenzene is less toxic than benzene itself. Nevertheless it is possible to have severe poisoning from chlorbenzene, as can be seen in the cases reported by Mohr.[11] Ten instances of severe and typical poisoning are described by Mohr in men who, after exposure to chlorbenzene and DNB or in three instances to chlorbenzene alone, developed the symptoms after drinking a few glasses of beer.

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[11] Mohr. Deutsche medizinische Wochenschrift. 1902, XXVIII, 73.
[28] Perkins, R. G. United States Public Health Reports, 1919. Vol. 344, p. 2335.
[49] Apfelbach, G. L. Bulletin of Department of Factory Inspection of Illinois, 1913, p. 55.
[46] Kobert. Lehrbuch der Intoxikationen. Stuttgart, 1911.

Nitrochlorbenzene ($C_6H_4ClNO_2$).—The nitrochlorbenzenes are very much more poisonous than the chlorbenzenes. Systemic symptoms from paranitrochlorbenzene have been observed in connection with the reduction of this compound to paranitrochloranilin. Sturm[50] found orthonitrochlorbenzene very volatile and the fumes decidedly toxic to animals when present in less than 2–10 mg. per liter of air. It is more toxic than para. Para is an intermediate for sulphur blue, ortho for anisidin.

Dinitrochlorbenzene ($C_6H_3Cl(NO_2)_2$), used in the manufacture of sulphur blacks, has probably caused more dermatitis than any other compound used in color manufacture. In one American plant every man employed was more or less affected in this way, and for a while in summer the place had to close down for lack of labor. One of the men described the symptoms as beginning with itching behind the knees and at the bend of the elbow and along the inner surface of the thighs. Little red points appeared, which later coalesced to form a swollen mass, which itched and burned unbearably. Sometimes the face was involved and the eyes swollen shut. In another plant the chemists suffered so severely from dinitrochlorbenzene itch that they were forced to take prolonged alkaline baths.

Benzyl chloride ($C_6H_5CH_2Cl$) is toluene with 1 atom of chlorine taking the place of an atom of hydrogen in the CH_3 group, and *benzal chloride* is similar, only with 2 such atoms of chlorine ($C_6H_5CH(Cl)_2$). These are therefore side chain products and not so toxic as the so-called *chlorinated toluenes* in which the hydrogen of the ring is replaced by chlorine ($C_6H_4CH_3Cl$). Benzyl chloride, which is used for green dyes, is one of the many "tear gases," producing rapid and intense irritation of the eyes with blinding tears. Benzal chloride, which is used to produce the important intermediate benzaldehyde, is still more irritating to the eyes. In the only place in which the author saw benzyl chloride manufactured chlorine gas is passed into toluene and the resulting benzyl chloride, carrying doubtless chlorinated toluenes with it, is poured out and washed in an open shed; otherwise the fumes would be unbearable.

A case of mixed poisoning, probably from chlorinated toluenes, benzyl chloride, and toluene is the following: A chemist was employed in the production of benzyl chloride and was working in an atmosphere which at times was heavy with fumes. During the nine months he worked in the laboratory he lost some 25 or 30 pounds, his color changed to a cyanotic hue, he suffered from insomnia and so great a loss of strength that toward the end he found himself unable to perform the simplest sort of physical work. His eyes were affected, but transiently, and he traced it to the benzyl chloride, for the inflammation varied according to presence of benzyl chloride fumes in the air. He also seemed to have some injury to the liver, for he complained of pain and tenderness in the liver region. No physical examination was ever made in this case, and we have only the history to go by, but it seems pretty clear that this was a case of poisoning from chlortoluenes and benzyl chloride.

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[50] Sturm. Quoted by Curschmann. Deutsche Vierteljahrsschrift für öffentliche Gesundheitspflege, 1911. XLIII, 225.

HYDROXY COMPOUNDS.

Phenol, hydroxy benzene, has already been mentioned. *Naphthol* ($C_{10}H_7HO$), which bears the same relation to naphthalene as phenol does to benzene, resembles phenol in its action but is less soluble and less corrosive. Alphanaphthol is more strongly antiseptic than beta and probably more poisonous. The use of beta-naphthol in industry seems to give rise to little if any trouble, except for its effect on the skin. Even the fumes are said to be irritating to the skin, but the caustic soda used in the production of beta-naphthol is responsible for more trouble than the beta-naphthol itself. *Nitroso-beta-naphthol* formed in the production of H acid gives rise to dermatitis.

Dinitronaphthol ($C_{10}H_6O(NO_2)_2$) is the dye called Martius yellow and also Manchester yellow. It has the usual action of a nitro derivative of the benzene ring on the blood and on the nervous system, but it is one of the weaker members of this group.

PYRIDINS.

The *pyridins* used in the making of anthraquinone and in other processes for indanthrene dyes are said to make the men "dopy," to give them headache, dizziness, and dulling of the intelligence. They have also a peculiar effect on the skin similar to that which has been described in England as a result of the handling of tarry substances in briquette factories. The skin is raw and sensitive as if from sunburn, and the man suffers, especially after washing his face and hands and forearms and then going out into the open air.

PHOSGENE OR CARBONYL CHLORIDE (COCl).

Phosgene was first made by John Davy in 1812 by exposing a mixture of equal parts of chlorine and carbon monoxide to sunlight, and he gave it the name because of the part played by light in its formation. It was used for some years before the war in dye manufacture, especially in the production of Michler's ketone, and it was responsible for some industrial poisoning, but its use in gas warfare led to a thorough study of the toxic properties, and we know now very clearly what happens when phosgene is inhaled.[51]

It owes its poisonous action to the fact that it decomposes readily in the presence of water to hydrochloric acid and carbon dioxide. This decomposition takes place within the body when the gas reaches the finer bronchioles and the alveoli of the lungs and is acted on by the watery vapor there, and also probably when the gas is absorbed and reaches the tissues of various organs, undergoing slow decomposition. The effect of phosgene differs from the effect of hydrochloric acid because it is not immediately caustic, therefore while the latter attacks the upper respiratory passages and produces violent inflammation of the larynx, trachea, and bronchi, phosgene does not produce its effect till it has penetrated deeply into the lungs.

In men dying from phosgene gas the lungs are found deeply congested and filled with fluid. Around the fine bronchioles there are

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[51] Collected Studies on the Pathology of War Gas Poisoning. Medical Science Section of the Chemical Warfare Service. M. C. Winternitz, Major, M. C., U. S. A. Yale University Press, 1920.

islands of inflammation which form broncho-pneumonic areas and may spread if life is prolonged, become infected, and result in miliary abscesses. The edema and the fibrin which obstruct the circulation in the lungs lead to heart strain and dilatation, which may be the immediate cause of death, especially if the victim has had to exert himself after gassing.

The German factory inspection reports for the year 1913 mention three cases of poisoning from phosgene, but none of the men died. The treatment that was given consisted in the administration of fumes of alcohol mixed with oxygen. So far no fatal cases of poisoning from this substance have been reported from English dye works, although several have occurred in the United States. It is impossible to say how many there have been in the years since 1914, for a great deal of secrecy has been observed with regard to them, and positive statements concerning only three have been obtained. One of these, which should really be attributed to the gas warfare industry rather than to the dye industry, is worthy of special mention, because it shows the extent of the danger of an accident which allows phosgene gas to escape.

In a plant which was manufacturing phosgene for use in the war something went wrong and a quantity of gas escaped at a moment when about 180 men were in the vicinity and were supposed to have breathed more or less of the fumes. They were all put under medical treatment at once, and 20 developed symptoms, fairly serious in some cases, but not fatal. An Italian teamster, who is said to have been more than 1,000 yards away, was not thought to have been exposed and was allowed to go on with his work. He went home at the end of the day and complained of breathlessness. A doctor who was summoned said he was developing pneumonia, but by 5 in the morning he was dead, and the case was pronounced to be one of phosgene poisoning. One of the physicians in charge of the other men said that they suffered from intense headache which lasted about 72 hours, a strangling, exhausting cough without sputum, exhaustion, and a weak heart. One man, a Negro, developed edema of the lungs but recovered.

ALIPHATIC OR FATTY COMPOUNDS.

The compounds of this series that are used in dye manufacture are methyl and ethyl alcohol, acetates, chlorides, aldehydes, and ketones.

According to Fraenkel,[6] the members of the methane series are less toxic than those of the ethylene or acetylene series. The toxicity increases as the number of carbon atoms increase, but there is an important exception to this rule—methyl alcohol is less rapidly toxic than ethyl, but its effects are more serious because it is so much less rapidly oxidized. The ethyl series have a special affinity for the central nervous system, and most of the ethyl substitution products are more poisonous than the methyl. Chlorine increases the narcotic effect of all fatty compounds and also the depressant effect on heart and blood vessels. As a general rule the toxicity increases with the increase of Cl atoms, carbon tetrachloride being more toxic than

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[6] Fraenkel, Sigmund. Die Arzneimittel Synthese auf Grundlage der Beziehung zwischen chemischer Aufbau und Wirkung, Berlin, 1912.

chloroform. Introduction of the HO group lessens toxicity increasingly, changing alcohols to glycolls and glycerines. The displacement of an HO group by a methyl or ethyl group increases toxicity, especially the hypnotic effect. ·Esters, ethyl acetate, and amyl acetate have a different effect from alcohol, increasing respirations and benumbing the central nervous system without any exciting effect.

Methyl or wood alcohol (CH_2OH).—Industrially, ethyl alcohol can be disregarded. One hears tales of workmen having been made drunk in the early days of dye manufacture when they went in to clean out the stills, but the work of still cleaning has been much improved of late years; air is blown in or Draeger helmets provided. Methyl alcohol is more of a danger. One case of serious systemic poisoning, but without effect on the eyes, occurred as the result of a boil-over, the man inhaling the fumes. Two cases of mixed poisoning are on record in the files of the New York Department of Labor. The men were dipping wood alcohol and anilin from receptacles and mixing them.

It is usually assumed that the use of denatured alcohol is free from danger, but this is far from being true. According to the regulations of the United States Revenue Service, revenue-free denatured grain alcohol can be produced by the addition of methyl alcohol to grain alcohol in quantities from 2 to 20 per cent. There is also a small quantity, about one-half of 1 per cent of pyridin, a nauseous, ill-smelling coal tar distillate. The denatured alcohol generally used in industry contains 2 per cent or 4 per cent of wood alcohol, but in dye manufacture the 10 per cent formula is often used because the Government imposes less rigid restrictions on the use of this variety of denatured alcohol. In one color works it was this 10 per cent methyl alcohol mixture that was held responsible for ill health in the making of metanil yellow by coupling metanilic acid to diphenylamine in denatured alcohol containing 10 per cent of methyl alcohol. There are also cases of suspected methyl alcohol poisoning in connection with the making of methyl anilin and in producing anisidin from nitroanisol.

Experience in Germany and in Austria has shown that denatured alcohol which contains only 2 per cent methyl alcohol may cause symptoms of poisoning in susceptible workers. The variation in individual susceptibility to methyl alcohol is very striking, as was shown in the famous poisoning in the Berlin lodging house in 1911, when more than a hundred men were made sick by drinking adulterated brandy. It was shown then that the same amount of brandy which had produced death in one man and permanent blindness in another, produced only trifling symptoms in a third. Recently a case of complete blindness, resulting from the use of denatured alcohol with 4 per cent of methyl alcohol, was reported by J. M. Robinson,[52] of Duluth.

Of the aldehydes of this series, *formaldehyde* is the important one in dye manufacture. It is used in the production of synthetic indigo. Iwanoff[53] tested it on animals, and found that if he exposed them to heavy fumes, or to lighter fumes for eight or nine hours, they developed purulent bronchitis and edema of the lungs. Loeb[54] describes

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[52] Robinson. Journal of American Medical Association, 1918. LXX, 148.
[53] Iwanoff. Archiv für Hygiene, 1911. LXXIII, 307.
[54] Loeb. Arch. für experimentelle Pathologie und Pharmakologie, 1912. XLIX, 114.

also affections of the lungs, but in addition he finds that all the aldehydes of the fatty series cause destructive changes in the coats of the arteries, with loss of elasticity and the formation of aneurisms.

The ketones, of which *acetone* is the best known, seem to be harmless, at least no harmful effect on human beings has so far been reported. During the war a good deal of acetone was used in making smokeless powder, but no harm resulted. Kobert[46] believes that industrial poisoning from acetone is impossible, although there is a nonindustrial case on record which resulted from the application of a celluloid dressing which had been softened by acetone. This would tend to show that if the skin is in contact for a long time with acetone, poisoning may occur. Archangelsky[55] has tested acetone on animals and has found that it is possible to recover it from the brain and to a less extent from blood and liver. It seems to have a special affinity for the central nervous system. It is narcotic, but only slightly toxic. Large quantities can be given and can accumulate in the body without causing death. In large doses a narcosis is produced like that of alcoholic intoxication, from which recovery is rapid unless excessive quantities have been given, when it may persist for hours. This narcosis can also be produced by the breathing of acetone fumes.

Dimethyl sulphate ($(CH_3)_2SO_4$) is used in dye works in England, Germany, and the United States to methylate anilin. It is not essential for this reaction and its use is not by any means universal, for dimethylanilin can be produced by the use of methyl chloride or methyl alcohol, provided the reaction is carried on in an autoclave with heat and pressure. But it is cheaper to use dimethyl sulphate because heat with pressure is not required. The poisonous properties of this compound are well known and in many of the plants visited here and abroad it was considered too dangerous to use, but in others it was freely used, and the management insisted that the dangers had been greatly exaggerated. It is hard to believe this when we are told that it was one of the gases selected by the Germans for use in trench warfare.[56]

The cases of industrial poisoning which aroused the German dye manufacturers to a realization of the danger of dimethyl sulphate were described in 1902 by Weber,[57] of Schmiedeberg's laboratory in Strassburg. There were three, two of them fatal, and they had occurred in the Boehringer factory, near Mannheim, and in the Ludwig Casella factory, near Hanau. The first case was in a laborer 48 years old, who worked for four hours over a kettle from which heavy gray fumes of dimethyl sulphate were arising. At the end of this time he felt a severe burning pain in his throat and chest. He went to the doctor and 48 hours later was sent to the hospital in a dying condition with pneumonia of both lower lobes and distinct evidence of a local caustic action on the throat. The mucous membrane of the pharynx and uvula was destroyed and there were also burns covered with scabs on the eyelids. He died that same day. The autopsy showed destruction of the mucous membrane in

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[46] Kobert. Lehrbuch der Intoxikationen. Stuttgart, 1911.

[55] Archangelsky. Archiv für experimentelle Pathologie und Pharmakologie, 1901. XLVI, 347.

[56] Auer. Proceedings of Society for Experimental Biology and Medicine, 1918. XV, 104 and 106.

[57] Weber. Arch. für experimentelle Pathologie und Pharmakologie, 1902. XLVII, 113.

larynx, trachea, and bronchi, small hemorrhages into the serous covering of brain, lungs, and heart, cloudy swelling of liver and kidneys, double pneumonia.

The second case occurred at the same time and in the same room. Another laborer, 19 years old, was working at a distance from the dimethyl sulphate kettle. He was obliged to stop work because of burning in the chest, constant cough, and running in the eyes. For a week he suffered from hoarseness and painful cough, pain in swallowing, difficulty in breathing, burning in the chest. On the third day the cough began to produce a very abundant purulent bloody sputum and he also vomited mucus. He had a slow recovery, the hoarseness lasting three weeks, abundant sputum four weeks. His lungs were not normal till the tenth week, and the inflammation of the eyes persisted for three months. He lost 12 pounds in weight.

The third was a chemist who broke a receptacle containing dimethyl sulphate and spilled about 20 cc. over his clothes. This happened in the morning. In the evening he began to have severe pains in his body, especially the legs, pain in his eyes and burning in the chest. Early the next morning the physician who was summoned found that he had burns of the first to the third degree on the abdomen, genitals, and thighs. He had severe inflammation of the throat, bronchitis with an incessant painful cough, edematous swelling of the eyelids, and his eyes could not stand the light. There was no involvement of the lung tissue, of the heart, or the nervous system. The burns improved, but the secretion from the bronchi grew more profuse. Inflammation of the lungs set in, then jaundice and albuminuria, with a high fever, a rapid pulse, and death on the fourth day. There was no autopsy.

Dimethyl sulphate is an oily colorless fluid which boils at 188° C. (370.4° F.), but vaporizes at room temperature, giving off gray fumes at 50° C. (122° F.) which consist of dimethyl sulphate itself. Weber found that its toxicity depends on the whole molecule, not on any group which may be split off, such as methyl alcohol or sulphuric acid. The striking peculiarity of dimethyl sulphate is the intensely caustic effect on all tissues, not only by direct contact with the skin but by the action of the vapors on the lung tissue. In animals it produces also coma and convulsions. There is no possible antidote for it; prevention is the only cure.

Recently experiments have been carried on by Auer,[56] of the Rockefeller Institute, testing the effect on cats of exposure to the fumes of dimethyl sulphate, which he calls a war gas. Auer reviews a Russian article by Naiding, published in May, 1917, in which the anesthetic effect of certain war gases was mentioned. Naiding found that soldiers gassed with chlorine and phosgene had lost pain sensation in the skin. Auer brought about a very marked generalized loss of sensation to pain in cats by exposing them to dimethyl sulphate fumes, and this was so pronounced that severe operations could be performed without any sign of pain. If the animal survived the analgesia was sometimes still well marked six months afterward. The effect on the respiratory tract was like that which has been described in man, a diphtheritic inflammation of large and small bronchi and bronchials followed by edema of the lungs.

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[56] Auer. Proceedings of Society for Experimental Biology and Medicine, 1918. XV, 104 and 106.

In factories in which dimethyl sulphate was found in use, the only precautions taken are against a caustic action on the skin. The men are given goggles and rubber gloves, but in one plant they were not using even those and were handling it with less care than they gave to caustic soda. It was said in this plant that only one really bad case of blistering had occurred and that burns on the skin or inflammation of the eyes were the worst accidents that could be expected.

The surgeon in charge of the National Aniline and Chemical Co., Buffalo, Dr. Ferdinand D. Mohlau, has recently published[58] an account of two cases of dimethyl sulphate poisoning, the first reported in America. Two men, aged 53 and 55 years, were exposed on May 26, 1920, to contact with liquid dimethyl sulphate and to the fumes. They did not notice any effect at first beyond a slight irritation of the throat and eyes, but during the evening of that day the irritation of the eyes and throat became intensified, and inflammation of the bronchi developed. Cyanosis appeared. A physician was summoned to see one of the men, C., that night, but Dr. Mohlau did not see the case till the afternoon of the following day. He found him "delirious, with a severe congestion of the throat, symptoms of bronchitis, a severe inflammatory condition of the eyes, intense pain, photophobia, and a severe migraine." The second man, S., was then visited and found in a similar condition, but later on his symptoms became much aggravated, acute congestion of both lungs, edematous condition of throat and larynx, and considerable cyanosis. S. passed into a comatose state, and during recovery from his pneumonia he relapsed several times with an aggravation of all symptoms. C. had a quick crisis and recovered promptly, but at the time of writing, some six weeks later, both men were still suffering from photophobia and from the damage to throat and larynx. S. has also complete loss of color vision and his visual field is reduced to one-tenth. His optic nerve shows pale outer edges but no degenerative changes are discernible.

The urine examination showed in both cases an increase in the phosphates and sulphates, with a faint trace of albumin, an occasional hyaline cast, and no sugar.

In this same article is given the result of experiments on a rabbit, carried on by Charles A. Bentz and R. L. Cameron, both of Buffalo. The animal was exposed to the fumes of dimethyl sulphate under a bell jar and died promptly. The blood was dark and fluid and gave the characteristic bands of methemoglobin, the liver and kidneys were congested and had undergone intense degeneration, and the lungs were edematous.

The use of *methyl chloride* or chlormethyl is not unattended with danger, as the Germans have found. Kobert says it is one-fourth as poisonous as chloroform. It is very volatile, and in a report by Gerbis[59] histories of two cases are given of poisoning by fumes of methyl chloride in machinists who had to clean from time to time a gasometer through which methyl chloride passed. Both were elderly men, which may explain their susceptibility. They had attacks of somnolence, once preceded by delirium, and both had marked impairment of sight.

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[58] Journal of Industrial Hygiene, November, 1920, vol. 2, No. 7, p. 238.
[59] Gerbis. Münchener medizinische Wochenschrift, 1914. LXI, 879.

INORGANIC COMPOUNDS.

The heavy acids, *hydrochloric*, *sulphuric*, and *nitric*, are used in dye manufacture in large quantities, and the fumes from these acids or from their anhydrides form one of the most difficult problems of factory management. Hydrochloric acid and chlorine fumes are encountered especially in the making of anilin hydrochloride, of benzidin sulphate from benzidin hydrochloride and the making of nigrosin and indulin. Nitrous fumes are given off in all nitration processes and must always be removed through fume pipes. As a usual thing such pipes are not provided with exhaust suction and are efficient only when everything works well. If the wind is in the wrong direction, and still more if the nitrator is overheated, these fumes may escape. There are records of serious poisoning from nitrous fumes in making dinitrotoluene, mononitrobenzene, paranitranilin and nitroso-beta-naphthol. The fumes of sulphur dioxide may be given off in all sulphonation processes, and during the early stages especially these fumes may be very distressing.

All these compounds except sulphur trioxide have a very caustic irritating action on the respiratory tract. It is characteristic of them that the effects do not show themselves in their full intensity till some hours after, usually when the man has left work and gone home. There is always more or less strangling, with burning of the throat, at the time the gas is being breathed in, but usually these symptoms can be controlled by simple treatment. The man apparently recovers and then, some 6 to 12 hours later, he exhibits the symptoms of acute congestion of the lungs.

Sulphur dioxide may be formed, but rarely, at high temperatures in certain reactions. In moist air or in contact with the mucous membranes of the throat and nose it takes up water and changes to sulphurous acid, which is very caustic. Irritation from SO_2 begins at as low a point as 0.01 in 1,000 parts of air, and a new workman may be made ill by 0.03 part, but tolerance is quickly established, and men can work in an atmosphere much more highly contaminated than that. Sulphur trioxide is irrespirable. It is very disagreeable and choking, but not harmful, for it can not combine with water and is breathed out again unchanged.

The fumes of hydrochloric acid are very caustic to lips and tongue and throat. The danger limit is said to be between 0.1 and 0.2 part per 1,000 parts of air. Chlorine, which is almost two and a half times as heavy as air, is asphyxiating, paralyzing to the central nervous system, and irritating to the respiratory tract. There is an abundant literature on chlorine poisoning because of the use of this gas in chemical warfare. Fortunately, both hydrochloric acid and chlorine fumes are so immediately strangling in their effect that workmen exposed to them get away as quickly as possible and so escape the severer effects.

The most serious effects result from nitrous fumes. Both chlorine and sulphur dioxide are more immediately painful and choking than nitrogen oxide fumes, and therefore a man makes more effort to escape from them and seldom is so severely poisoned. Nitrous fumes can be breathed more freely, and in many industrial cases these poisonous gases reach the whole of the lung surface so that when inflammation develops there is no normal tissue left, and death is inevitable.

More than one industrial physician employed in dye works has said that he dreaded nitrous fume cases more than any other.

According to Haldane, exposure to 0.5 part per 1,000 parts of air for half an hour is enough to kill mice, death coming on after 24 hours.

In dye manufacture the really serious cases of nitrous fume poisoning result usually from an accidental leak of fuming nitric acid, or a job of cleaning or repairing in an acid tank. A typical case of the latter was related recently. The man went into a tank which had contained nitric acid, but which was supposed to be empty. There was, however, a small amount of residue at the bottom. He " choked up " several times, and when his work was finished he was coughing and had a burning pain in his chest. On his way home he stopped in to consult his doctor, but the latter found no signs in the chest except a slight bronchitis. Early in the morning the doctor was summoned to see him and found him dying of edema of the lungs.

The cases of industrial poisoning from nitrous fumes that have been reported are usually severe acute poisoning, and if the man recovers it is assumed that his recovery was complete. The physician does not follow up his later history. Therefore we have little information about the permanent damage to the lung tissue which may be produced by such an accident, even when the man has apparently recovered from the acute symptoms. There is one report from an American source of an accident involving 20 men whose subsequent history was followed up for nine months. (Hall and Cooper.[60]) Four of them died of pulmonary inflammation, but only two from an acute attack developing immediately, the other two were not affected till several weeks after the accident. There were relapses in one-third of the survivors, with symptoms like the original attack. Eight recovered their health practically entirely, after periods running from 90 to 210 days, but the others suffered loss of weight, "nervousness," stomach troubles, cough, pleuritic pain, difficulty in breathing, especially if the air was smoky. The loss of weight among these men was from 20 to 40 pounds.

Hydrogen sulphide or sulphuretted hydrogen.—In the making of sulphur dyes, when sulphur and sodium sulphide are fused with various amido compounds, hydrogen sulphide may be evolved in gaseous form. The danger of this is greatest in connection with the sulphur browns and khaki, less in connection with sulphur black, least with sulphur blue. It is poisonous in very small quantities, danger to life beginning at 0.75 per 1,000 parts and 1 to 1.5 per 1,000 is rapidly fatal. It is very much dreaded in the dye industry, not because many fatalities have resulted from it, nor because it gives rise to a great deal of ill health, but because of its startlingly rapid action. It seems to be the general opinion that sulphuretted hydrogen is either rapidly fatal or does little damage. Men who are " knocked out " by the gas either die without recovering consciousness or they come to after an hour or two and seem none the

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[60] Hall and Cooper. Journal of American Medical Association, 1905. XLV, 396.

worse for it, although a careful physician does not allow them to go back to work for a day or so. Many instances have been given of the rapid action of this gas. One man went into an empty pressure tank in a sulphur brown department too soon after it was emptied and was completely knocked out in five minutes. A second man who bent over the manhole to help him was also overcome, but neither died. The physician who told of this thought it dangerous to let a man go into a receptacle which had an opening no larger than a manhole. Several cases have been reported of pipe fitters or carpenters who were working on a platform in sulphur dye departments being overcome by the fumes so that they fell from the platform and were injured. One pipe fitter who was affected by these fumes was sick for four days, although he did not suffer from any accident. Rumors of fatal poisoning have been heard, but have not been substantiated.

Hydrogen arsenide or arseniuretted hydrogen.—There is a very general impression in the minds of the public that arsenic is used in the manufacture of anilin dyes and that some of them are poisonous because they contain arsenic. This belief, which is also held by many physicians, is founded on old and long discarded methods of manufacture. In an early article, written by Sonnenkalb in 1864, there is a description of the original methods used to produce fuchsin and the colors derived from it. As at present, anilin was made by the reduction of nitrobenzene with iron filings and acid; only acetic acid was used, instead of hydrochloric. Rosanilin, which is colorless, was then formed by oxidation and was the starting point for the colors, which were produced by the action of organic and inorganic acids. The oxidizing substances used were the oxide and nitrate of mercury, red lead, arsenious acid, and other less poisonous compounds. Fuchsin was made with arsenious acid (H_3AsO_4), and its poisonous qualities were due to its arsenic content. This method is, of course, no longer used.

The arsenical poisoning which occurs now in the manufacture of anilin dyes is caused by the accidental evolution of hydrogen arsenide (AsH_3) which may occur in connection with certain processes, especially acid reduction, and alkaline reduction when followed by acidification. These processes are described fully in a later section (see p. 53). It is a subtle and powerful poison, causing extensive destruction of the elements of the blood and, as a consequence of this, an acute degeneration of liver and kidneys. When the exposure to the fumes is great enough to set up acute poisoning, the man is seized with symptoms which may suggest, and, in fact, probably often do suggest, acute anilin poisoning. He is nauseated, complains of cramps in the stomach, vomits, complains of headache, dizziness, and faintness. The urine is dark, another resemblance to anilin poisoning. But the condition lasts longer than that caused by anilin, or even by dinitrobenzene. The case does not clear up, but grows worse, the urine becomes bloody, anemia is profound, jaundice appears, and signs of inflammation of the liver. The man may pass into a typhoid condition lasting for days, or he may die within a few days, deeply jaundiced, with constant vomiting of greenish fluid, with strangury and bloody urine. Autopsy then shows hemorrhagic inflammation of liver and kidneys.

This form of poisoning has been recognized in Germany for a good many years and carefully guarded against. It has also been studied recently by physicians of the British Factory Inspection Department and by physicians attached to the British works. According to these authorities, it is only prudent to take into consideration the possibility of arsenical poisoning in any case of supposed poisoning by a nitro or amido compound when the symptoms do not clear up, but profound anemia or jaundice appear. In such cases the urine should be tested for arsenic. A record of 16 such tests was shown by one of these physicians. In almost all, traces of arsenic were found in the urine, but only five had enough to be of significance. Four of these five men were working in the benzidin department, where most of the accidents from hydrogen arsenide fumes have taken place. The fifth was also engaged in a reduction process, producing amidodiphenylamine by the use of zinc dust, iron filings, and hydrochloric acid. No symptoms were complained of by two of the men, but their color was livid and their urine dark. The symptoms of the other three might easily have passed for anilin poisoning, jaundiced skin, dark colored urine, headache, and abdominal pains. Obviously it is very important to distinguish this low-grade, chronic, arsenical poisoning from poisoning by a nitro or amido compound. It is distinctly more serious, because arsenic is a cumulative poison in a sense in which no organic compound can be.

To illustrate this sort of accident in dye manufacture, three American cases which occurred in a small plant in New Jersey are selected. This factory was making naphthionic acid from alphanaphthylamine and sulphuric acid, and also benzidin base and sulphate by a reduction process involving contact between hydrochloric acid and zinc dust. The construction of the plant was crude, and fumes from the different processes were allowed to escape into the room. One night five men were at work in the benzidin department, and when the acid was added at the end of reduction there was a " boil over." The fumes affected all of the men so that they were obliged to quit work. Their subsequent history was obtained partly by personal interview with one of them and partly from the records of the hospital to which two were sent.

The first man, C, had been employed in the plant for 18 months, and had often suffered from the fumes in the benzidin department. On this night he went home feeling very ill, so that he could not even get into bed, but dropped down on the floor. He did not send for a doctor, thinking it no worse than former attacks until he saw that his urine was the color of blood, when he became alarmed, for this had never happened before. He was ill for about three months, suffering from pains in the kidney region, a band-like feeling around the lower part of his abdomen, intense pain in the back of his head and neck, vomiting, poor appetite, depression, and loss of strength. During this time his wife said that he looked like " a yellow corpse." When seen about 18 months later he still had pains in the kidneys, headache and buzzing in the head, and his strength had not returned.

The second man, D, was treated at home for about two weeks for supposed typhoid fever, and no details as to this part of his history can be obtained, but probably, judging from the diagnosis, he had symptoms of abdominal distress of an aggravated kind. When he was finally brought to the hospital the Widal test disposed of the typhoid-fever theory. He was then, on the fifteenth day after the accident, in a semiconscious condition; there were ulcers in mouth, throat, and tongue; he had diarrhea and vomiting, and his body was shaken with tremors of the muscles. Albumin was found in the urine, but no blood. There was a very marked anemia, the red blood corpuscles being reduced to 1,780,000. Both spleen and liver were enlarged. In spite of his partial delirium he showed great pain and difficulty on urination, and this symptom increased, together with retention of urine, diarrhea, and frequent vomiting, during the two days in the hospital. He died on the third day, but no autopsy was made.

E went to the hospital 48 hours after the accident. He was then jaundiced, complaining of great pain in the lower chest and over the bladder, vomiting greenish fluid, voiding blood-red urine. There was also pain and difficulty in urination. These symptoms persisted for two days, then slowly improved, and he was discharged on the sixth day, "cured" according to the hospital record, but according to C he has never recovered his health since then nor been able to do a full day's work. No blood count was made in this case, but hemoglobin was found in the urine.

As for the other two, one never reported back to the plant, and C knew nothing of his history. The fifth, a cousin of C, recovered completely.

There seems little doubt that these were cases of poisoning from the escape of hydrogen arsenide when acid and zinc dust, one or the other containing arsenic, came together in the process of making benzidin. That the diagnosis of anilin poisoning should have been made is natural, for anilin also is a blood poison, one that destroys the red corpuscles, thus causing the appearance of hemoglobin in the urine and later possibly jaundice. Anilin poisoning is also accompanied by more or less pain in the abdomen and by vomiting, but all these symptoms were more accentuated and persistent in the cases in question than they are in anilin poisoning. No case of the latter is on record in which the victim passed into a typhoid condition lasting for days and terminating in death. On the other hand, the histories of all these cases are very typical of arseniuretted hydrogen poisoning.

Caustics.—The caustics used in dye manufacture are *sodium hydrate*, or caustic soda, NaHO, which is used in so-called hydrolyzing or caustic fusion (see p. 51); *sodamid*, $NaNH_2$, used to change phenylglycine to indoxyl, in the course of which reaction fumes of ammonia may be given off; and *monochloracetic acid*, which is used in the manufacture of indigo.

It is not necessary to describe the effect of caustic soda upon the skin and mucous membranes of nose and throat and on the conjunctiva, for this effect is familiar to every one. Sodamid is not so powerful a caustic. In contact with a sweating skin it changes to NaHO, and therefore it acts more slowly than caustic soda. Monochloracetic acid causes severe blistering and extensive desquamation, the skin coming off in sheets, but if the burn is treated promptly and not allowed to become infected, there is almost no pain connected with it.

Fumes of *ammonia* have given rise to two cases of serious inflammation of the lungs, with edema, in the dye industry, in connection with the manufacture of indigo and of aurantia.

RECORDS OF SICKNESS IN GERMAN DYE MANUFACTURE.

A careful search through German factory inspection reports for the seven years just preceding the war shows the following substances to be responsible for occupational poisoning in the color industry:

Anilin.
Nitrobenzene.
Paranitranilin.
Toluidins, ortho, and para.
Paranitrotoluene.
Alpha and beta naphthylamine.
Dinitrobenzene.
Hydroquinone and other quinones.
Chloranthracene.
Dimethylsulphate.
Hydrogen sulphide.
Chlorine gas.
Phosgene.
Nitrous fumes.
Pyrogallic acid.
Potassium bichromate.
Monochloriodide.
Phosphorus pentachloride, and oxychloride.
Methyl chloride or chloromethyl.

Several detailed studies have been made of sickness in certain German plants. For instance, such a report is given of a factory employing 251 men, in which there were during a year's time 33 cases of industrial poisoning, with 500 days of sickness. For the workmen not employed in the anilin department the average was 0.97 attack of illness per man, each attack averaging 14.6 days. For the anilin department the average was 1.74 attacks of illness, with 23.48 days. Ten per cent of the cases in the nonanilin departments were skin diseases; 41.8 per cent of those in the anilin department were skin diseases. Digestive troubles made up 17.4 per cent of the nonanilin workers; 45.4 per cent of the anilin workers. Some unusual cases are described. One was a boiler tender who was using water from an anilin still. Some of it boiled over and soaked the floor and the coal, and he had a severe attack of anilin poisoning. A case of bloody urine occurred in a man making naphthol, and another in a man making "fuchsin melt." There was one death from benzene poisoning. A workman went into a room which he had been warned not to enter because benzene had run out on the floor.

Grandhomme,[61] who was for many years physician to one of the great German dye works, analyzed 1,163 cases of sickness in the force in five years, 1874 to 1879. In the manufacture of anilin colors there was an average of 60 per cent of sickness, in making alizarin colors 46 per cent, and in the mechanical department 40 per cent. But the average length of disability was greater among the men in the alizarin department than in the anilin because there was a greater proportion of skin affections, and these are notoriously slow to heal. There is far less sickness shown in the more recent reports, as indicated in the next paragraph.

In the report for the year 1913 a factory with 9,376 men had 12 cases of anilinism, with 98 days of sickness. The two serious cases in this factory were caused, one by the spilling of anilin, the other by repair work in an imperfectly cleaned apparatus. The first man got his clothes soaked with anilin, was made to strip at once and take a thorough bath, but in spite of that half an hour later he became cyanosed. The second man was a lead burner working in a receptacle which had contained nitrobenzene and had not been thoroughly cleaned. He was ill with nitrobenzene poisoning for eight days.

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[61] Grandhomme. Vierteljahrsschrift für gerichtliche Medizin, 1880. XXXII, 120 and 280.

RECORDS OF SICKNESS IN AMERICAN DYE WORKS.

Cases of poisoning have occurred in the United States from the following substances used in the making of dyes and dye intermediates:

Benzene.
Toluene.
Mononitrobenzene.
Dinitrobenzene.
Paranitrochlorbenzene.
Orthonitrochlorbenzene.
Dinitrochlorbenzene.
Anilin.
Paranitranilin.
Metanitranilin.
Dimethylanilin.
Diethylanilin.
Anilin hydrochloride.
Paranitrochloranilin.
Nitroso dimethylanilin.
Paranitrotoluene.
Dinitrotoluene.
Orthotoluidin.
Paratoluidin.
Paranitrotoluidin.
Orthonitrotoluidin.
Acetylparatoluidin.
Benzylchloride.
Chlorinated toluene.
Paranitrophenol.
Paraamidophenol.
Dinitrophenol 1–2–4.
Paraphenylendiamine.
Metaphenylendiamine.
Nitrosobetanaphthol.
Alphanaphthylamine.
Betanaphthylamine.
Benzanthrene.
Anisols.
Quinones.
Phenylcarbylamine.
Phenylhydroxylamine.
Solvent naphtha.
Pyridin.
Nitric acid and nitrous oxides.
Sulphuric acid and sulphur dioxide.
Hydrochloric acid and chlorine.
Hydrogen sulphide.
Hydrogen arsenide.
Monochloracetic acid.
Sodamid.
Sodium hydroxide.
Ammonia.
Methyl alcohol.
Phosgene.

Cyanosis from the handling of nigrosin has been reported, but probably should be attributed to anilin. Cases of dermatitis are said to occur among men making azo colors, and the condition is called " azo itch." It is doubtful whether the cause is to be found in the finished colors. It would seem more probable that it should be attributed to one of the nitroso intermediates.

In treating dimethylanilin with sodium nitrite the nitroso compounds of the corresponding bases are formed and these are known to be very irritating. It is possible that in making azo dyes some nitroso might be formed, as, for instance, when the amine to be treated with the nitrite is impure and contains phenols or secondary or tertiary amines.

In an industry so new as the anilin color industry, it is very important to know not only which are the possible dangers which threaten the workmen, but which are really serious and which are only exceptionally serious. We have records from three large American factories which throw some light on this question. In one of these the different processes have been classified according to their danger, so that the examining physician may decide, on the basis of the physical condition of the applicant for work, in which department he can be safely placed. There are three classes of processes. Class 1 includes operations or processes in which nitro or amido compounds are used and which experience has shown involve risk of poisoning to the workman. Under this classification come the following departments: Naphthionic crudes, dinitrobenzene, the diamines, the so-called " anilin dyes "—rosanilin, magenta, fuchsin, anilin blue, alkali blue—phenylglycin drying, anthraquinone, pyridin, indanthrene yellow.

Class 2 includes operations or processes involving the handling of nitro or amido compounds, but which are attended with less risk, either because the poisoning set up is less severe, or because the equipment is so arranged that there is no contact with the poisonous substances. In this class come paranitranilin purification, betanaphthylamine, anilin reduction, benzidin manufacture, auramine, and benzanthrene.

Class 3 includes operations which do not involve handling nitro or amido compounds, or in which such compounds are present but no ill effects have thus far resulted from such work. This class is large and includes the ortho and paratoluidin department, sulphonating processes of all kinds, all low-pressure autoclave work, naphthionic purification, picramic acid, benzoic acid, chloracetic acid, salicylic acid, chlorine, hydrochloric acid, chlorbenzene, benzaldehyde, sodium sulphide, nitranisol, eosin, victory green, malachite green and sulphur black and indigo.

The record of a plant in which about 850 process men are employed and about 400 laboratory men is as follows for one month of hot summer:

	Cases.
Poisoning from nitro and amido compounds, new cases	29
Poisoning from nitro and amido compounds, old cases still under treatment	26
Acid burns of cornea	20
Acid burns of cornea with conjunctivitis	29
Dermatitis	122
Alkali in eye, inflammation	26
Alkali burns	82
Chlorine fumes	1

The improvement that has taken place in this plant within the last year is shown by the record of days lost on account of occupational disease in relation to the output of the plant. There was at first a great deal of trouble in the ortho and paratoluidin area, and for a time the cases of poisoning were very frequent. Then exhaust ventilation was installed to remove fumes not only from the liquids but from the solids also. The men were given rubber boots and gloves and they were strictly watched and sent to the hospital for treatment at once if the slightest sign of illness appeared. The days lost on account of poisoning, which in December had been 61 for an output of 125,000 pounds, had reached zero in June with an output of 340,000 pounds.

For a second plant the records for six months in 1918, from January to July, are available.

The number employed at this time was about 1,600, something over 700 of whom were process men and about 100 engaged in laboratory work. The company considered only cases of acute fume poisoning or of injury to skin or eyes by acids and caustics as "occupational" in character, so in order to get at the amount of illness in the different departments one must look through the list entitled "nonoccupational." This gives the number of cases among 1,640 men in six months as follows:

	Cases.
Gastro-intestinal diseases	63
Colds, catarrh, coughs, grippe	69
Lumbago, rheumatism, etc	12
Headache	13
Abscesses, boils, etc	27
Skin eruptions	37
Conjunctivitis and sundry eye diseases	72
Unclassified	43
Total	336

The different classes of employees suffered in the following proportions during the six months:

Class.	Number of employees.	Cases of sickness.	Per cent sick.
Mechanical and yard	627	116	18.5
Office force, police, etc	200	11	5.5
Laboratory	97	18	18.6
Intermediates	300	85	28.3
Colors	270	73	27.0
Raw materials	146	33	22.6

During the same period a record of accidents was kept, both those involving loss of working time and those needing treatment but without loss of time—minor accidents.

Character of injury.	Accidents causing loss of time.	Days lost.	Minor accidents.
Acid burns	1	3	20
Caustic soda burns			16
Steam and liquid burns	4	37	34
Burns from explosions	3	1,605	
Sundry burns	1	13	3
Anilin poisoning	4	15	2
Nitrous fumes	6	21	1
Sundry fumes	5	74	2
Injuries to eye (not mechanical):			
From acids	2	6	15
From caustics and lime	2	5	10
Total	28	1,779	103

It is impossible to read these figures and not see the influence of the occupation on even the supposedly nonoccupational diseases given in the second table. The workmen who come in contact with the raw material, intermediates, and colors, have a decidedly higher sickness rate than have the workmen not so exposed.

PROCESSES IN DYE MANUFACTURE.

It is not the purpose of this report to describe the very complicated processes of dye manufacture except so far as it must be done in order to point out the possible dangers to the workmen. Only a bare outline is presented of the principal reactions, in connection with the consideration of the special risks involved in each. It is impossible to generalize about the dangers of the color industry, the various departments of which differ so much in character.

There are certain fundamental chemical processes that are used in dye production and that carry with them dangers which are sometimes constant, inherent, and well recognized; others that are accidental and perhaps quite unforeseen by all but very experienced men. These processes are as follows:

1. *Sulphonation*, or treatment with fuming sulphuric acid, usually added in excess. This very common procedure results in the replacement of an H atom in an organic compound by the sulphonic acid (SO_2HO) group, and often the change from a toxic to a nontoxic or weakly toxic body. The troublesome features of sulphonation lie in the nature of the body to be sulphonated, anilin, toluidins, etc., and in the fumes of SO_2 that may be given off if a good fume pipe system has not been installed or if sulphonating tubs are left partially uncovered. These fumes may be very disagreeable, especially during the early stages of the reaction. In one plant the foreman remarked that when the sulphonators were charged they expected "a gas attack lasting about five minutes, during which time everyone takes to cover." SO_3 is not dangerous, but at a high temperature it may, through the oxidation of organic matter, change to SO_2, as when anilin sulphate is heated. Then sulphonation and partial oxidation result in the formation of sulfanilic acid and SO_2.

2. *Caustic fusion, or caustic melting or hydrolyzing.*—It is usually a sulphonated product that is fused with sodium hydroxide, and the SO_2OH group is replaced by a hydroxyl (OH) group. In this way benzene monosulphonic acid yields hydroxy-benzene or phenol, and naphthalene monosulphonic acid yields alpha and beta naphthol. The danger here is from the sodium hydroxide, not only from contact with the solid or liquid form but even from exposure to steam which carries it. Caustic burns, sometimes very severe, are fairly common in connection with this process, and even in the best-managed factories the danger has not been entirely done away with. If the sodium hydrate is added to a liquid in the kettle there is great danger of splashing; it should always be put in first. Methods of handling the caustic differ much in different plants; sometimes it is handled in solid form, shoveled or scooped, but this gives trouble with dust, especially in hot weather when it dissolves on the sweating bodies and causes a great deal of irritation. Or the container is heated and the liquid contents are blown to the hydrolyzer. This is much safer if all goes well, but productive of more serious accidents if anything goes wrong and the liquid caustic splashes about. Another disastrous accident is the blowing up of an autoclave used for caustic fusion, scattering the hot caustic and causing terrible burns of skin and eyes.

In the making of betanaphthol, which is always disagreeable work, hot, sloppy, steaming, ill smelling, it is chiefly the use of caustic soda that gives trouble. Naphthalene is sulphonated, the resulting alpha and beta salts are separated by liming (treatment with calcium to form the soluble alpha and insoluble beta salt), the calcium is replaced by sodium, and the sodium salt of betanaphthalene sulphonic acid is fused with caustic soda. It is here that the escaping steam may carry caustic with it.[62]

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[62] The most recent process for making betanaphthol is without liming. Naphthalene is sulphonated, the sulphonation mixture is neutralized with soda ash and salted out, the beta salt is filtered out and fused to betanaphthol.

In boiling p-nitracetanilid with sodium hydrate, if the boiling is carried too far decomposition may take place and anilin and ammonia be given off. There is always an effort made to provide for the possible escape of fumes here.

3. *Nitration.*—A mixture of nitric and sulphuric acids is used for nitration, the latter being added to take up the water liberated in the reaction, which would otherwise result in too great a dilution of the nitric acid. The most usual nitration process in dye manufacture results in the production of a mononitro compound, a single NO_2 group replacing one hydrogen atom in the benzene ring. For dinitro and trinitro compounds further nitration is carried on in successive steps usually. The danger in this process is that which always attends the use of nitric acid. Not only may severe burns result from splashed acid, but the fumes of mixed nitrogen oxides that are given off when nitric acid is exposed to the air or when it is added to the organic substances to be nitrated constitute one of the gravest risks to which the workman in the dye industry is exposed.

It must also be remembered that the product resulting from nitration is more toxic than the original compound and requires great care in handling. Reference has already been made to the difficulty encountered with the making and use of dinitrobenzene, nitranilins, dinitrophenol, to mention only the worst of these compounds. The waste acid from the nitrators is also a source of danger, for it often carries enough of the product of nitration to cause poisoning. In making DNB, the first waste acid may contain as much as 20 per cent DNB, and must be used again and again to recover it. The manufacture of DNB from mononitrobenzene is almost always the most troublesome department of all, and in some plants this one place, with only an insignificant force of men, may send as many cases of occupational poisoning to the physicians as all the rest put together. This is when the DNB is allowed to flow out and solidify in open pans or on a filtrose bed, and then is broken up and shoveled or scooped up into trucks or barrels.

The best arrangement of this kind seen allows the product from the nitrators to flow into a covered hot washing tank with an air exhaust, then out into a cold-water tank outside the building under a shed, where it is pelleted by the cold water. This, then, is carried by a screw conveyor to the barrels. The worst one seen had admittedly so much poisoning among the DNB men that sometimes it seemed as if the plant must shut down for want of help. The nitrated product ran out into open pans and solidified there; the men then broke up the solid mass, shoveled the fragments into trucks, and emptied them into a crystallizer, heated, where the DNB was melted and crystallized. This was inclosed. The crystallized DNB was then screened, and although the screen was inclosed a fine powder escaped in quantities when the screened product was poured into barrels through a canvas chute, for this leaked badly. Near the screen stood open barrels of lumpy DNB, which had been dug out of the crystallizer through an opening and which was fed into the screen with a shovel.

In a German plant visited in the summer of 1919 the DNB is never transported in the open; it is melted and blown through pipes. When it is packed a false cover is used, with two openings—one connected with the hopper of DNB, the other with the dust-collecting system. In this way all dusty shoveling and scooping and all direct contact are avoided. Even the packed and closed barrels are regarded as a source of possible danger, for DNB volatilizes at ordinary temperature, and still more on a hot day; so the Germans store these barrels in an open shed, lest the fumes from them affect men working in that department.

4. *Reduction.*—Acid reduction is carried on with the aid of hydrochloric acid and iron filings; alkaline reduction, with zinc dust and usually caustic soda; neutral reduction, with zinc dust alone. The former is used in the production of anilin from nitrobenzene, ortho and para toluidin from nitrotoluene, alpha naphthylamine from nitronaphthalene. It is also used in the reduction of dinitrobenzene to phenylendiamine, dinitrotoluene to toluylendiamine, nitronaphthodisulphonic acid to amidonaphthodisulphonic acid, nitrophenol to amidophenol, and so on. Since reduction begins with a nitro compound and ends with an amido compound, it follows that there is a decided risk in connection with the reaction, a risk more or less recognized and more or less guarded against in every plant. When the process goes forward normally, without any hitch, there is little trouble with sickness among the men. To be sure, the taking of samples from time to time, if carelessly done so that the liquid spills on the hands, may give rise to mild poisoning or fairly serious, according to the compound undergoing reduction, and in hot, heavy weather, especially on the night shift, the fumes, which escape from the feed hole, may cause enough discomfort to force a man to quit work for that shift though he is able to return for the next one. But frequent and serious cases of acute poisoning and a general condition of anemia among the men in the reduction department is found only when the mechanical arrangements for reduction are faulty. It is when, for some reason, poor construction of the reducer, poor charging, failure of motive power, or some other defect, the iron filings fall and cake around the paddles and the reaction has to be interrupted, the manhole opened, and the "sludge" cleaned out for a fresh start, it is then that serious poisoning occurs. There is a wide variation between anilin reduction departments in different plants, it being a matter of ordinary observation that while in some of them the caking of a reducer is a rare accident, which may not happen oftener than once in three months, in others it seems to be an ordinary occurrence. The first kind of a plant has a scrupulously clean reduction department, with only a slight odor of anilin, or, perhaps, it is quite free from odor; the second is an untidy, sometimes filthy, spot, the floor covered with a wet mass of black iron filings, which are tracked over the floor by the men's feet; the anilin water runs partly through the gutters in the floor, but some of it spreads over and lies about in pools. The men work through the open manhole, prodding the caked mass with iron rods and hoes and then drag it out. Their hands and clothing show the contact with this anilin-laden sludge, which their work necessitates. In such a place anilin poisoning is looked upon as a serious thing and one very hard to control, while in well-managed plants it is considered a rarity unless in very slight form.

In the reduction of dinitrobenzene to phenylendiamine the danger is much greater than in reducing mononitrobenzene to anilin, and, unless the charging is done with great care, trouble inevitably results sooner or later. This is also true, although to a less extent, with the reduction of dinitrotoluene to toluylendiamine. The English and the Germans know much more about the dangers of these compounds than we do and use special precautions in handling them. A good device for charging the reducer with dinitrobenzene was seen in an English factory. The covered truck had an opening just on a level with the feed door of the reducer, and when the lid of this opening was dropped down it formed a bridge between truck and reducer over which the DNB could be pushed without scooping or dropping. In contrast to this was the method used in one of the American plants visited, where the DNB was shoveled from an open truck into a pail and this dumped into the reducer. It is impossible for a man doing work like that to keep from contact with the stuff, and, aside from the contact, there is the continual volatilization.

In making phenylendiamine by reduction of DNB in one American plant there was much poisoning among the men so long as the product was filtered hot, but this has been avoided by sending in a stream of cold water which prevents fumes from the filter press and also from the sludge. The sludge contains only 1 per cent of DNB, but enough to give trouble if it is hot.

The usual dangers of acid reduction are well known and understood, but there is one possible danger in connection with it and still more in connection with alkaline reduction, which is not generally recognized in American plants, although it has long been known in Germany and has recently attracted a good deal of attention in England. This is the evolution of fumes of hydrogen arsenide, spoken of in the former section of this report.

There are several processes in dye manufacture in which the conditions may occur which give rise to the formation of hydrogen arsenide, namely, the contact of an arsenic-bearing metal, zinc or iron, with hydrochloric acid or sulphuric, or the contact of an arsenic-bearing acid with one of these metals. In one of the cases reported from England a plumber went into an empty acid tank to repair it. That is, the tank was technically empty, it had been washed out and only about a bucketful of fluid was left at the bottom. But the acid, chamber acid, contained enough arsenic to poison him and he died of hemorrhagic nephritis two days later. A similar but even more disastrous accident took place not long ago in New Jersey. Here three men went into an iron tank that had contained chamber acid but was supposed to be empty and clean. All were quickly overcome by fumes of AsH_3 and two died from its effects. It does not take much arsenic in this form to cause severe poisoning. According to Rambousek an amount corresponding to about one-hundredth of a milligram of arsenic is sufficient.

The other sources of hydrogen arsenide in the dye industry are reduction processes, both acid and alkaline. In reducing nitrobenzene to anilin, nitrotoluene to toluidin, etc., this gas may be given off and therefore it is dangerous to send cleaners or pipe fitters into the reducer, aside from the danger of the nitro and amido bodies. The arsenic may be contained in the iron but is more likely to be in the acid. One English manager said that he had had four men on sick leave at once as a result of such an accident as this. The same risk must be thought of in connection with the reduction of nitro to amido naphthosulphonic acid.

But it is especially in the making of benzidin, as this is done in English plants and in some American plants, that precautions against arsine poisoning must be taken, for it is here that a large number of English workmen have recently been found to be suffering from mild or severe poisoning. This method of making benzidin is as follows: Nitrobenzene is reduced to hydrazobenzene by means of zinc dust and caustic soda. One of the Home Office experts believes that at this point hydrogen arsenide may be given off, but the industrial chemists are skeptical. There is no doubt, however, as to the danger of the next stage, when hydrochloric acid is used to dissolve out the zinc dust and leave hydrazobenzene. This process must be carried out in the cold, for otherwise some of the hydrazobenzene might be converted to benzidin, pass into solution and be lost, and therefore it is customary in these factories to open up the acidifying tub and drop chunks of ice into the acid. This is the point at which the accidents have usually arisen, for if arsenic is present in the zinc dust, or in the acid, there may be a sudden evolution of AsH_3 when they meet and the liquid may "boil over," as the men say. Usually the zinc is the substance at fault in the most serious accidents, for the acid seldom carries as much arsenic as may be carried by the zinc. Since the latter is in powder form, the conditions are ideal for the production of the gas; and since the tub must be opened to admit the ice, its escape is easy.

The next stage is also attended with some danger, and here, too, cases of poisoning have developed. The contents of the tub with the zinc chloride in solution and the crystals of hydrazobenzene are sent into a filter press and if AsH_3 is present, bubbles may be given off from the liquid and from the paste. In one of these English plants it was evident that just this had happened and the chemist in charge spoke with much emphasis of the necessity of providing good drains under the filter press and thoroughly flushing the floor from time to time, never letting any of the fluid lie about in pools. He said that the use of compressed air to blow out the filter press was an advantage also because this served to carry off whatever fumes might be left. In the last stage, when the hydrazobenzene is heated to boiling by steam to convert it into benzidin, it is possible that some unchanged azobenzene may be given off with the steam and this compound is decidedly poisonous.

In consequence of the accidents which have occurred, the English factory inspectors are insisting on changes in the equipment of benzidin departments, provision of fume pipes for the reduction, acidifying, and final conversion pans, proper drains for the filter presses, and so on. In one, the management has put in a long sluiceway to the manhole of the acidifying pan, with a valve at the end and the ice is sent down this sluice by the workmen, who can thus stand at a distance from the manhole, too far to inhale whatever fumes might escape. This was the plant that had the most trouble in its benzidin department. In another, the cases of hydrogen arsenide poisoning had occurred in connection with the reduction of nitro to amido naphthosulphonic acid and since then they have used arsenic-free acid (contact acid) for this reaction, but even so the iron may contain arsenic, so they test the fumes from time to time with mercuric chloride paper.

This way of making benzidin is rather crude and is not used in our largest plants. It is perfectly possible to produce the proper degree of cold by means of brine coils and so avoid the opening of the acidifier for ice. This is done in one of our plants. It does not, however, do away with the risk of escaping fumes if for any other reason the manhole is opened or if there is a leak, nor does it prevent fumes at the filter press, nor the risk of poisoning the men who repair or clean the acidifying kettle. The process in use in the better American plants does not require the use of acid and is quite free from any danger of arsenic at any stage. By this method the zinc dust is not changed to the chloride and dissolved out, but is separated by passage through a very fine screen which catches the crystals of hydrazobenzene and lets the dust through.

In smaller American plants the procedure may be the same as that in England, and carried on without any precautions. In going through the records of a hospital in a New Jersey town, histories of two men poisoned while on a night shift were found; both were made very ill, and one of them died some three weeks later.[a] They had been employed in a plant which was making napthionic acid from alphanaphthylamine and sulphuric acid, and also benzidin base and sulphate by the process just described. The company had installed a fume pipe but had never completed it and it was never used. According to the information obtained, the men in the hospital were two out of five affected on the same night shift by some gases of unknown nature. The diagnosis given was, very naturally, "anilin or alphanaphthylamine poisoning."

Quite different dangers attend reduction by means of sodium sulphide as in the making of sulphur dye intermediates. Paranitrophenol is reduced to paraamidophenol, picric acid—which is trinitrophenol—is reduced to picramic acid—amido-dinitro phenol—by means of sodium sulphide, and if the reaction is acid, fumes of hydrogen sulphide may be given off.

In making 1–2–4 amidonaphthosulphonic acid, reduction and sulphonation are brought about simultaneously by the use of sodium sulphide and sulphuric acid and here the fumes of sulphur dioxide may be bad.

5. *Chlorination.*—The introduction of the chlorine atom may take place in the benzene ring or in a side chain. The resulting product may be inert, or highly poisonous, or it may resemble closely the nonchlorinated compound, as anilin hydrochloride differs from anilin only in being a solid instead of a liquid. The escape of fumes of hydrochloric acid used for the production of chlorine gas and of the gas itself constitute a danger and it is always necessary to provide a vent or an absorbent chamber for the gas, which is best taken up in water and neutralized. It is especially in the making of anilin hydrochloride and of nigrosin that these fumes are troublesome. The use of cylinder chlorine in the manufacture of pyrone dyes is hardly ever troublesome, for only small quantities are needed.

6. *Alkylation.*—This consists in the introduction of methyl or ethyl groups into a hydroxy or amido group. The important ex-

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[a] See page 45.

amples of this class of compounds are dimethylanilin and diethylanilin. The latter is made by treating anilin with ethyl alcohol. Dimethylanilin may be made by the action of methyl alcohol or methyl chloride on anilin under heat and pressure, or by the action of dimethyl sulphate without pressure. The trade poisoning that has occurred in the usual processes of alkylation is to be attributed to the anilin rather than alkyl derivatives, which are less toxic. When dimethyl sulphate is used for methylation, a new danger is introduced which has already been discussed.

In making methylanilin, some trouble has been experienced from the methyl alcohol used. Methyl alcohol is also employed to bring about alkylation of fuchsin to form other triphenylmethane colors.

7. *Oxidation.*—The substances used as oxidizers are usually inorganic salts, such as sodium dichromate, sodium chlorate, or permanganate, manganese dioxide, lead peroxide with a mineral acid. Anthraquinone, the intermediate for alizarin dyes, is produced by oxidizing anthracene with sodium dichromate. In making fuchsin, orthonitrotoluene may be used as an oxidizer, or mononitrobenzene. In this case, fumes from these compounds must be guarded against. The use of sodium and potassium dichromate has led to serious chrome ulcers in England, but apparently, from the literature, it is in using it as a mordant that the trouble is encountered, not in the production of dyes. Certainly in the United States chrome ulcers are practically unknown in alizarin dye works. Nor does the use of red lead seem to give rise to enough lead poisoning to make itself known. Oxidation may result in the production of poisonous quinones, and this is a danger not generally recognized.

8. *Carboxylation.*—This is generally effected by the action of caustic soda and pure carbon dioxide gas upon a phenol as a result of which the COOH group is introduced into the ring. For instance, carboxylation of phenol yields salicylic acid, which is much used in the dye industry. This process is not so dangerous as caustic fusion, because it does not require nearly so much free alkali and the resulting compound is less poisonous than the original compound.

9. *Liming.*—Lime or chalk, or sometimes caustic lime, may be added, usually to a sulphonated product to separate one salt from another. For instance, in the production of betanaphthol the separation of the alphanaphthalene sulphonic acid from the beta is brought about by adding lime, because the lime salt of the alpha acid is very soluble in cold water and that of the beta acid is only slightly so.

10. *Condensation.*—This process consists in the union of two compounds, or two molecules of the same compound to form a new compound by the loss of water or HCl or H_3N. Sometimes hydrochloric or sulphuric acid is used with phosphorus, zinc, sulphur, or tin to bring about this reaction. There is no special danger involved except in the liberation of the volatile substances if the apparatus is faulty, or in the case of accident allowing the workmen's hands or clothes to become splashed with such a substance.

11. *Diazotizing and coupling.*—An amido compound on treatment with nitrous acid (sodium nitrite and hydrochloric acid are generally used) yields a compound called diazo. This is then coupled with an aromatic amine or phenol to form an azo compound. Although

the compounds that are diazotized are toxic, the fact that the reaction of diazotizing or coupling is carried on in the cold lessens very much the danger of both fumes and contact. An instance of the many dyes that are made in this way is chrome brown, which is made by diazotizing picramic acid (dinitroamidophenol) and coupling with betanaphthol.

The making of intermediates is on the whole attended with more risk of poisoning than the making of finished colors, and the benzene intermediates are much more dangerous than the naphthalene and anthracene intermediates. Toluene and xylene are included with benzene in this statement.

COLOR MANUFACTURE.

The *azo dyes* are made with a primary amine, anilin or toluidin or toluylendiamine or benzidin or some similar body, which is treated with nitrous acid in the cold. The diazo compound produced is then coupled with an aromatic amine or phenol to form an azo compound. Diazotizing is done at about zero, centigrade. The making of azo dyes is the safest branch of the color industry, and a plant which does not make its own intermediates and makes only azo dyes may probably be kept practically free from occupational disease. Typically, the work is carried on in one high building with three levels, the coupling tanks into which the intermediates are blown being on the top level, so that whatever fume escapes is taken care of up there and does not contaminate the air on the other levels. It is said that if the sodium nitrite used for diazo production is run in too quickly nitrous fumes may be given off.

Anthracene dyes may be produced also without much risk of trouble. The most important of these dyes is alizarin, which is synthetic madder. To produce this, anthracene is oxydized usually with potassium or sodium bichromate to anthraquinone, and this is sulphonated and then fused with caustic soda and chlorate of potash to form alizarin, or dioxyanthraquinone. Indanthrene is produced from anthracene by oxidation to anthraquinone, sulphonation, amidation (with ammonia and catalytic copper), caustic fusion. Indanthrene blue is formed by air oxidation; greens and violets are produced by the use of chlorine gas, nitrobenzene, and nitric acid. Obviously, there are decided risks in the making of indanthrene colors, especially from chlorine, nitrous fumes, and nitrobenzene, for although during the uninterrupted reaction no fumes may escape, any accidental interference with the process, and these are not uncommon, may result in a very bad state of things. Benzanthrene causes dermatitis.

Indigo is made in three large plants which were visited, the process differing slightly in each. In two, formaldehyde and anilin are used and sodium cyanide is either added to or formed in the course of the reaction. In the course of this ammonia fumes may be given off. This reaction is followed by hydrolysis, usually with caustic potash, to phenylglycine. It is in the filtering, drying, and transporting of phenylglycine that most of the illness among the workmen occurs. It is a very light and fluffy powder, and although it is usually said to contain no more than 1 per cent of anilin, it may set up very serious acute and chronic anilism if unusual precautions are not taken, especially in emptying the filters and drying, dumping, transporting, and barreling the powder.

In the third plant anilin and monochloracetic acid are used to form phenylglycine. During this process the fumes that are given off contain anilin, hydrochloric acid, and chlorine. Monochloracetic acid is strongly caustic.

In one of the three plants the filter press stands in a separate building, which is really a shed, with ample ventilation. While the air is being blown through the press the vapor is bad, but usually it is not necessary to have anyone inside the shed at that time. The presses are then opened, the crystals dumped and scraped up and shoveled into barrels. For this work rubber aprons, gloves, and respirators are provided. From the filter the crystals go to a tank with caustic potash, the temperature being kept as low as possible to prevent too much ammonia fumes. A second filtration to remove dirt follows, and then evaporation in an inclosed badger. The liquor falls over great hot metal rolls, on which a thin layer of powder forms, which scrapes off and falls into a box. The powder is kept from flying about by heavy canvas curtains. This dryer is in a separate room with a high, windowed roof, and only one operator works on each shift. He is required to spend all but 15 minutes of each hour in a little sheltered porch just outside the room, for it is extremely dusty, and everything is covered with white powder like a flour mill. He is given gloves and a respirator. Boxes of the powder go to the next room, and are emptied into a barrel packer of a good mechanical type, but nevertheless there is a great deal of white powder in this room.

The second plant has a better method. The phenylglycine is evaporated in a vacuum dryer, and a traveling screw carries the dry powder to an inclosed hopper, from which it falls into a barrel, standing underneath. A canvas chute connects hopper and barrel, and there is an exhaust with an opening right beside the top of the barrel. At the time when visited no dust was visible anywhere around this apparatus.

The third plant was very bad. The synthetic indigo department was well housed in a great new building, amply ventilated for ordinary purposes, but the air was full of fumes and dust, so that a short stay there was enough to affect one's head quite noticeably. Two of the men at work there were quite livid, one of them startlingly so.

The *di and tri phenylmethane* dyes are often called anilin dyes, others are called toluidin dyes. The intermediates used are derivatives of benzene, toluene, and xylene, and there is probably more typical nitro and amido poisoning in connection with this class of dyes than any other. The only diphenylmethane color of importance is auramine, in the course of the manufacture of which strong fumes of ammonia may be given off, and also sulphuretted hydrogen. The waste water from the auramine building may carry a good deal of H_2S.

The triphenylmethane dyes are very important, and require the use of large quantities of nitrobenzene, nitrotoluene, anilin, the toluidins, especially para, the anisidins and methyl and ethyl derivatives of anilin. The malachite green series belong in this group. Malachite green is made from benzaldehyde and dimethylanilin, Victoria green from benzaldehyde and diethylanilin. Fuchsin, the starting point for so many colors, is made with anilinhydrochloride, or formaldehyde, ortho and para toluidin and anilin oil. This forms what is called the "red oil mix." If formaldehyde is used instead of anilin hydrochloride there is risk of a boil over, and this may also happen with anilin hydrochloride if it is added too fast. The red oil mix is oxydized with nitrobenzene or orthonitrotoluene and "fuchsin melt" is formed. This department is frequently mentioned in German factory inspection reports as the place in which a case of intoxication occurred. The fuchsin melt is treated with caustic soda to make fuchsin base, and this is phenolated by means of anilin and benzoic acid to opal blue, oil-soluble, which is changed by sulphonation to water-soluble alkali blue. Fuchsin can also be alkylated to other colors of this same group by displacement of the H atoms in the amido nucleus by ethyl or methyl groups, but it is simpler to start with an alkylated amine. For instance, methyl violet can be made with dimethylanilin, sodium chloride and chloride of copper, cresol and phenol, and then treatment with hydrogen sulphide.

Eosins and *fluoresceins* are closely allied to the so-called "anilin" dyes (the tripheylmethane dyes), and are sometimes classified with them, sometimes called pyrone dyes, sometimes resorcin dyes. Chlorine, bromine, and iodine are used, also fuming sulphuric acid and caustic soda, but the gases are provided in cylinders and not enough are used to give any trouble.

Nigrosin and *indulin* are made by melting anilin and nitrobenzene, ferric chlorid and hydrochloric acid. This "melt" is ground, then washed. Fumes of anilin and of hydrochloric acid, especially of the latter, may be quite heavy in these departments.

The *nitro* or *nitroso* dyes are in themselves poisonous. It is only recently that a man in Germany was poisoned by handling aurantia, which is hexanitrodiphenylamine. The greatest risk of industrial poisoning, however, is in the manufacture, which involves nitration processes and the possible escape of nitrous fumes. Aside from aurantia, the best-known nitro colors are picric acid, trinitrophenol, and Martius yellow or dinitronaphthol, and naphthol yellows.

There is probably more risk of occupational poisoning in the making of *sulphur dyes* than any other class of colors, for the introduction of sulphur and sodium sulphide may result in the liberation of sulphuretted hydrogen fumes. The preparation and use of the intermediates also involve exposure to compounds which have decidedly toxic properties, and set up not only very troublesome skin eruptions but systemic poisoning as well. For instance, chlorbenzene is nitrated, during which process nitrous fumes may be given off. The resulting ortho and para nitrochlorbenzene must be separated, the para crystals from the ortho liquid. This operation was seen done in an open centrifuge, and although the centrifuge was in a small compartment with a strong suction fan drawing away the fumes, it was necessary to provide a current of fresh air directly beside the man who was obliged to go in from time to time and empty the centrifuge. Even with these precautions the vapors were strong beside the centrifuge. The paranitrochlorbenzene is washed and saponified to paranitrophenol, which is a prolific source of dermatitis unless it is handled with great care. Reduction of paranitrophenol to paraamidophenol is done for sulphur blue. For sulphur black, dinitrochlorbenzene is used, and the production and use of this compound in the early days of American dye manufacture gave rise to so much distressing skin disease as to necessitate changes in method or it would have been impossible to keep the men at work.

Sulphur browns and yellows result from the treatment of phenylendiamine with sulphur and benzidin. Phenylendiamine results from the reduction of paranitranilin, one of the most dangerous of the nitro and amido compounds made from anilin through acetanilid and paranitracetanilid. The process of saponifying or hydrolizing paranitracetanilid is often attended with the liberation of fumes.

Primulin is made from paratoluidin, which is fused with sulphur to a " melt," then ground and sulphonated. Sulphuretted hydrogen is sometimes evolved in making the melt and a typical case of toluidin poisoning was reported in a man who was in charge of the making of the melt.

The danger from fumes of hydrogen sulphide is greatest in the manufacture of khaki and sulphur browns and yellows, less in connection with sulphur black, and very slight in making sulphur blue. As a usual thing an effort is made to burn the H_2S to a mixture of sulphur oxides. In one plant powerful suction carries H_2S to an iron column where it is absorbed by caustic soda.

PREVENTION OF OCCUPATIONAL POISONING.

It is true in the anilin dye industry, as in every American industry, that no generalizations can be made about the protection that is given to the workmen against the dangers inherent in his occupation. This differs widely, not only in completeness but in character. In one plant the emphasis will be placed on rigid cleanliness of the premises and removal of fumes, while less stress will be laid on the medical department. In another there is much less effort made to prevent the men from coming in contact with different toxic compounds, but there is a very complete, admirably equipped plant dispensary. It seems that no American plant as yet has developed both these sides as thoroughly as possible, although one of the older companies has come very near it.

Perhaps it may be well to begin the consideration of the care which should be given to anilin dye workers by a description of the methods used in some of the German factories. That of Meister, Lucius & Brüning, in Hoechst, was described as follows by Grandhomme back in 1880. At that time this factory employed 1,000 men, 40 superintendents, and 25 chemists. It manufactured anilin colors; resorcin colors (eosins) ; naphthol colors, yellows, reds, and browns; and alizarin colors. The buildings were one-storied with saw-tooth roofs, the windows in the roof being kept open. Fumes were carried off in underground flues; the floors were of brick laid in cement, impermeable to moisture, and furrowed with many cement-lined gutters to carry off fluids. In all rooms where steam or other vapors were formed the walls were whitewashed twice a year. Each room had at least one large door to the outside, usually two. In the anilin department everything was inclosed. The sludge was driven out with compressed air and discharged through pipes to a distant field where, after thorough drying, the iron was recovered.

In the factory inspection report for 1910–11 a description is given of the welfare work in the Aktiengesellschaft für Anilinfabrikation. The plant dispensary held clinics twice a day, with two physicians and two nurses. There were also two visiting nurses for the workmen's families. The bathhouse was available for the use of the families twice a week. There was an infant welfare station, and milk was provided at cost. Free care was given in a maternity home to the women employees and the wives of the workmen during confinement and for three weeks after. The mother was given 3 to 5 marks a week if she nursed her baby. There were illustrated lectures on hygiene, and the medical care included light baths, electric treatments, vibrations, massage, ultra-violet rays. Coffee was provided free, and also milk if the man would pledge himself to drink no alcohol during work time. The report states that "anilism has been practically abolished by a closed system for mixing, grinding, transporting, and for producing nitro and amido compounds; by excellent ventilation, scrupulous cleanliness and rigid insistence on baths."

Koelsch, one of the principal authorities on industrial hygiene in Germany, gives the following advice to manufacturers of anilin dyes and intermediates: Medical examination must be made of all applicants for work, and men must be rejected who are weakly, anemic, or with affections of heart or kidneys. Nobody under 20 years of age or over 50 should be accepted. Persons with skin diseases should be rejected, and it is better not to employ women because of their greater tendency to hemorrhage and because of the possible effect on their offspring. The hours should not be too long. He advises alternation of employment unless the ideal can be attained of a selected force of trained and immune workers. It is important to prevent heat and humidity as much as possible, for experience shows that there is always more poisoning on hot, windless days, and the same condition is brought about by allowing steam to escape into the workroom.

The rules in force should be made to fit the different compounds. It is not necessary, for instance, to make the men working with the toluene compounds bathe daily and have a clean suit of working clothes every day. He believes that medical inspection for these men need not come oftener than once in six or eight weeks, and there is no reason why they should not work 10 or 12 hours. For men working with benzene compounds far greater precautions must be taken. They must have proper working clothes and caps, frequently changed; they must bathe daily; they should not work more than six hours, and in hot weather this period should be divided, three hours in the early morning and three in the late afternoon. It is very important to provide thick, impervious footwear and to see that the feet are kept clean, especially if the man perspires much. Koelsch objects to gloves, especially if the work is greasy, for their use simply results in keeping the hands in more intimate contact with the substance to be avoided than they would be if no gloves were used. It is wrong to place dependence upon respirators; dust and fumes must be removed at the point of origin. No eating in workrooms should be allowed, and it is well to provide a big cup of hot coffee at the end of the day's work.

In case of poisoning, Koelsch advises removing the man to fresh air, but not walking him up and down. He must be made to lie down. His clothes must be removed and he must be given a thorough bath. If there is dyspnea, oxygen inhalation with artificial respiration is advised. If there is marked blood destruction, it may be well to bleed and give saline injections, but this is not necessary if the pulse is good. Make the man drink abundance of milk or hot black coffee or weak tea, and give him mild laxatives. During convalescence give him milk, iron, and arsenic, but no alcohol. Curschmann insists on the value of cool sponging or douches as a stimulant to heart and respiration. He also advises the administration of abundant quantities of milk.

In a large German dye works visited in July, 1919, the prevention of occupational poisoning had been carried to a much higher point than that seen elsewhere. It is not extravagant to say that the passageways between buildings and the roadways through the grounds were cleaner than are the floors in some American factories. There was no odor anywhere. One could not have guessed what was being produced in the anilin reduction room. It was explained that each department was under the charge of a chemist who was responsible for all the sickness occurring there. No fluid was ever allowed to drip or spill on the floor. If an accidental case of poisoning should occur, the chemist would be called to account, not before the heads of the plant, but before a committee of the associated anilin industries, the "Berufsgenossenschaft," for it is they who have to pay the sickness compensation, and they make a strict inquiry into every case. This system seems to result in a more rigid control of the sources of industrial accident and disease than is obtained when each establishment carries its own insurance and is alone responsible for the cases which occur in it. Naturally an association of all the members of a branch of industry can exert pressure upon one member which will result in a more careful supervision on the part of the chemists and physicians than is to be expected when what happens in the plant is known only to that one plant and the loss falls only on it. Merely to save his face and avoid the disagreeable experience of examination at the hands of his colleagues the man in charge will do all he can to keep off accidents and accidental poisoning. After all, the criticism of one's own class is the criticism most to be dreaded, and it is probable that the influence of the "Berufsgenossenschaft" is more potent than the authority of the factory inspection department.

The freedom from odors and the striking cleanliness of the plant were the result of this strict supervision. No apparatus which was wet with any sort of fluid was placed on the floor. Near the opening of the manhole of each kettle or autoclave was a smooth metal shelf upon which the workman was instructed to lay any wet piece of machinery as well as the lid of the manhole. The chemist in charge was responsible for the cleanliness of this metal shelf. All vapors, even plain steam, were removed by fume pipes, which could be connected up with the air exhaust system, and always before opening an autoclave or kettle the exhaust must be turned on and left on so long as the receptacle was open. It was explained that this rule was based on experience, for in processes of this kind it is impossible to be sure of all the reactions, and the only safe thing is to guard against the possible escape of such fumes as hydrogen arsenide and hydrogen sulphide.

The dust prevention was excellent, every effort being made to catch even the color dust, so that the men engaged in color packing showed very little color on their clothes and faces. The small packages were filled under glass and an exhaust provided at that point. Barrel packing was done in the open room, but through a lid with two openings, one connected with the dust recovery system and the other with a hopper containing the ground color.

This particular German factory had a lavish supply of basins and showers, 1,200 for 3,000 men, and also several bath tubs. It is not compulsory in Germany for the employer to provide overalls for the men, but in this place good two-piece suits of blue denim were provided, mended, and laundered. At the end of three to six months, according to the process in which the man was employed, a new suit was provided and the old one given to the man for his own. The guide said that this inclined the man to take good care of his overalls. The men employed there are decidedly high-grade workmen, as is shown by one little significant item—the absence of doors to the lockers. The locker room has open compartments for the men's street clothing, one for each man. It was said that it was much more healthful to let the clothing air and dry than to shut it up behind doors, and that there was no danger of the men stealing each other's clothing.

The new applicants for employment in Germany are examined by a physician and doubtful cases rejected, but there seems to be at present no routine examination of the working force, such as is carried on in England and in some American plants. All cases of occupational illness are strictly investigated, as explained above.

The rules for the control of the dye industry in Great Britain are those which were passed in 1908, but the factory inspection department of the Home Office is preparing a new code which will be more detailed and comprehensive. Already the local inspectors have issued orders supplementing the rules of 1908 as new dangers came to light with the great increase of the industry. On the whole, the construction and management of the British plants is about on a level with the American, if one leaves out of consideration our worst specimens. As is invariably true in every industry studied, the United States contains some factories which are dirtier and more neglected than any in England. This is partly because of the varying standards for factory inspection in our different States. The provision of working clothes for the men in the English factories is, as it is in ours, sometimes ample, sometimes inadequate. The provision of washing facilities in the best English factories is quite as lavish as in the best American, but the worst is not nearly so bad as our worst. Shower baths are required in England, but at least one American dye works which manufactured phenol during the war, is now manufacturing dye intermediates as well as dyes, and employs 2,000 men, has not a single shower bath.

No American dye works has yet reached the point of doing everything possible to protect the workers from the dangerous compounds which are used or produced, or which may be accidentally evolved in the course of production. The faults in these plants depend in the first place on the construction of the buildings and here, curiously enough, some of the newest are most at fault. Of two factories observed, one has been running for years and is situated in a large city; the other is hardly more than two years old and is out in the country, with practically unlimited space to spread over. The first is excellent in construction, the buildings are high and well ventilated, the floors of concrete or some similar substance, properly drained. The second consists of small buildings, often with low ceilings, huddled together so that they shut off light and air from each other, the floors are chiefly of wood already rotting and roughened, and the walls and windows look as if the plant were 20 years old instead of 2.

Even if the construction is good, the method of carrying on the different processes may result in a continual leakage of vapors or fluids, or dusts, or the frequent need for repairs, which always means untidiness and sometimes a dangerous state of affairs. To compare two anilin reduction plants: In one, the smooth concrete floors are clean and dry; the high ceiling and open windows insure good air because the only source of fumes is the occasional taking of a sample or perhaps a puff from the feed opening. The sludge is run out into the open and the reducers do not have to be opened and cleaned out oftener than about once in three months. In the other plant the notes taken at the time of the visit read as follows: "The reduction building is dirty, and it is plain that there is a good deal of trouble with the working of the apparatus. It seems to be a common occurrence to have a reducer stop and then the iron falls on the paddles and cakes them, and they have to be dug out. They take certain precautions to lessen the danger of this work; they drive in steam, but it is admitted that the steam can reach only the upper layers of the iron filings, and as soon as the man begins to dig he reaches the anilin. One reducer had just been opened up because the iron was caked, and the door at the bottom, about 4 feet by 2½, was open. A man must climb in through this door to finish the cleaning, and although he is allowed to stay in only 10 minutes, it is admittedly a bad job, for, of course, he can get very thoroughly smeared with anilin sludge in that time. Another reducer had just been cleaned out. The sludge from the two lay in heaps on the floor and little rivulets of anilin water ran from the heaps. The fumes were quite strong, although the building is big and high and well provided with windows. According to the physician, there is trouble every time a reducer is cleaned out, even though compressed air is driven in while the man is at work inside. Various improvements were discussed, such as making an opening in the bottom of the reducer and passing in an air hammer to break up the caked filings and then running the sludge out with water, but it seems obvious that what they need is some way of keeping the paddles of the reducers running and prevent caking."

The cleanliness of the plant also depends on the standards of the men in charge. This sounds like a truism, but it is really worth repeating. There are perhaps two plants among those visited in which one can go dry shod through every department, but it is need-less to say that this is an exception and that ordinarily one must be prepared to wade through puddles on almost all the ground floors. The statement is commonly made that most of the cases of anilin poisoning come from the anilin water that has soaked through the men's boots, and several superintendents have said with pride that they provide wooden-soled boots for their men. It seems not to have occurred to them to try to provide dry floors instead.

In German factories the rule seems to be to prevent the escape of any fumes or vapors, no matter how harmless—a rule based upon long experience. In the United States each factory seems to be acquiring its own experience, rather at the expense of the workmen. If a case of sickness develops in connection with a given process, the matter is investigated more or less promptly, and the dangerous fumes are prevented, not always immediately, but eventually. In a few rare instances the scientific knowledge which is so abundantly available in these factories has been taken advantage of and those fumes which are known to be poisonous are carried off by suction, even though there may never have been an actual case of poisoning from them in that plant.

In Great Britain the centralized control and the presence of experts in the factory inspection department make it possible to apply in all the factories the experience which has been gained in one. For instance, the occurrence of hydrogen arsenide poisoning in one benzidin department resulted in precautions being installed against such an accident in all the other works which made benzidin.

The actual care taken of the individual workman differs very widely in our American dye factories. The matter of providing working clothes for the men is admittedly important, for all practical men, as well as physicians, know that these poisons are absorbed through the skin, and that clothing impregnated with a nitro or amido compound acts like a poisonous poultice. Yet one of the largest plants in the country, employing over 1,200 men in process work and laboratory work, has never made any provision of overalls for the men, although the safety expert says that plans have been made to do so. Another plant for the manufacture of intermediates and dyes employs 2,000 men and provides neither overalls nor adequate washing facilities. In contrast to this are several factories where the provision is ample and generous. In one large plant clean clothes are provided for the DNB and DNT men daily; for the anilin men twice a week. A plant making printer's inks and employing 380 men provides not only the usual denim overalls but clean underwear, shirts, socks, and heavy boots with wooden soles an inch and a quarter thick. The clothing is repaired and two suits a week are provided. In the paranitranilin department of another plant, since closed, the men were given underwear as well as overalls and socks, a clean supply every day. These men were required to bathe at the end of the day's work, and if any man was engaged in an unusually dusty job he was made to bathe as soon as it was over and change all his clothes. One of the oldest plants, and probably the cleanest of all, which employs between 1,500 and 1,600 men, supplies working clothes, but makes the men pay for the first suit. The process men have a clean suit every other day, unless after a cleaning or repairing job, in which case they change at once. Color men wear theirs until they are badly torn or worn out.

There is a decided difference of opinion as to the wearing of gloves. Some foremen hold that the men get on much better without them when working in nitro and amido compounds; that it is impossible to prevent leaks, and a leaking glove is much worse than none at all. They maintain that the men are much better protected if they are encouraged to wash their hands frequently during the day than they are by wearing gloves. This can, of course, be done only if there is a supply of hot water and soap in the department itself, which is not always the case. No experienced man depends on respirators to protect his employees from poisoning. To exhibit with pride a collection of rubber sponge respirators is a mark of inexperience. On the other hand, an abundant supply of warm water at different points in the plant is an evidence of experience. Even if warm water can not be provided, there must be a supply of cold water readily accessible in every department where caustics are handled, or where the mineral acids are handled, for severe burns can be prevented only by prompt and thorough washing with water.

The great majority of American dye works have good and well equipped wash rooms and bathrooms and shower baths for their process men. This is required by law in the States in which most of these plants are situated (Massachusetts, New York, New Jersey, Pennsylvania, Illinois), but, unfortunately, it seems not to be required in Wisconsin. Usually soap or some washing powder is also provided; less often, towels. There is a great difference in the degree to which the employees of the different plants avail themselves of these facilities. For instance, in one factory 90 per cent of the men use the shower baths; in another only 25 per cent. The difference probably comes back to the personality of the welfare manager, or perhaps of the individual foreman.

It is not so important in this industry to provide against the men eating their lunch in their workrooms as it is in connection with lead work. Nevertheless it is desirable to have rooms provided in which no work is carried on, and in which hot food or at least hot drinks may be bought by the employees. Factories which are situated far from town are usually obliged to have a cafeteria for the men, but the provision is not as general as it should be, and the whole matter of proper feeding of the process men should be taken more seriously than it is in American factories.

Much more attention is paid in Europe to the proper feeding of men in all the dangerous trades than is true over here, and in the dye industry it is recognized that a poor dinner and an inadequate breakfast may have an important influence on industrial poisoning among those employed. The English have long laid stress on the necessity for proper feeding in the lead trades, and they have now applied the same principles to the coal-tar industries. They look on the dinner pail, so common in our factories, as distinctly bad, with its cold, soggy sandwiches and pie. A hot digestible meal in the middle of the day or night is considered essential, and therefore all these plants are provided with kitchens, simply but sufficiently equipped with a stove for boiling water for tea and an oven to keep food hot. Opening one of these ovens, one finds them filled with bowls of meat and vegetable stew, or the meat pie the English are so fond of. If they wish, the men may bring a rasher of ham or bacon and a couple of eggs and have them cooked at noon. All day long tea may be brewed, and it is customary to allow 10 or 15 minutes in the middle of the afternoon for this; sometimes also in the middle of the morning. Nobody can deny the refreshing and restful effect of a cup of hot tea with milk and sugar in the course of the afternoon. Aside from the other effects of indigestion, one must not forget that it lessens elimination of a poison, makes it harder for the system to rid itself of what has been absorbed.

The conviction that industrial poisoning is greatly facilitated by poor and insufficient breakfasts has made these English employers provide milk for their workers in the morning as soon as they go on. A pint apiece is the allowance, and it is given free. The Germans are not so liberal since the war, but they provide hot coffee in the morning and afternoon, coffee and soup at noon, for one-tenth the usual price. Hot milk as an antidote for anilin poisoning holds a high place in English estimation. One manager said he had treated a man overcome from having his hands in anilin water—he was a bricklayer and had mixed his mortar with wash water that had a little anilin in it—by pouring hot milk and porridge down his throat till the man could hold no more. Hot coffee with milk is also used and is doubtless a good stimulant in such cases.

There is one American factory which gives the men in the dinitrobenzene department all the milk they will drink.

The need for continual, careful medical supervision in the manufacture of dyes and intermediates is greater now than it will be in a few years' time, for so long as the industry is still new and unfamiliar, so long as it is still in the experimental stage, it will be necessary to have the men's physical condition constantly under the observation of a doctor experienced in detecting the early signs of intoxication. All of the American plants employing large forces of men have some medical service, not always adequate, but some of the smaller ones dispense with medical supervision altogether. A plant in Massachusetts employing 90 men has not even a part-time doctor. As for the larger ones, it would be hard to explain the difference one finds in the proportion of doctors and nurses to the numbers employed in the different plants. Certainly it does not depend on the comparative dangers nor on the cleanliness or filthiness of the premises. In a dye and chemical works employing 1,600 men there are three nurses and one part-time doctor. In another employing 1,600 men there are five nurses and one full-time doctor with an assistant. A plant with 2,000 men manages to get on with the services of one doctor for two hours daily, one nurse, and one visiting nurse, while another with the same number of men has five full-time physicians and seven men nurses.

It must be remembered that a large part of the physician's time, sometimes almost all of it, is taken up with the examination of new applicants for work, so that unless he has ample assistance, he has little time to give to the very necessary work of protecting the men who are actually employed. The enactment of workmen's compensation laws in the different States has made the employer feel that he must protect himself against claims for physical disabilities which possibly may have been present when the man entered his employment, and therefore he insists on this preliminary examination. That this may involve an enormous amount of medical work can be seen by the record of one plant in which 420 to 470 new men are examined each month in order to keep up a force of 2,000.

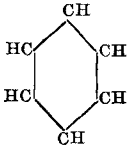
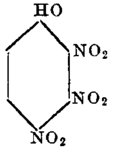
There are several companies that maintain a high standard of medical work. This means that the physician does not confine himself to office work, but makes frequent trips through the plant, familiarizing himself with the various processes, and learning just where the dangers are. Routine blood examinations are made of men who are in the more dangerous processes and who show slight signs of poisoning, and a fall in hemoglobin is the signal for suspension from work. In connection with this it is well to remember that the usual method of estimating hemoglobin does not give satisfactory results when the blood has a brownish tint, for then it is difficult to match it up with the color standard.

It should be a rule to suspend from process work any man whose hemoglobin is as low as 85 per cent, and not to return him to process work till he has gained at least 5 per cent. Sometimes extravagant claims are made by industrial physicians with regard to the improvement of men under treatment. One physician said that a man whose hemoglobin had been 98 per cent when he was employed and had fallen to 72 per cent, as a result of acute poisoning, had, under treatment, brought his hemoglobin back to 91 per cent in four days, the treatment consisting in light outdoor work and proper food. This seems perhaps not impossible, but certainly unexpectedly rapid. As a usual thing the return to a normal hemoglobin content is slow. Of course the man should always be removed from contact with the poison, but it is not enough for the doctor to order him out of doors. Sometimes the outdoor job is heavier and more fatiguing than his former work, and he is only telling the truth when he comes to the doctor complaining that he feels worse than he did when he was on his own job.

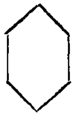
The question of rejections is very important. The procedure carried on in one large dye works already referred to is recommended—that is, a careful classification of work according to the risks involved. Here the men accepted for employment are assigned to one of the three classes of occupations, according to the doctor's findings. The blood pressure is taken and an examination is made of the urine as well as the usual physical examination. Men with slight abnormalities are not admitted to the more dangerous work, nor are any men under 18 or over 48 years of age. This classification also permits the doctor to shift a man from a dangerous job into a safe one with ease. It must be remembered that the mechanical department often contains the most dangerous work of all, cleaning and repairing, and that these men are usually less on their guard against dangerous compounds than are the process men, because they are not familiar with the nature of the compounds with which they come in contact.

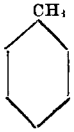
APPENDIXES.

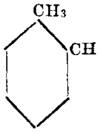
APPENDIX 1.—STRUCTURE OF THE BENZENE RING AND ITS PRINCIPAL DERIVATIVES, ISOMERIC FORMS, ETC.

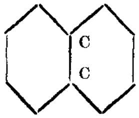
The benzene molecule is for convenience represented by a " ring " or hexagon which, if unmodified, stands for C_6H_6, or  Usually the carbon and hydrogen elements in a graphic formula are not written out, for it is understood that all replacements for the formation of new compounds take place at the expense of the hydrogen atoms and that no matter how complicated a series of such replacements may be, the original 6 carbon atoms of the ring remain unaltered. To illustrate, the formula for picric acid, trinitrophenol, is usually written thus,  the unoccupied angles of the hexagon are understood to be taken by the original hydrogen atoms.

Benzene is C_6H_6. Toluene is methyl-benzene, $C_6H_5CH_3$. Xylene is dimethyl benzene, C_6H_4 $(CH_3)_2$. The graphic formulas are these:

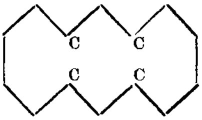




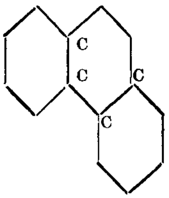


In naphthalene two benzene rings are joined directly together, at the expense of two hydrogen atoms, which results in the formula $C_{10}H_8$ or 

Anthracene is three such rings joined together, or $C_{14}H_{10}$.



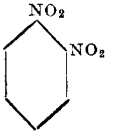
Phenanthrene has the same number of atoms as anthracene and its formula is also $C_{14}H_{10}$, but the three rings are differently grouped.

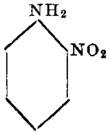


When the hydrogen of the benzene ring is displaced by HO, phenols result:
$C_6H_6+HO=C_6H_5HO$, hydroxybenzene, or phenol or carbolic acid.
$C_6H_6+2\ HO=C_6H_4(HO)_2$, dihydroxybenzene or resorcin.
$C_6H_6+3\ HO=C_6H_3(HO)_3$, trihydroxybenzene or pyrogallic acid.
$C_6H_5CH_3+HO=C_6H_4CH_3HO$, hydroxytoluene or cresol.

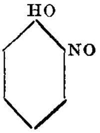
The introduction of the nitro group into the ring produces nitro compounds, such as nitrobenzene, $C_6H_5NO_2$, and dinitrobenzene, $C_6H_4(NO_2)_2$; nitrotoluene, $C_6H_4CH_3NO_2$, and trinitrotoluene, $C_6H_2CH_3(NO_2)_3$; nitronaphthalene, $C_{10}H_7NO_2$, and dinitronaphthol, $C_{10}H_5HO(NO_2)_2$.

Reduction of a nitrocompound changes the NO_2 radical to NH_2 and produces amido compounds. From nitrobenzene comes amidobenzene or anilin, $C_6H_5NH_2$. From dinitrobenzene, diamidobenzene, or phenylendiamine, $C_6H_4(NH_2)_2$. From nitrotoluene comes amidotoluene or toluidin, $C_6H_4CH_3NH_2$. From nitroxylene comes amidoxylene or xylidin, $C_6H_3(CH_3)_2NH_2$. The reduction may be partial, as when dinitrobenzene is reduced to nitranilin, thus:

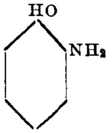




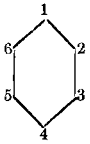
and this may be further hydrolyzed to nitrophenol:



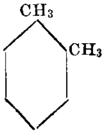
and then reduced to amidophenol:



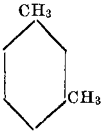
For convenience the angles of the benzene hexagon have been numbered in the order of the figures on the face of the clock.



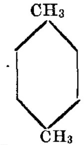
When only one hydrogen atom is replaced by a new atom or radical it is no importance which of the six is replaced, but when more than one is substituted several so-called isomers or isomeric forms are produced, bodies which have the same number of the same atoms, but are differently grouped and differ decidedly from each other in physical properties and in toxicity. For instance there are three xylenes, or dimethylbenzenes, $C_6H_4(CH_3)_2$.



Orthoxylene.

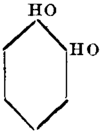


Metaxylene.

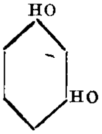


Paraxylene.

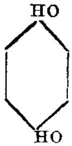
There are three dihydroxybenzenes, $C_6H_4(HO)_2$.



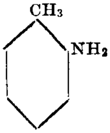
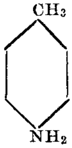
ortho, or pyrocatechin.



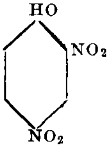
meta, or resorcin.



para, or hydroquinone.

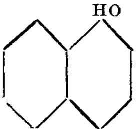
Orthotoluidin,  is an oily liquid at a temperature at which paratoluidin  is crystalline.

The prefixes commonly used, ortho, meta, and para, refer then to the different forms which result from the displacement of two of the hydrogen atoms of the ring. When there are more than two substitutions a much greater number of isomeric forms is possible, and these are designated by the numbers of the angles, 1-2-3, 1-2-4, 1-3-5, etc. Dinitrophenol 1-2-4 is this:

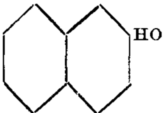


It differs toxicologically from all the other isomers.

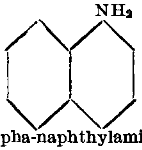
When two or more benzene rings are joined, as in naphthalene, two monosubstitution products are formed, according as the substituting atom or radical is combined with a carbon atom, which is in direct union with one of the common carbon atoms, or not. These two forms, known as alpha and beta, may be illustrated as follows:



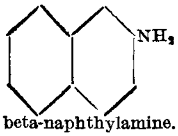
alpha-naphthol.



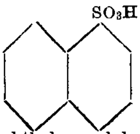
beta-naphthol.



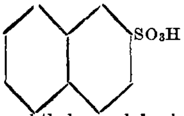
alpha-naphthylamine.



beta-naphthylamine.



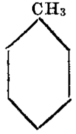
alpha-naphthalene-sulphonic acid



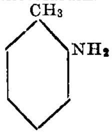
beta-naphthalene-sulphonic acid.

The compounds thus far described are all substitution products formed by replacement of the hydrogen of the ring. They differ in chemical and physical properties and in their effect on human beings from the substitution products, which are formed by displacement of hydrogen from a side chain, such as the radical CH_3. Thus if the hydrogen of the ring in toluene is displaced by NH_2, amidotoluene or toluidin, is formed, while if the replacement takes place in the CH_3 radical, we have benzylamine. A third compound, with the same elementary composition, results when the replacement is in the NH_2 group of amidobenzene, or anilin, and a CH_3 radical enters. This last is methyl anilin. These three compounds are very different in action and in properties.

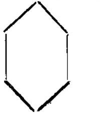
Toluene.



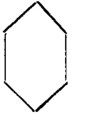
Orthotoluidin.



Benzylamine.

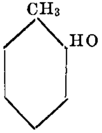


Methyl anilin.

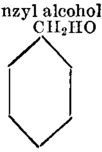


This distinction is very important, for the ring substitutions have in general the physiological action of benzene, while many of the products formed by replacement of hydrogen in the methyl group act like the alcohols. The following are some instances of these two kinds of products:[1]

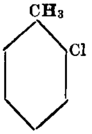
Orthocresol.



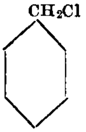
Benzyl alcohol.



Chlortoluene, formed by chlorine gas in toluene with heat.



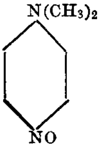
Benzyl chloride, formed by chlorine gas in toluene with cold.



Bodies similar to benzene substitution products may be formed from ammonia, H_4N, by substitution of one of the hydrogen atoms. Anilin is $C_6H_5NH_2$. Diphenylamine is $NH(C_6H_5)_2$.

These ammonia substitution products are slightly toxic if at all.

An instance of a body which is both a substitution and an addition product is nitrosodimethylanilin



When an amido compound of the benzene ring is acted on by nitrous acid, HNO_2, there results a series of intermediate compounds known as diazo com-

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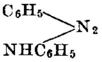
[1] Substitution products of toluene are usually called tolyl or toluyl compounds. Toluylendiamine is $C_6H_3CH_3(NH_2)_2$. Side-chain products are called benzyl. Benzaldehyde is C_6H_5CHO.

pounds which contain two nuclei bound together by—N_2—. Diazoamidobenzene is



$$\begin{matrix} C_6H_5 \\ NHC_6H_5 \end{matrix} > N_2$$

.Anilin, para and meta phenylendiamine, etc., yield these diazo compounds, and the latter unite with other amido compounds or with phenols to form azo coloring matters. For instance, the diazo compound of benzidin acting on alphanaphthylamine and sulphuric acid forms Congo red.

ALIPHATIC, FATTY, PARAFFIN SERIES.

These bodies are hydrocarbons derived from petroleum. They form the methane or marsh gas series, beginning with CH_4 and adding successive radicals of CH_2; the ethylene series, beginning with C_2H_4 and adding CH_2; and the acetylene series, beginning with C_2H_2. Substitution products formed with HO are alcohols; with COOH, acids; with Cl,Br.I, chlorides, bromides, iodides. Alcohols may be oxidized to aldehydes. Amines are ammonia substitution products.

To illustrate:

CH_4, marsh gas or methane.
CH_2OH, methyl or wood alcohol.
CHOH, formaldehyde.
CH_3Cl, methyl chloride.
$CHCl_3$, chloroform.
CH_2COOH, acetic acid.
C_2H_6, ethane.
C_2H_5HO, ethyl or grain alcohol.
C_2H_4O, acetaldehyde.
$C_2H_5NH_2$, ethylamine.

The combinations of CH_3,C_2H_5, etc., with the benzene ring, have already been spoken of.

Methylanilin.	Dimethylanilin.	Diethylanilin.
$C_6H_5NHCH_3$	$C_6H_5N(CH_3)_2$	$C_6H_5N(C_2H_5)_2$

APPENDIX 2.—PRODUCTS DERIVED FROM COAL.

The diagram facing this page and showing the products derived from coal and some of their uses is reproduced by permission of the Barrett Co., of New York City, by whom it was prepared.

APPENDIX 3.—MASSACHUSETTS: RULES AND REGULATIONS SUGGESTED FOR SAFETY IN THE MANUFACTURE OF BENZENE DERIVATIVES AND EXPLOSIVES.[2]

Evidence of the danger to the life and to the health of persons employed in the manufacture and use of various benzene derivatives has accumulated in this State during the past year. The experience of countries where manufacturing processes have been carried on in an extensive way for many years shows that the industry can be regulated without hindrance to its development and with comparative safety to the workers engaged in the manufacturing processes.

The State Board of Labor and Industries presents the following regulations to insure safety to the workers in this State, and will welcome any observations manufacturers or employees may desire to make on these proposals.

CLASSIFICATION.

The following substances shall come within these regulations:

Nitrobenzol.
Dinitrobenzol.
Dinitrotoluene.
Trinitrophenol (picric acid).
Trinitrotoluene.
Anilin hydrochloride.
Anilin oil.

Also all compounds in which any of the foregoing is a part of the manufacturing process.

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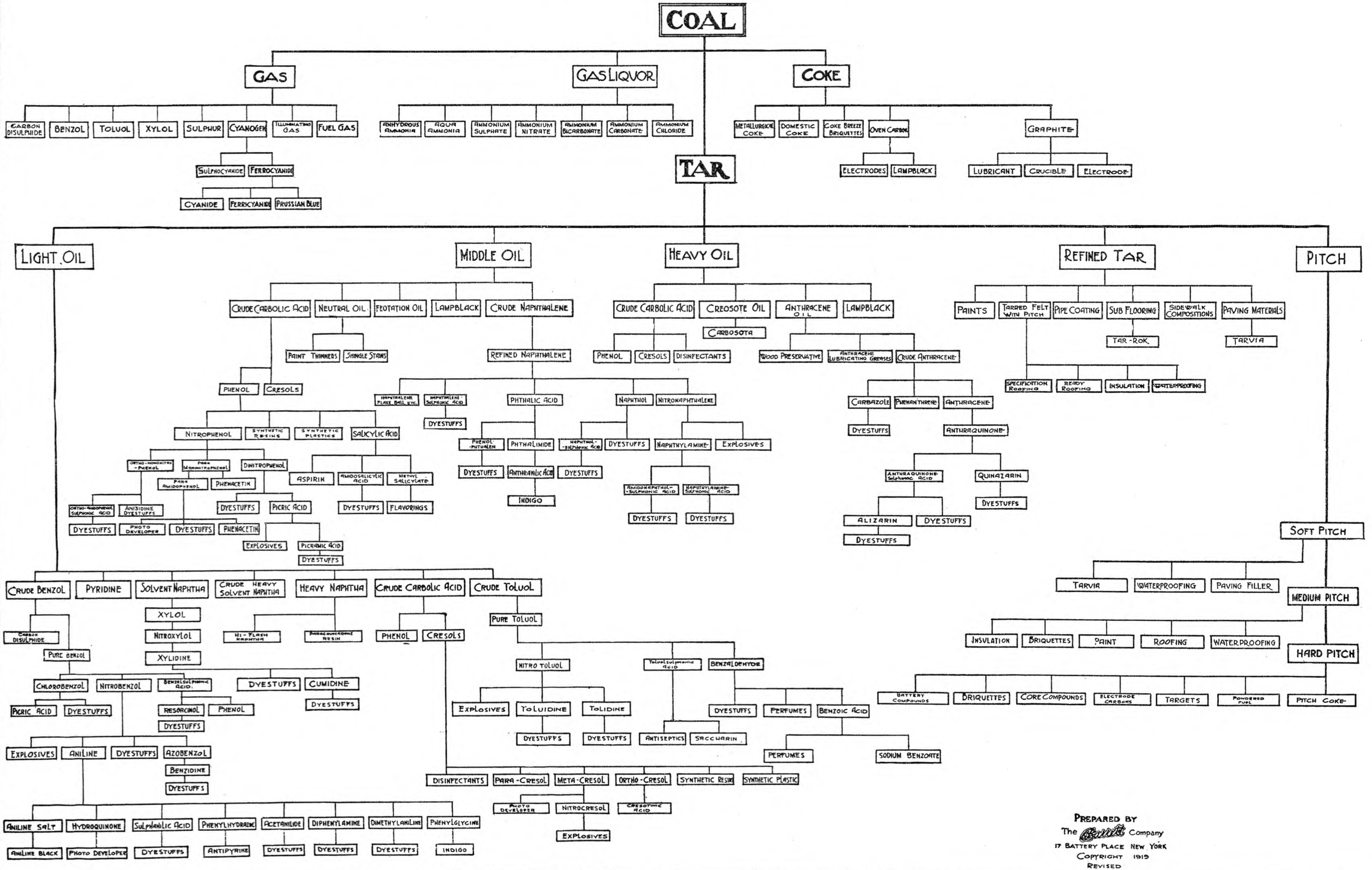
[2] Massachusetts. State Board of Labor and Industries. Industrial Bulletin No. 11. Boston, 1916.

PRODUCTS DERIVED FROM COAL



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DANGERS.

In the various processes of manufacture in which any of the foregoing substances are used, a danger to health arises in three ways, viz:

1. From the inhalation of fumes before the process of crystallization is completed.
2. From the inhalation of dust given off in the breaking up or crushing of the crystallized mass.
3. From the absorption through the skin by contact with the material in either the liquid or solid state.

PREVENTION.

The danger to health can be reduced to a minimum by—

1. The removal of fumes and dust.
2. The prevention of absorption of the poisonous material through the skin.

To make prevention effective the fumes and dust must be removed at or very near to the point where they are produced, and the following means employed:

A. VENTILATION.

1. Every vessel containing any substance included in these regulations shall, if steam is passed into or around it, or if the temperature of the contents be at or near the temperature of boiling water, be covered in such a way that no steam or vapor may be discharged into the open air at a less height than 25 feet above the heads of the workers.
2. In every room in which fumes from any of the substances included in these regulations are evolved in the process of manufacture and are not removed as provided in section 1 there shall be provided and maintained thorough ventilation by means of a fan or other exhaust system.
3. No substances mentioned in these regulations shall be crushed, ground, mixed, or packed in a crystalline condition except with an efficient exhaust system, so arranged as to carry away the dust as near as possible at its point of origin.
4. No substances mentioned in these regulations shall be broken by hand in a crystallizing pan, nor shall any liquid containing it be agitated by hand, except by means of an implement at least 6 feet long that shall prevent the workers' hands and faces from coming into close proximity with the substances used.
5. In the filling of cartridges with any of the substances mentioned in these regulations, the process shall not be done by hand except by means of suitable scoops.
6. Drying stoves shall be efficiently ventilated to the outside air in such a manner that hot air from the stoves shall not be drawn into the workroom. No person shall be allowed to enter a stove to remove the contents until a free current of air has been passed through it. All openings in stoves, retorts, vats, etc., for the admission of workmen into the interior of such stoves, vats, etc., shall be sufficiently large to permit the easy passage of the body of such workmen.

B. WASHING FACILITIES.

There shall be provided and maintained in a cleanly state, in good repair, and properly lighted for the use of all persons employed on the substances mentioned in these regulations—

1. At least one washbowl, sink, or other appliance for every five persons, and provided with running hot and cold water.

The number of bowls, sinks, or other appliances required shall be based upon the maximum number of persons entitled to use the same at any one time. Twenty inches of sink will be considered as equivalent to one washbowl.

2. A lavatory within reasonable access and under cover, with a sufficient supply of clean towels and of soap, and nail brushes.
3. Sufficient and suitable bath accommodations (shower or other) with hot and cold water, and a sufficient supply of soap and towels.

C. TOILET FACILITIES.

Rules and regulations for toilet facilities adopted by the State Board of Labor and Industries shall prevail in all establishments where the manufacturing processes concerned in these special regulations are carried on.

D. SPECIAL CLOTHING.

There shall be provided and maintained for the use of all persons employed in the manufacturing processes included in these regulations—

1. Suitable overalls or suits of working clothes. Overalls included in these regulations shall be washed or renewed at least once every week.
2. India-rubber gloves, which shall be collected, examined, and cleansed at the close of the day's work and shall be repaired or renewed when defective. Equivalent protection for the hands, when they come in contact with the substances mentioned in these regulations, may be substituted for gloves.
3. Clogs or other suitable protection for footwear that shall guarantee against contact with the substances mentioned in these regulations.
4. A suitable clothes room for changing and for keeping clothing put off during working hours.
5. A suitable locker, separate from the clothes room and meal room, for the storage of overalls and other work clothes.

E. DINING ROOM.

1. In establishments included in these regulations a suitable meal room shall be provided unless the establishment is closed during the meal hours. This dining room shall be separated from any room in which a process using materials mentioned in these regulations is carried on.
2. Suitable provisions shall be made for the keeping of food brought by persons employed.
3. Adequate washing facilities, equipped with running hot and cold water, shall be provided in or adjacent to the meal room.
4. No person shall introduce, keep, prepare, or partake of any food, drink, or tobacco in any room in which a process using substances mentioned in these regulations is carried on.

MEDICAL REQUIREMENTS.

Each establishment in which manufacturing processes using materials mentioned in these regulations are carried on shall employ and keep in employment one or more duly qualified physicians to act as medical officer or officers, who shall be in attendance at all necessary times while such work is in progress, so as to guarantee constant medical supervision and care of workers engaged in these processes of manufacture.

Such medical officer shall also be charged with the duty of enforcing the following regulations:

1. Examine every person employed in these processes of manufacture either before said person begins employment, or within seven days after beginning said employment.
2. Reexamine every person employed in these processes at least once in each calendar month, or at such other intervals as may be necessary to insure protection to the workman against poisoning from the substances used in the process of manufacture; also before permitting a workman to return to work after absence or suspension on account of illness.
3. The medical officer shall have the power of suspension because of physical unfitness of any person employed on any of these processes of manufacture, and no person, after such suspension, shall be reemployed without written sanction of the medical officer.
4. The medical officer shall give such instruction to employers and to employees concerning the danger to health from the particular process of manufacture being carried on in the establishment as will best qualify such persons to—
   (*a*) Recognize the signs of poisoning.
   (*b*) Apply suitable first-aid treatment to workmen taken ill upon the premises.
5. The medical officer shall keep a full and complete record of all examinations made by him, which record shall contain the date on which examinations are made, name, address, age, height, weight, physical condition of heart and lungs of all persons examined by him; also a full and complete record of all illnesses, accidents and deaths occurring among the employees under his charge. These records shall be open to the inspection of the State board of labor and industries or its representatives, and a copy thereof shall be forwarded to said

board within 48 hours following the occurrence of the accident, illness, or death, stating as fully as possible the cause of said illness, accident, or death of employees.

No statement contained in any such report shall be admissible as evidence in any action arising out of said accident, illness, or death herein reported.

6. There shall be provided a suitable medical or hospital room for the care and treatment of workmen taken ill upon the premises. This room shall be conveniently located, properly lighted, heated, and ventilated, and shall contain the following minimum equipment:

(*a*) A couch or bed.
(*b*) Pair of blankets.
(*c*) Two hot-water bottles.
(*d*) Tank of oxygen, with apparatus for using the same.
(*e*) A lungmotor.
(*f*) An oxygen helmet for rescue work.
(*g*) Suitable ropes for rescue work.
(*h*) Medical and surgical chest as prescribed by the rules of the State board of labor and industries.

PRINTED NOTICE POSTED.

A printed notice in language intelligible to all the workers, and in type sufficiently large to be legible to all workers, labeled "CAUTION," shall be conspicuously posted and maintained in all departments where any of the substances mentioned in these regulations are used in any processes carried on therein. Said notice shall contain the following:

1. In large conspicuous type the common name of the poisonous substance in use in that particular room.

2. That the substance named is capable of causing poisonous symptoms if precautions are not observed.

3. Signs and symptoms of poisoning, viz, throbbing of blood vessels, giddiness, dizziness, headache, weakness of legs, palpitation of heart, nausea, blueness, cyanosis, unconsciousness.

4. First-aid treatment, viz.:

(*a*) Remove poisoned person to the fresh air. Keep him quiet and warm.
(*b*) Do not let person walk home until advised by physician.
(*c*) Use hot coffee as stimulant.
(*d*) If person is unconscious, apply artificial respiration; lungmotor; oxygen inhalation; keep patient warm.

5. Prevention:

(*a*) Avoid dust, fumes, and chemical compounds on hands, feet, and clothes.
(*b*) Wash hands before eating and after day's work is finished.
(*c*) Do not eat food nor chew tobacco in workroom.
(*d*) Do not wear same clothes in workroom and at home.
(*e*) Use extra protection on hands, feet, and clothes while at work on any of the substances mentioned in these regulations.
(*f*) Bathe regularly.
(*g*) Consult a physician if losing color or weight.
(*h*) Do not enter stoves, vats, or retorts for repair work unless in the presence of another workman.
(*i*) Have emergency appliances ready for use in all dangerous repair work.
(*j*) Watch for leaky joints in pipes, ducts, valves, etc., carrying the gas or chemical compounds.

APPENDIX 4.—SAFETY STANDARDS FOR THE MANUFACTURE OF NITRO AND AMIDO COMPOUNDS ADOPTED BY NEW JERSEY AND PENNSYLVANIA.

SECTION 1. For the purpose of these regulations the following nitro and amido compounds shall be considered injurious to health.

(*a*) The nitro compounds of benzol, toluol, xylol, etc., as well as their chlorine derivatives.

(*b*) The nitro compounds of naphthaline.

(*c*) The twice or higher nitrated compounds of phenol and naphthol.

(*d*) Aniline and its homologues (toluidine, xylidine, cumidine, etc.), anisidine, phenetidine and their chlorine, nitro, and alphyl derivatives, as dimethyl and diethyl aniline, diphenylamine, etc. The salts of these compounds are comparatively innocuous and do not come under these regulations.

(*e*) Phenylenediamine, tolylenediamine.

(*f*) Benzidine, tolidine, dianisdine.

(*g*) The naphthylamines. The salts of these compounds are comparatively innocuous and do not come under these regulations.

(*h*) Phenyl and tolyl hydrazin.

Factories in which the above compounds are regularly recovered in considerable quantities are mainly:

Fuchsin, aniline blue, violet, and nigrosin factories.

SEC. 2. BUILDINGS.—The buildings in which nitro and amido compounds are manufactured or are regularly recovered in considerable quantities shall be properly ventilated.

Buildings in which twice or more nitrated compounds of benzol or of toluene or of phenol are manufactured shall be of fire-resisting material or shall be separated from other buildings.

SEC. 3. PLATFORMS.—In the above buildings, operating platforms may be erected, provided they do not cover more than three-fourths of the ground floor. In buildings constructed after the adoption of these regulations, the distances of platforms (under which workingmen may be required to work) from the floor and from each other shall be at least 9 feet. In buildings already constructed this distance shall be at least 7 feet. (It is recommended to leave between platforms and the outer walls either a free space or a space covered by slats 18 inches to 3 feet wide; and the area of this space is to be added to the free space in calculating the latter.)

On top of melting kettles and distilling apparatus, only such platforms shall be built as are absolutely necessary for the proper handling of the apparatus, and care should be taken that all apparatus be so constructed that vapors and gases can not escape, and thereby injure those obliged (by reason of their duties) to be upon said platforms.

Platforms on which work is regularly carried on with nitro and amido compounds shall be light and easy to clean; covered with sheet lead where advisable.

Platforms shall be equipped with railings and toe boards, in accordance with the safety standards on these subjects of the department of labor.

SEC. 4. FLOORS.—The floor of the workrooms and the storage room shall be nonabsorbent, smooth, and easy to clean. Where necessary, wooden or cement floors are permissible.

SEC. 5. WALLS.—The walls of the workroom shall be kept clean. If painted with calcimine they shall be repainted at least once a year. Windows which can be opened shall be provided on at least two sides of the room.

SEC. 6. ROOF.—The roof shall have a sufficient number of ventilators or other appliances, which allow sufficient ventilation of the workroom, and which can be kept open, even if it rains. Windows or skylights shall be so constructed that they can be operated from the floor or platform. Skylights in the roof shall be constructed of wire glass.

SEC. 7. MANUFACTURE.—The work in the above factories shall be regulated in such manner that the men do not come in direct physical contact with nitro and amido compounds. It is therefore recommended, when practicable, that liquid nitro and amido compounds be transported through closed pipe lines either by pumping, blowing, suction, or by gravity.

As a general rule gravity or suction is to be preferred, because in the use of compressed air fine parts of the compounds go off with the air. It is also necessary that spent compressed air be vented outside. If, in the latter case, this is obnoxious to the neighborhood, it is suggested that the spent air shall be purified before being expelled. The same refers to the air which is expelled from vacuum pumps of distilling apparatus, as it frequently contains small quantities of anilin, etc.

Liquid nitro and amido compounds shall be kept and stored only in covered vessels. Wherever the above nitro and amido compounds are handled in such a manner that dust, gases, or vapors are generated (especially in powdering, sifting, and packing operations), the work shall be carried on as far as practicable in covered or closed apparatus. The vapors from receivers of distillates shall be excluded from work buildings.

Chiseling out of solid nitro and amido compounds, which are explosive, is strictly forbidden; and, when these are poisonous, is permitted only if proper precautions are taken.

Drying should be done in separate buildings used for drying only, or in properly constructed apparatus.

Frequently drying can be avoided by melting the nitro and amido compounds, and breaking them up when cold.

Where boilers are fed with water containing aniline the boiler shall be fitted with suitable safety valves and water glasses, which absolutely prevent the entering of steam or water containing aniline into the workroom.

Nitrating apparatus.—In nitrating benzol and similar compounds, which are readily inflammable or generate inflammable or explosive vapors, the following precautions must be observed:

(*a*) The service pipe from the acid container to the nitrating vessel, where possible, shall be of such a diameter that at no time can an excessive amount of acid be conducted into the nitrating tank. The diameter of this pipe must, of course, depend entirely on the size of the container which it supplies with acid.

(*b*) The nitrating tank shall be fitted with a safety device so that the faucet of the acid tank can not be opened until the stirring apparatus of the nitrating tank has been put in motion. This rule is due to the fact that if a large quantity of acid accumulates in the bottom of the nitrating vessel (due to its not being constantly stirred) a powerful chemical reaction will occur when the stirrer suddenly starts up, and there is sudden combination with the benzol.

(*c*) The protruding end of the shaft of the stirring apparatus shall be fitted with a pendulum or similar device, so that persons in charge may, from a distance, know that the stirring apparatus is actually in motion and keeping the mixture constantly agitated, thus preventing undue generation of heat.

(*d*) The nitrating vessel must be equipped with a large pipe (which is to act in the capacity of a safety valve) extending through the roof, and provided on top with a suitable arrangement, which, while keeping the pipe closed ordinarily, will open when a dangerous pressure developes in the nitrating vessel.

When, in the judgment of the commissioner of labor or his authorized representative, it is deemed necessary, all apparatus and machinery in which nitro and amido compounds are manufactured, transported, treated, distilled, centrifuged, filtered, dried, ground, mixed, etc., packed or filled, shall be fitted with reliable attachments to remove such dust, gases, or vapors as may be generated.

Special care shall be taken so that all vapors generated in the opening, discharging, and filling of dry rooms, melting kettles, autoclaves, and other pressure vessels will be harmlessly disposed of, when in the judgment of the commissioner of labor or his authorized representative it is deemed necessary to do so.

SEC. 8. CLEANLINESS.—The workroom shall be kept as free from nitro and amido compounds as possible. If any of the above compounds are spilled they shall be removed as soon as possible. The floor shall be cleaned at least once every 24 hours.

SEC. 9. HEALTH PRECAUTIONS.—The employer shall inform the workingmen employed in the manufacture, etc., of the above nitro and amido compounds as to the poisonous quality of these products and the necessity of strictly observing the following precautions:

Shirts, overalls, caps, stockings, shoes, gloves, and other wearing apparel which have become saturated with poisonous nitro or amido compounds in such manner that the skin comes in immediate contact with them shall be immediately taken off; the skin washed first with vinegar and then with water; and the employee must then put on clothing which has not been in contact with these substances.

Employees shall be warned that the use of alcoholic liquors and chewing tobacco is harmful to their health. Smoking in the workroom is strictly forbidden.

Food shall be neither kept nor eaten in the workroom. A suitable dining room, absolutely separate from the workroom, shall be provided. Employees shall not be allowed to enter this room until they have washed both face and hands. For this purpose wash and dressing rooms and bathrooms, absolutely separate from the workroom, shall be provided. These rooms shall be suitably fitted up, kept clean, and properly heated. Nobody shall be allowed to keep any wearing apparel in the workroom. All process men shall dress in the dressing or wash room provided. Each process man shall be provided with two lockers, one for his working and one for his street clothing, or a properly divided double locker, or such other method for storing clothing as shall be approved by the commissioner of labor or his authorized representative. An approved number of washing appliances shall be provided. Soap and towels shall be furnished in suitable number and free of charge.

It is recommended that every working man who comes in contact with the above nitro and amido compounds shall take a bath daily before he leaves the factory.

Men who suffer from inflammation of the bladder should not be employed in the above factories.

Men who are addicted to the use of alcoholic liquors must not be employed, and no employee upon whom the odor of alcoholic liquor is detected shall be allowed to enter the factory.

It is recommended that process men be between the ages of 22 and 50 years. It is also recommended that applicants for employment presenting evidences of anemia or of emaciation should not be employed as process men by reason of their increased susceptibility.

The employment of females except in the office, or works hospital, or welfare room or building, is prohibited.

Toilets shall be provided in accordance with the sanitary code of the department of labor.

The employer shall provide and maintain a sufficient number of sanitary drinking fountains, readily accessible, for the use of all employees.

All process men should be cautioned of the danger of commencing work on an empty stomach.

It is recommended that those who suffer from excessive perspiration should not be employed as process men.

Bodily cleanliness is essential to good health. It is recommended that those employees who do not take frequent baths be not employed as process men.

Process men are those employees whose work brings them in immediate contact with nitro and amido compounds, either in the manufacture of these compounds or in the repair of apparatus used in their manufacture. The term does not include employees whose duty is in the power plants or other employees whose work does not bring them in such contact.

Sec. 10. Repairs.—All repairs and changes on the machinery, apparatus, and pipes for nitro and amido compounds shall be made only after they have been thoroughly cleaned.

All work in the inside of apparatus, vessels, boilers, etc., shall be done in accordance with the following rules of procedure:

If it is necessary for an employee to enter vats, tanks, or other containers in which there have been used, stored, or manufactured gases, fumes, or vapors of an asphyxiating or poisonous nature, or materials which give off gases, fumes, or vapors of an asphyxiating or poisonous nature, the following procedure shall be pursued:

(*a*) Empty containers. Disconnect and blank off all connections.

(*b*) Clean containers thoroughly by repeated washings with water, soda water, steam, compressed air or other suitable means.

(*c*) If the person in charge then considers conditions satisfactory, employees may enter such containers. They must use an approved type of helmet, and have attached to their bodies a life line or rope if the person in charge considers it necessary.

(*d*) The life line or rope shall be under the control of one or more fellow-workmen, who shall remain outside of the container in order that they may render assistance if necessary.

(*e*) After the work is finished the men should take, at once, a bath and change their clothing, including shoes, if the foreman or other person in charge shall deem it necessary. Facilities for taking such baths shall be provided.

The superintendent of the plant shall be held responsible for the enforcement of these regulations.

A copy of the rules for procedure as given above will be furnished by the department of labor and shall be conspicuously posted at every place in each plant where asphyxiating or poisonous fumes, gases or vapors may be found.

Sec. 11. Resuscitation.—For every 50 process men or less employed in such plant and exposed to such risk there shall be present at all times at least 2 persons who are trained or competent to apply means of resuscitation by the prone pressure or Shaeffer method, or by mechanical devices approved by the commissioner of labor.

A sufficient number of helmets of a type approved by the commissioner of labor shall be kept at each plant, in order that they may be available for use by every employee who has occasion to enter places where there may be asphyxiating or poisonous gases, fumes or vapors.

All employees who are required by the employer to wear helmets in making repairs or in maintenance work shall be thoroughly instructed in the use of such apparatus; and be physically examined by a licensed physician at least once in ninety days or after absence from work due to either sickness or accident. The physician shall certify to the proper physical condition of the men so employed; and no employee shall be permitted to do such repair work unless so examined and certified. The examining physician shall report the results of these examinations, within 48 hours after each examination, to the commissioner of labor, upon blanks which will be furnished upon request.

Oxygen inhalation apparatus shall be kept on hand and the foremen and authorized employees shall be instructed in its use. In all cases in which the apparatus has been used, a physician shall at once be called or the sick employee removed to a hospital. A supply of oxygen or the means for its production must be kept on hand.

If oxygen tanks are used at least two must be kept on hand at all times, one of which shall be full.

SEC. 12. PHYSICAL EXAMINATION.—All applicants for employment as process men shall be physically examined by a licensed physician, either before commencing work, or before the expiration of 24 hours after their employment.

All process men shall be physically reexamined by a licensed physician at least once every 30 days, and before resuming work after an absence due to sickness or to accident or to any other cause.

These examinations shall each consist in the determination and recording of the following facts, either in a book or upon a card:

Name ____ Age ____________
Address ____ Process ____________
Height ____ Weight ______________
Examination of urine: Reaction ______________ Specific gravity ______________
Pulse ______________ Blood pressure ______________ Hemoglobin ______________
Albumen ________________ Sugar ________________ Casts ________________

The records of these examinations shall at all times be open for inspection by the commissioner of labor or his authorized representative.

The examining physician shall report the results of these examinations to the commissioner of labor within 48 hours after such examinations, upon blanks which will be furnished upon request.

It shall be the duty of the examining physician to request the factory manager or superintendent to suspend from work any process man whom he believes to be suffering from poisoning; and it shall be his further duty to report such case to the department of labor upon the following blank:

STATE OF ______________________
DEPARTMENT OF LABOR,
BUREAU OF HYGIENE AND SANITATION.
Report of case of occupational disease.

Please mail this report in all cases of either suspected or diagnosed industrial disease to Bureau of Hygiene and Sanitation, Department of Labor, ____________, which will furnish additional copies of this blank upon request.

Name of patient____

Address, street, and number______________________ City or village______________ County______________

Sex__________ Age__________ Color__________ Nativity__________

S. M. W. D. Number of dependents______________________

OCCUPATION.

A. Present trade, profession, or work______________________

B. Exact occupation in this trade______________________

C. Date of entering this trade______________________

D. Date of commencing this work______________________

E. Previous occupations______________________

Name of occupation.	Entered.	Left.
1. ______________	______________	______________
2. ______________	______________	______________
3. ______________	______________	______________

F. Previous illness, if any, due to occupation______________________

1. ____
2. ____
3. ____

G. Employer's name______________________

H. Employer's address, street and number______________________

City or village______________________

I. Employer's business______________________

A. Diagnosis of present illness______________________

B. Chief symptoms______________________

____

____

____

____

C. Date first symptoms appeared______________________

D. Complicating diseases______________________

____

____

____

____

E. Additional facts______________________

____

____

F. Date of diagnosis______________________

G. Date of this report______________________

Signed______________________M. D.
Address, street and number______________________
City or village______________________

When in the judgment of the commissioner of labor it is necessary, it will be the duty of the employer to provide, without expense to the employee, a hospital room or dispensary, separate and apart from the workroom or rooms; which room shall be equipped with a couch, bed, or surgical table, two pairs of woolen blankets, two hot-water bottles, two tanks (one completely full) of oxygen, and the necessary apparatus for administering the same; an oxygen helmet for rescue work; such device or devices for artificial respiration as are approved by the department of labor; and a shower bath with hot and cold water; and a toilet, which toilet shall comply with the sanitary code of the department of labor.

At least one stretcher shall be provided.

It shall be the further duty of all employers to keep in a book or on a card a record of all employees, showing their exact employment and all changes to other work; which record shall at all times be open for inspection by the commissioner of labor or his authorized representative.

TRINITROTOLUOL.

Section 13. Scope.—Beyond the regular regulations for the erection and conducting of factories in which poisonous nitro and amido compounds are manufactured, or regularly recovered in considerable quantities, the following additional regulations shall govern the manufacture of trinitrotoluol and ammunition derived from it.

Sec. 14. Buildings.—Trinitrotoluol shall be manufactured in a special plant which is an approved distance from other factories or portions of factories.

Buildings in which twice or more nitrated compounds of benzol, or twice or more nitrated compounds of toluol are manufactured, shall be of fire resisting material or shall be separated from other buildings.

Trinitrotoluol factories which are not on the land of an explosives factory shall be surrounded by a fence, which prevents the entrance of outsiders. At the gates proper signs shall be provided, which prohibit the entrance of unauthorized outsiders. Smoking upon the premises shall be prohibited.

Sec. 15. Nitration.—Nitration shall be performed in high airy rooms, allowing easy escape of vapors, and in which no nitrated product is stored or handled in a dry condition. There shall be an approved number of easily accessible exits.

Sec. 16. Storage of acids.—Spent acids shall be stored in tanks, standing in the open air and only roofed over.

Sec. 17. Washing and centrifuging.—All washing and centrifuging operations shall be performed in a building in which no nitrated product is stored. Ample ventilation shall be provided.

Sec. 18. Recrystallization.—The recrystallizing of the crude trinitrotoluol with easily inflammable solvents, such as alcohol, benzol, or toluol, shall take place in a building standing alone. All solution tubs, crystallizing vessels, centrifuges, and conveying apparatus, shall be closed in such manner that vapors in dangerous quantities can not escape into the workroom. Proper ventilation of the workroom shall be provided. All platforms in this building shall have an exit into the open air.

Sec. 19. Drying.—The drying of the trinitrotoluol shall be carried on in a building standing alone. The separation of the pure trinitrotoluol from the solvent may be done in the building for the recrystallizing, if the apparatus provided avoids accumulation.

Sec. 20. Packing.—All packing shall be done in separate packing houses.

Sec. 21. Storage.—Trinitrotoluol shall be stored in separate stock rooms, protected by an approved type of barricade. The location of the stock rooms from the nearest manufacturing building shall be at an approved distance.

Sec. 22. Storage of inflammable solvents.—The storage of tanks of inflammable solvents or of toluol shall be constructed in such a manner that the contents of the tanks, in case of leakage, can not run over the surroundings. Wherever practicable storage vessels should be below ground. If the above solvents are stored above ground they shall be stored in an approved manner. Storage in open air in iron drums in a suitable place is permissible.

Earth embankments of sufficient height to hold the contents of tanks in case of leakage shall be placed around all tanks of inflammable materials when such tanks are located above ground.

SEC. 23. MANUFACTURE OF AMMUNITION.—The manufacture of ammunition from trinitrotoluol shall be conducted in a separate building or plant. For the storage of the ammunition the same regulations govern as for the storage of the trinitrotoluol.

SEC. 24. DOORS.—All doors which lead into the open air shall open outward.

SEC. 25. NITRATING APPARATUS.—All nitrating vessels shall have reliable appliances for stirring and for the regulation of the temperature, as well as ventilating apparatus for the removal of the vapor.

SEC. 26. DRYING APPARATUS.—If the drying is done on small drying hand trays the heating elements shall be arranged in such a manner that the material to be dried, or the dust, can not come in direct contact with them. The temperature in the drying chambers shall not exceed 60° centigrade [140° Fahrenheit]. All drying apparatus shall be constructed in such manner that the gases can escape easily without dangerous pressure, if the trinitrotoluol should ignite.

If the drying is done in large drying pans, hot water or low-pressure steam, at not over 20 pounds pressure per square inch, shall be employed for heating. The contents shall be kept in constant motion, and the apparatus shall be constructed so as to prevent the escape of vapors into the workroom.

SEC. 27. DUST.—The drying and sifting apparatus shall be so constructed as to prevent as far as practical the escape of dust. All walls, floors, radiators, electric bulbs, etc., shall be kept free from the accumulation of trinitrotoluol dust. All employees shall be provided without cost with respirators, cloths, or sponges, for their protection against dust.

SEC. 28. FIRE PREVENTION.—In rooms in which there are easily inflammable solvents or dried TNT (trinitrotoluol), electric motors, electric bells, or other sparking apparatus shall not be employed. Centrifugals shall neither have a brake, nor shall it be allowed to brake them in any improvised manner. Oily waste shall be kept outside the workroom in safety cans, which shall be cleaned frequently. In all drying, breaking, and sifting operations the friction of iron against iron shall not be permitted.

SEC. 29. REFUSE.—Impure trinitrotoluol shall be refined and purified before being used. All refuse from the nitration or recrystallizing rooms which is still useful shall be removed from the above rooms, and shall be kept in a special room until it is refined. It shall not be permissible to bury any refuse which contains trinitrotoluol. Such refuse shall be placed in containers, and shall be destroyed from time to time under the supervision of an experienced foreman.

SEC. 30. REPAIRS.—Repairs on apparatus and other tools which have been in contact with trinitrotoluol are permissible only after they have been thoroughly cleaned. The remelting of old vessels, lead pipe, etc., is permissible only after they have been burned off on an open fire. All other vessels, etc., which have become useless, shall be treated in the same manner or shall be destroyed by explosion.

SEC. 31. NITRIC ACID.—In view of the danger to the worker from inhalation of nitrous fumes in case of fire or of the breakage of carboys, carboys containing nitric acid shall be stored in detached sheds, with sandstone, brick, or other suitable flooring; and in quantities not to exceed 100 carboys placed in not more than four rows. Nitric acid in carboys may be stored in the open in unlimited quantities.

The following notice will be supplied by the department of labor on application, and shall be posted at all places in plants where there is danger of poisoning by acid fumes:

ACID FUMES—WARNING.

THE INHALATION OF DENSE ACID FUMES MAY CAUSE DEATH.

Employees are strictly prohibited from entering buildings where dense acid fumes exist, or tanks or confined spaces which are not entirely clear of acid fumes, unless they wear a helmet.

Employees working in such places shall, in addition to the helmet, wear a life line, which is at all times in the hands of an assistant stationed outside of the tank.

Employees who have been exposed to acid fumes and who feel weak, sick, short of breath, or who are attacked with cramps or coughing, shall report this condition to their foremen, or to the works dispensary, or hospital, at once, so that proper treatment can be given. They must not wait to get home. Delay may be fatal.

Responsibility for complying with these regulations shall rest with the foreman or other person designated for that purpose by the management of the plant.

By order of—

——— ———,
Commissioner of Labor.

Water shall always be available for use in case of evolution of nitrous fumes caused by breakage or other accident to carboys, and all workers handling such acid shall be warned against sprinkling sand, sawdust, earth, or anything other than water or alkalies upon any spilled nitric acid.

At all places where there is danger of an employee becoming burned by contact with acid there shall be a shower bath.

Sec. 32. Avoidance of accumulations.—No more trinitrotoluol shall be kept in the workroom than is necessary for concurrent use.

CHEMICALS.

Section 33. Scope.—The handling and storage of all acids and other chemicals necessary for the operation of plants not herein provided for, shall be governed by regulations as set forth in the code governing the operation of chemical works.

Sec. 34. Heating.—The workrooms, when desirable, shall be heated by an approved system of steam, indirect hot air radiation, or hot water. The temperature of the steam shall not exceed 120° Centigrade [248° Fahrenheit]. The radiators shall be at least 1 inch distant from all wooden walls or other inflammable material, and shall be attached in such a manner that they can be easily inspected and cleaned.

APPENDIX 5.—GREAT BRITAIN: REGULATIONS FOR THE MANUFACTURE OF NITRO AND AMIDO DERIVATIVES OF BENZENE AND OF EXPLOSIVES WITH USE OF DINITROBENZOL OR DINITROTOLUOL.[3]

Whereas the manufacture of nitro and amido derivatives of benzene, and the manufacture of explosives with use of dinitrobenzol or dinitrotoluol, have been certified in pursuance of section 79 of the factory and workship act, 1901, to be dangerous;

I hereby, in pursuance of the powers conferred on me by that act, make the following regulations, and direct that they shall apply to all factories and workshops in which the said manufactures are carried on.

Provided that regulations 1 (*a*), 2, 3, 4, and 14 (*c*) shall not apply to any process in the manufacture of explosives in which dinitrobenzol is not used.

DEFINITIONS.

" Employed " means employed in any process mentioned in the schedules.

" Surgeon " means the certifying factory surgeon of the district or a duly qualified medical practitioner appointed by written certificate of the chief inspector of factories, which appointment shall be subject to such conditions as may be specified in that certificate.

" Suspension " means suspension by written certificate in the health register, signed by the surgeon, from employment in any process mentioned in the schedules.

DUTIES.

It shall be the duty of the occupier to observe Part I of these regulations.

It shall be the duty of all persons employed to observe Part II of these regulations.

PART I.—DUTIES OF OCCUPIERS.

1. (*a*) Every vessel containing any substance named in schedules A or B shall, if steam is passed into or around it, or if the temperature of the contents be at or above the temperature of boiling water, be covered in such a way that no steam or vapor shall be discharged into the open air at a less height than 20 feet above the heads of the workers.

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[3] Great Britain. Home Office. Statutory Rules and Orders, 1908. No. 1310.

(*b*) In every room in which fumes from any substance named in schedules A or B are evolved in the process of manufacture and are not removed as above, adequate through ventilation shall be maintained by a fan or other efficient means.

2. No substance named in schedule A shall be broken by hand in a crystallizing pan, nor shall any liquor containing it be agitated by hand, except by means of an implement at least 6 feet long.

3. No substance named in schedule A shall be crushed, ground, or mixed in the crystalline condition, and no cartridge filling shall be done, except with an efficient exhaust draught so arranged as to carry away the dust as near as possible to the point of origin.

4. Cartridges shall not be filled by hand except by means of a suitable scoop.

5. Every drying stove shall be efficiently ventilated to the outside air in such manner that hot air from the stove shall not be drawn into any workroom.

No person shall be allowed to enter a stove to remove the contents until a free current of air has been passed through it.

6. A health register, containing the names of all persons employed, shall be kept in a form approved by the chief inspector of factories.

7. No person shall be newly employed for more than a fortnight without a certificate of fitness granted after examination by the surgeon by signed entry in the health register.

8. Every person employed shall be examined by the surgeon once in each calendar month (or at such other intervals as may be prescribed in writing by the chief inspector of factories) on a date of which due notice shall be given to all concerned.

9. The surgeon shall have power of suspension as regards all persons employed, and no person after suspension shall be employed without written sanction from the surgeon entered in the health register.

10. There shall be provided and maintained for the use of all persons employed—

(*a*) Suitable overalls or suits of working clothes which shall be collected at the end of every day's work, and (in the case of overalls) washed or renewed at least once every week; and

(*b*) A suitable meal room, separate from any room in which a process mentioned in the schedules is carried on, unless the works are closed during meal hours; and

(*c*) A suitable cloakroom for clothing put off during working hours; and

(*d*) A suitable place, separate from the cloakroom and meal room, for the storage of the overalls.

For the use of all persons handling substances named in the schedules—

(*e*) India-rubber gloves, which shall be collected, examined, and cleansed, at the close of the day's work, and shall be repaired or renewed when defective, or other equivalent protection for the hands against contact.

For the use of all persons employed in processes mentioned in schedule A—

(*f*) Clogs or other suitable protective footwear.

11. There shall be provided and maintained in a cleanly state and in good repair for the use of all persons employed—

A lavatory under cover, with a sufficient supply of clean towels, renewed daily, and of soap and nail brushes, and with either—

(*a*) A trough with a smooth impervious surface, fitted with a waste pipe without plug, and of such length as to allow at least 2 feet for every five such persons, and having a constant supply of warm water from taps or jets above the trough at intervals of not more than 2 feet; or

(*b*) At least one lavatory basin for every five such persons, fitted with a waste pipe and plug or placed in a trough having a waste pipe, and having either a constant supply of hot and cold water or warm water laid on, or (if a constant supply of heated water be not reasonably practicable) a constant supply of cold water laid on and a supply of hot water always at hand when required for use by persons employed.

For the use of all persons employed in processes mentioned in schedules A and B—

(*c*) Sufficient and suitable bath accommodation (douche or other) with hot and cold water laid on and a sufficient supply of soap and towels. Provided that the chief inspector may in any particular case approve of the use of public baths, if conveniently near, under the conditions (if any) named in such approval.

12. No person shall be allowed to introduce, keep, prepare, or partake of any food, drink, or tobacco in any room in which a process mentioned in the schedules is carried on.

PART II.—DUTIES OF PERSONS EMPLOYED.

13. Every person employed shall—

(*a*) Present himself at the appointed time for examination by the surgeon as provided in regulation 8;

(*b*) Wear the overalls or suit of working clothes provided under regulation 10 (*a*) and deposit them, and clothing put off during working hours, in the places provided under regulation 10 (*c*) and (*d*);

(*c*) Use the protective appliances supplied in respect of any process in which he is engaged;

(*d*) Carefully clean the hands before partaking of any food or leaving the premises;

(*e*) Take a bath at least once a week, and when the materials mentioned in the schedules have been spilt on the clothing so as to wet the skin. Provided that (*e*) shall not apply to persons employed in processes mentioned in schedule C, nor to persons exempted by signed entry of the surgeon in the health register.

14. No person employed shall—

(*a*) After suspension, work in any process mentioned in the schedules without written sanction from the surgeon entered in the health register;

(*b*) Introduce, keep, prepare, or partake of any food, drink, or tobacco in any room in which a process mentioned in the schedules is carried on;

(*c*) Break by hand in a crystallizing pan any substance named in schedule A or agitate any liquor containing it by hand, except by means of an implement at least 6 feet long;

(*d*) Interfere in any way, without the concurrence of the occupier or manager, with the means and appliances provided for the removal of the fumes and dust, and for the carrying out of these regulations.

SCHEDULES.

A. Processes in the manufacture of—
  - Dinitrobenzol.
  - Dinitrotoluol.
  - Trinitrotoluol.
  - Paranitrochlorbenzol.

B. Processes in the manufacture of—
  - Anilin oil.
  - Anilin hydrochloride.

C. Any process in the manufacture of explosives with use of dinitrobenzol or dinitrotoluol.

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