BLOOD CHANGES IN INDUSTRIAL DISEASE*

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I am honoured to be invited to give the second Ernestine Henry Lecture. I had the privilege of knowing this distinguished lady and of appreciating her interest in industrial medicine. She remained an inspiration to many and particularly to her son—Dr. Sydney Henry—whose work in this field is widely known.

A discussion of blood changes in industrial disease is justifiable for two reasons: all physicians should be aware of changes in the blood produced by toxic agents, and industrial physicians in particular should know how to make use of these changes in the medical supervision of workers. They must appreciate the limitations and sources of error of blood examinations. While full advantage should be taken of any objective method of measuring damage, it is important that figures used for this purpose are not endowed with false values. Blood changes may be considered separately as those that occur in the circulating blood and in blood formation. Poisons do not usually restrict their action to one organ nor are their effects likely to be restricted to one enzyme system in the blood. These changes are extremely complicated but with the growing knowledge of biochemistry more and more is being understood about them. For instance, though a poison may produce methaemoglobinaemia it is unlikely that this is the only change taking place in the cell. Less obvious and often more permanent changes occur; a minor degree of haemolysis may be found and morphological changes, such as Heinz bodies and siderocytes, may result from the disturbance of the normal biochemical processes. Fig. 1 shows diagrammatically how certain industrial poisons affect the blood.

Changes in the Circulating Blood

Changes produced in the circulating blood range from simple pigment changes, as for instance when

reduced haemoglobin is present in excess, to gross haemolysis produced by arsine. The pigment changes will be considered first.

Carboxyhaemoglobinaemia.—One of the best known of these pigment changes is that produced by the action of carbon monoxide. There is nothing to add to the extensive review by Killick (1940) except to draw attention to a recent recommendation that pure oxygen should be used in resuscitation rather than a mixture of oxygen and carbon dioxide which has been the practice for the last 30 years (Medical Research Council, 1952a).

Tolerance to repeated small exposures of carbon monoxide has been shown to occur in animals

FIG. 1.—Effect of industrial poisons on the blood.

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which respond by an increase in the number of erythrocytes and in the haemoglobin level. Clinical evidence exists of a similar polycythaemia in men whose work exposes them regularly and frequently to carbon monoxide. Karasek (1911) records a red cell count of 9.68 millions in such a worker.

Methaemoglobinaemia.—Methaemoglobinaemia is the term used to describe the blood changes leading to cyanosis, caused by poisons producing an excess of unusual pigments. The pigment is often methaemoglobin but this is not always true. Sometimes sulphaemoglobin is responsible for the cyanosis, while occasionally methaemalbumin is also present.

Probably about 1% of the total haemoglobin in the red corpuscles is normally present as methaemoglobin. Reducing systems are present in the erythrocyte to keep all but this small percentage of the total haemoglobin active and they accomplish this unless the formation of methaemoglobin is abnormally high or they themselves become damaged. High concentrations of methaemoglobin are reduced at a rate of rather more than 10% in the hour. As the concentration drops, however, so does the speed of reduction. Methaemoglobinaemia occurs on rare occasions as a familial disease and is not uncommon as the result of the toxic action of certain drugs such as the sulphonamides.

Methaemoglobinaemia in industry is usually the result of the absorption of the nitro and amino derivative or compounds of the aromatic series. There is a great variety of substances in this group and their number is continually increasing. Many of these compounds are in that large group of industrial poisons which are readily absorbed through the skin and respiratory tract. Toxic substances which can gain access to the body by both these routes are likely to present serious health problems. Table 1 gives some of the compounds which produce methaemoglobinaemia.

Aniline Poisoning.—Aniline is a good example of this group and has given its name to the condition of cyanosis widely known as "anilism". Methaemoglobinaemia following the absorption of aniline is caused by the products of its metabolism, such as phenylhydroxylamine and p-aminophenol.

Methaemoglobin cannot transport oxygen, so in anilism there is a decrease in the available arterial oxygen. Moreover the dissociation of the remaining active haemoglobin is further impaired in accordance with the well known Haldane effect. Despite this, workers with obvious cyanosis due to the formation of methaemoglobin may be little

TABLE 1
SUBSTANCES PRODUCING METHAEMOGLOBINAEMIA

<i>Nitro Compounds</i>	
Nitrobenzene
Dinitrobenzene
Nitroaniline (esp. P)
Mononitrophenol (o.m.p.)
Nitrotoluene o.m.p.
Trinitrotoluene (2:4:6)
<i>Amino Compounds</i>	
Aniline
Diphenylamine
Methylaniline
Dimethylaniline
Chloraniline

the worse, and may not suffer from obvious dyspnoea. It is only when the methaemoglobin reaches levels of about 40% that dyspnoea on exertion occurs.

In more severe exposure, usually following accidental skin contamination, the patient becomes pale and then cyanosed. He complains of a fullness in the head and of a bursting, throbbing

headache. He feels weak and weary, sometimes he vomits and complains of abdominal cramps. Very heavy exposure is followed by a fall in blood pressure, rapid breathing, coma, and death. Such catastrophes are happily rare. Successful treatment of acute cases, as with all poisons which are absorbed through the skin, depends on the immediate removal of soiled clothing and on cleaning the skin. In the old days the workman, having been re-clothed, was put into an open car and driven furiously round the countryside. The purpose of this robust treatment is not clear, but it has now been superseded by giving methylene blue which is very effective in true methaemoglobinemia. It should be given in doses of 1-2 mg. per kg. of body weight; 10 ml. of a 1% solution in normal saline are usually sufficient for the ordinary man. Both theoretically and experimentally the value of oxygen in the treatment of pure methaemoglobinemia is doubtful, so that time and effort should not be wasted in giving it.

In the more chronic forms of aniline poisoning the blood changes are those of haemolysis and anaemia. Erythrocytes show stippling and there is evidence of marrow hyperactivity.

Dinitrobenzene after severe exposure produces methaemoglobinemia; when exposure is small and repeated it produces a marked anaemia, presumably because the red cells have been damaged. This is probably additional to the pigment change which has always been regarded as being reversible, though even in aniline poisoning Crick and Jackson (1952) believe that although the methaemoglobinemia clears rapidly the erythrocytes are changed for the remainder of their life.

It may well be that these chronic changes are due to the formation of other breakdown products. Barkan and Walker (1940) and Lemberg, Legge, and Lockwood (1941) have independently advanced the hypothesis correlating the formation of choleglobin with the breakdown of haemoglobin, the formation of Heinz bodies, the destruction of reducing enzymes, and the haemolysis of red cells. From what has been said it becomes clear that poisons which produce these pigments are likely also to produce anaemia and morphological changes in red cells.

Trinitrotoluene Poisoning.—The cyanosis after absorption of trinitrotoluene is usually due to methaemoglobinemia which develops slowly and may be present for prolonged periods with few obvious ill effects. In the early days of the last war, when work was being done in munition factories under bad conditions, large groups of workers sometimes showed the dusky complexion

of T.N.T. cyanosis. They seemed little the worse for the methaemoglobinemia but it is certain that this level of absorption was such that the more susceptible would eventually show other manifestations of T.N.T. poisoning. In a small percentage of these patients the pigment responsible for the change of colour was sulphaemoglobin (Jope, 1946). A slow reconversion of methaemoglobin to normal takes place, but this does not happen with sulphaemoglobin and the pigment remains as long as the erythrocyte remains intact.

Like the other substances producing pigment changes T.N.T. is a mild haemolytic poison and this is by no means confined to those patients who are cyanosed. Stewart, Witts, Higgins, and O'Brien (1945) observed a fall in haemoglobin concentration and in the red cell count in students exposed to T.N.T. Their work suggested that attempts by the bone marrow to compensate for this are inhibited and only begin to become fully effective 48 hours after removal from contact. These observations were carried out during the first five weeks of exposure to a concentration of T.N.T. varying from 0.3 to 1.3 mg. per 10 c.m. of air. My own clinical experience supports the suggestion of Stewart and her colleagues that after a time tolerance to T.N.T. is acquired and haemopoiesis returns to its normal level.

Blood examinations of T.N.T. workers are still carried out. Haemoglobin and red and white cell counts are thought to give useful information, but a critical appraisal of their value is needed.

Haemolytic Poisons.—One of the best examples of a haemolytic poison is arsine which can cause rapid death. It is given off when nascent hydrogen comes into contact with arsenic. The hydrogen is produced by the action of acid on a metal and the arsenic is usually present as an impurity. Locket, Grieve, and Phillips (1952) have recently reviewed the literature which includes reports of poisoning in a wide variety of industries such as electroplating and the smelting, refining, and galvanizing of metals. Dudley (1919) has reported arsine poisoning in the crew of a submarine. In the presence of oxygen arsine reacts with haemoglobin to form choleglobin and other pigments and the arsenic becomes fixed in the erythrocyte until haemolysis occurs. Where poisoning is severe this begins

The method of preserving specimens of blood is important. Oxalated blood may be used for the estimation of carbon monoxide but, where methaemoglobin or similar pigments are to be estimated, sodium fluoride should be used to preserve the specimen by inhibiting glycolysis. The blood should be collected in a blood sugar bottle and kept in the dark. Air should be excluded by filling the stopper with liquid paraffin and the estimation should be made as soon as possible and not delayed more than five hours.

to take place within about six hours of inhaling the gas. Early symptoms are headache, nausea, epigastric pain, vomiting and diarrhoea, and in about 10 hours some red or black urine may be passed. In 24 hours the skin may have the characteristic coppery colour. The red cell count may have dropped to one million and the haemoglobin to 20% (3 g.). If the patient recovers the anaemia sometimes persists due to depression of haemopoiesis but on the other hand the haemoglobin level may rapidly return to normal. Immediate oliguria is usual and in severe poisoning there is complete suppression of urine. It seems likely that death is due to renal damage and where this is less severe the patients survive. Treatment should be directed to maintaining the body fluids as near normal as possible. Oxygen should be given freely and slow transfusion of packed cells is of value if the anaemia is severe. B.A.L. is of doubtful value but may be of use if the condition is diagnosed within a few hours.

Lead Poisoning.—Lead is an extensively used toxic material. In lead poisoning there is a low grade hypochromic and normocytic anaemia rarely as severe as 60% (9 g.) with a fall in the number of red cells, with marked punctate basophilia, and with less constant changes in the leucocytes. The earlier workers attributed the anaemia of lead poisoning to haemolysis. Aub, Fairhall, Minot, and Reznikoff (1926) explained this by postulating a change in the red cell which made it more brittle and less able to withstand the trauma of circulation. The rise in reticulocytes was regarded as the normal response to this rapid destruction of circulating red cells. But Rimington (1938) advanced the hypothesis that the anaemia was due to a different cause, namely the blocking by lead of the entrance of iron into the protoporphyrin ring; he explained in this way the excretion of coproporphyrin III in such large quantities in lead poisoning. He discounted the haemolytic effect of lead since faecal urobilinogen was normal. Many aspects of haemopoiesis in lead poisoning still remain obscure. In 1942 Kench, Gillam, and Lane suggested that the excretion of coproporphyrin III was not sufficient by itself to account for the degree of haemoglobin deficit and suggested that lead interfered all along the line of enzymatic synthesis causing restricted formation of porphyrin and other intermediates.

McFadzean and Davis (1949) reconciled these newer theories of deficient haemoglobin formation with the older one of haemolysis. They studied the effect of splenectomy in rabbits poisoned with

lead, and concluded that the faulty haemoglobinization was associated with stippled red cells which were removed from the circulation by the spleen, producing a haemolytic type of anaemia. We have recently studied seven cases of lead poisoning (Kench, Lane, and Varley, 1952) and followed their coproporphyrin excretion and have shown that not only is coproporphyrin III greatly raised but also coproporphyrin I. This pigment is excreted in excess in haemolytic conditions characterized by hyperplasia of the bone marrow. These results support the view that lead is both a haemolytic and haemopoietic poison.

Changes in the white cells in lead poisoning have been described by numerous workers including Legge and Goadby (1912), Brookfield (1928), Ferguson and Ferguson (1934), and Shiels (1950). The most constant finding is an increase in the ratio of monocytes and large lymphocytes to small lymphocytes. The Fergusons found this change in ship breakers who were absorbing lead, while Shiels, working in Australia, found similar changes in a series of 400 workers employed in various lead trades.

In the medical supervision of lead workers blood examinations have long been used and there is certainly a place for a simple test which can be made by the examining doctor. In France routine periodic red cell counts are used to assess lead damage, and are required by law. It is doubtful, however, whether red cell counts are useful even in the more heavy exposures and certainly in modern industry, where exposures are far less than in the past, they have little value. I have found white cell changes of little value in the routine control of lead workers. McCord, Holden, and Johnston (1935) advocated the use of a basophilic aggregation test which enumerates both stippled cells and reticulocytes. I prefer the use of punctate basophil counts, provided they are done under standard conditions, in the medical control of lead workers, and I have previously discussed their value (Lane, 1949).

More recently the value of coproporphyrin excretion in the urine has been considered. There is little doubt that the level of excretion gives an early indication of the effect of lead on the blood and blood-forming system. Changes in excretion occur very early and before the appearance of other manifestations of lead poisoning. The ranges of coproporphyrin excretion of a small group of workers who had been heavily exposed to lead are shown in Fig. 2. It will be seen that urinary samples may be misleading if taken alone. As a simple method of medical control, I still prefer the punctate basophil count and haemoglobin

estimation, but urinary coproporphyrin levels are of value provided they are used for groups and not single persons. Nevertheless, none of these examinations can wholly replace the estimation of lead in the urine.

Changes in Blood Formation

Industrial poisons producing changes in the peripheral blood have so far been discussed, although in lead poisoning there is also an interference with blood formation.

There may also be aplastic changes in T.N.T. poisoning. Fatal cases of aplastic anaemia among T.N.T. workers were reported in this country in both world wars. Five T.N.T. workers who suffered from aplastic anaemia came under my care in the last war. In all there was profound anaemia, leucopenia, and thrombocytopenia. In one patient the red blood cells were below one million, the absolute polymorph count was under five hundred, and he had many haemorrhages. With repeated

LEAD POISONING

CHANGES IN URINARY COPROPORPHYRIN

FIG. 2.—Changes in urinary coproporphyrin excretion of six men with lead poisoning. Vertical lines give the ranges of observations.

T.N.T. POISONING

FIG. 3

transfusions he recovered and is now the father of a large family. This is the first case so far as I can find of a severe T.N.T. aplastic anaemia to recover (Fig. 3). With similar treatment all five of these

patients recovered and have been followed up to the present time, and none has shown any indication of being any the worse for these grave episodes. The blood changes during treatment are illustrated in Figs. 4 and 5 for two other of these patients.

The clinical picture before treatment is identical with benzene poisoning but the prognosis is quite different. I have yet to see a patient, suffering from benzene poisoning with severe aplasia and haemorrhages, recover, though transfusions may carry them on for a year or two.

The most important haemopoietic changes, however, arise from exposure to benzol and ionizing radiations.

Benzene (Benzol).—Benzol poisoning provides an interesting chapter in industrial toxicology and its vast literature has been reviewed by Browning (1937). The term benzol is a more satisfactory one than

FIG. 4

benzene because in industry pure benzene is rarely used. The commercial product (benzol) contains toluene and xylene as well as various other impurities in smaller amounts. This mixture of simple volatile substances can produce profound and long-term effects which are almost entirely confined to the blood. Schrenk, Yant, Pearce, Patty, and Sayers (1941) showed that the distribution of benzene in the body follows physico-chemical laws which account for the high concentrations in fat and bone marrow; these tissues contain some twenty times as much benzene as the blood. It may well be that this partition of benzene between water and fat is one factor which determines the selective action of this poison on blood formation, though its mode of action is still obscure.

Benzol is widely used in industry. The main dangers arise in its use as a solvent,

quantity in the atmosphere which is to be breathed continuously for eight hours a day. The usual clinical

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FIG. 5

in producing rubber cement, in the leather cloth industry, and in quick-drying inks. In this type of work it is often used under conditions which cannot be easily controlled. In the chemical industry, particularly in the dyestuffs section, it is used widely but here, as in its distillation from coal or coal tar, it is more readily controlled by complete enclosure. For over 50 years benzol has been known to be a dangerous poison yet this is still not appreciated by many employers and industrial chemists. Continuous daily exposures are more dangerous than single heavy exposures and there is no agreement as to what constitutes a safe limit. The Safety Code of the International Labour Office (1949) lays down 35 p.p.m. as a safe limit but some workers suggest that it is unsafe to allow any measurable

picture of benzol poisoning, aplasia with anaemia, leucopenia, and widespread haemorrhages, is frequently described. Further study, however, over the last 20 years has shown a great diversity in the manifestations of this poison. The examination in the U.S.A. of groups of workmen exposed to benzol by Hunter (1939), Greenburg, Mayers, Goldwater, and Smith (1939) as well as the pathological studies of Mallory, Gall, and Brickley (1939) have all added considerably to our knowledge. The effect of benzol on the marrow may be to produce a picture of heightened or reduced activity and these changes will be reflected in the circulating blood.

Not only are many of the descriptions of benzol poisoning that appear in textbooks out of date but the official description for the purpose of notification of industrial poisoning (Factory Department Form 1787, 1925) is no better, for it states that benzene produces "a severe form of anaemia with haemorrhages under the skin and bleeding from the gums, nose, and other passages in the last stages".

Some of the atypical cases are notified under the term "toxic anaemia", but a description of the variety of blood changes which it can cause would help in its early diagnosis and in the detection of the atypical cases which have been described by Bousser, Albahary, and Tara (1952) in France. Chronic benzol poisoning has for some time been recognized as a cause of leukaemia (Erf and Rhoads, 1939), more usually myeloid but sometimes lymphatic.

The variety of blood changes now accepted as being caused by benzol may be due to the fact that atypical poisoning was not recognized in the early years of the century, or that the mixture of substances now sold as commercial benzol has changed and this in turn has changed the clinical picture of the disease. The doctor responsible for the care of benzol workers should also be familiar with the early blood changes. In this connexion the work of Goldwater (1941) is valuable because he observed a number of workers over a long period and was able to study a comparable group not exposed to benzol. He found that among a group exposed to 11–1060 p.p.m. for a period of from six months to six years the abnormalities most frequently observed were anaemia, macrocytosis, and thrombocytopenia. Leucopenia was present in only a small percentage of the men but lymphopenia, both relative and absolute, was a common finding. The haemoglobin values were relatively high. It is significant, however, that of those patients showing severe blood changes, all had leucopenia, three-quarters

had thrombocytopenia, and half a reduced red cell count.

One of the striking features of benzol poisoning is the occasional delay in the onset of symptoms which may be as long as two years after exposure has ceased. Minor changes would probably have been detected had a careful search been made, but these patients appear to remain well for one or two years until perhaps some severe infection or other form of stress supervenes. There are considerable variations in susceptibility to benzol and cases are recorded where minute daily doses have been fatal, and there are others which have been exposed for years to potentially dangerous concentrations with no obvious ill effects. There is no conclusive evidence that women are more susceptible than men. On general principles, however, young people and pregnant women should be prevented from coming into contact with benzol, and my own experience suggests that those over 60 may be less resistant than younger adults.

A poison so widely used and capable of producing such a variety of blood changes presents a difficult problem in medical supervision. Routine blood examinations must be as simple and as rapid as possible. A leucocyte count used to be considered sufficient, and when it fell below 5,000 per c.mm. the worker was removed from exposure. The wide variation of the normal white cell count makes the interpretation of minor changes difficult. Complete red and white cell counts with differential counts should be done when possible. Browning (1952), who has considerable experience of this disease, recommends total white cell counts with differential counts. She is emphatic that a decrease in the polymorphs is the most significant early sign of benzol poisoning.

Two men suffering from benzol poisoning, referred to me by H.M. Medical Inspector of Factories, illustrate some of the points mentioned. They worked in a small leather cloth factory in which some 40 men had been exposed to benzol for 10 years before 1949. The extent of exposure varied but at least 12 men, including the two cases described, were approximately equally exposed.

F. M., a man aged 65, had been employed for seven years as an assistant spreader in the manufacture of leather cloth. He was first observed by one of H.M. Inspectors of Factories in 1948 when he had a considerably reduced polymorph count of 2,000; at two further examinations in 1949 the counts were 2,000 and 550. In May, 1950, when he was first seen in hospital he had a red cell count of $4\frac{1}{2}$ million and a white cell count of 3,500 with 11% polymorphs. The marrow at this time was generally depressed, the myeloid series being mainly affected. Three months later his red cell count fell

rapidly to 1.5 million with 30% haemoglobin (4.4 g.). His white cell count was 1,000 with 8% polymorphs (Fig. 6). Repeated transfusions failed to help him and he died in December, 1950.

J. L., a man aged 67, worked side by side with F. M. and was employed for a similar time. He was first seen by me in January, 1951. He had worked almost continuously as a spreader since 1941, but in 1949 the use of benzol was stopped. He had a large liver and spleen and a white cell count of 50,000 with 90% lymphocytes—the typical picture of chronic lymphatic leukaemia. Later counts have reached 200,000 lymphocytes. He has had various forms of treatment and the disease appears to be taking its usual course.

The use of A.C.T.H. in the treatment of toxic aplasias must be considered. The M.R.C. panel (1952b) has given little encouragement to such therapy in the idiopathic aplasias, but in their report the patients who showed most improvement from this treatment were the toxic cases of thrombocytopenia. Hart, Wraith, and Mansell (1952) record the successful treatment with A.C.T.H. of a patient with agranulocytosis due to drugs. This and the records given of two similar cases suggest that A.C.T.H. should be tried in aplastic anaemia due to benzol.

Toluene and xylene are widely used as a substitute for benzol. These two substances with a much higher boiling point and lower vapour pressure are much safer than benzol. Not only are they less volatile, but they are metabolized in a different way. In an investigation by Von Oettingen, Neal, Donahue,

Svirbely, Baernstein, Monaco, Valaer, and Mitchell (1942), of the U.S. Public Health Service, it was found that toluene had no effect on blood-forming tissues in animals.

Ionizing Radiations.—Small repeated doses of ionizing radiations may cause a depression of the bone marrow and the reticulo-endothelial system, giving rise to a leucopenia, sometimes preceded by a transient leucocytosis. This is often accompanied by a lymphopenia and if allowed to progress an aplastic anaemia may develop. As with benzol, leukaemia sometimes follows. A high incidence of leukaemia has been reported among radiologists by Levent (1932) and more recently in Japan among the populations who were exposed to the two atomic bomb explosions (Warren, 1952). The safe limit of exposure, which is now taken in Great Britain as 0.5 r (roentgen) per week, is constantly under review. It is important to know as accurately as possible the lowest exposure which can produce long-term effects.

The number of processes in which workers are exposed to ionizing radiations is rapidly increasing. Powerful x-ray machines are used to detect flaws in castings and welds, and radium is used for similar purposes. Luminizing—which involves painting dials with a paint containing minute quantities of radium—has been done for many years. The manufacture and use of fission products in atomic energy factories has introduced a new industrial hazard, and many laboratories employ tracer techniques which may be hazardous to the chemists concerned. Much is done both in industry and in hospital to reduce exposure to dangerous radiations to a minimum, and great strides in protection have been made, particularly in the design of x-ray apparatus. There are now probably few radiologists and industrial workers whose hazard is as great as that of the nurse who is looking after a patient being treated by radium.

In industry the possible danger of luminizing was recognized soon after the 1914–18 war. Several years after exposure had ceased a number of young women died of bone sarcomatosis (Martland, 1931). At the beginning of the last war, when a great increase in this work appeared likely, regulations were introduced in this country and arrangements were made for a clinical and haematological examination by a medical inspector of factories. The results of this work are recorded by

FIG. 6

Browning (1949). She concludes that, working under prescribed conditions, luminizers over a period of five years have shown no evidence of a depression of the bone marrow. She did, however, notice a slight hyper-stimulation. It was possible to follow up these girls for periods of one to four years after exposure ceased and these examinations showed that a complete reversion to normal had taken place. Browning concludes that the hyper-stimulation of the reticulo-endothelial system, suggested by the "high normal" white cell count, the relative lymphocytosis, and the appearance of young forms of the monocyte, is caused by inhalation of small amounts of radioactive material, and that it is transient only, since these changes disappeared after exposure had ceased. The immense labour involved in keeping this group of workers (at one time as many as 540) under review—scattered as they were throughout the country—is amply repaid by the evidence it has produced, namely, that luminizing is harmless if carried out in accordance with regulations.

The medical control of workers using x-rays has depended mainly on blood examinations. The British X-ray and Radium Protection Committee for X-ray and Radium Workers (1948) recommend an initial complete blood examination with rejection if the white blood count falls below 5,000 and if the lymphocytes are below 1,500, and repeated total and differential counts every three months. This standard has been widely adopted and in large Government factories, where processes involve exposure to ionizing radiations, blood examinations are extensively used. As a result considerable advances in knowledge are taking place, and Edson and Williams (1952) have recently suggested a modified standard. They regard a white cell count of 4,500 with 3,000 polymorphs or 1,000 lymphocytes as a warning level, at which men may continue to work but should be under strict supervision. A white cell count of 3,000, with 2,000 polymorphs or 700 lymphocytes, or a film in which numerous immature cells are constantly present, calls for rejection from work involving exposure to ionizing radiation.

An investigation was carried out at the Atomic Energy Research Establishment by Chamberlain and Turner (1951) to determine the reliability of white cell counts. Statistical evaluation of the counting techniques, which were standardized, showed a coefficient of variation of under 10% in leucocyte counts and 12–15% in neutrophil and lymphocyte counts. With extra special care the coefficient of variation for the total white count could be reduced to 5%.

Both daily and seasonal variations in the white cell counts were noted. Averages for counts in the winter were some 15% higher than for counts in the summer. Exercise and emotion as well as infection produce transitory changes in the leucocyte count. In much of the routine work that has been done in the past some of these normal changes have been ignored and false values have been attached to many of the blood counts made. To have any meaning, white cell counts should be done on men at a standard time of the day and they should not follow soon after severe exertion, a meal, or emotional disturbance. The initial count, before the man starts work, must often perforce ignore these restrictions. (He has often, for instance, cycled a considerable distance and is almost invariably under nervous stress.) It is not surprising, therefore, that the controls as well as workers exposed to radiation show a significant fall in the white count following this first examination. The authors conclude that in view of all these factors the six-monthly white cell count does not in fact afford the best protection to workers exposed to very low doses of radiation. They maintain that better protection is likely to result from a film badge which measures the exposure of the whole body to radiation. They advise the suspension of the routine six-monthly blood examinations of the many thousands of workers who are theoretically exposed to radiation, but recommend that a more frequent check is maintained on the smaller number who are exposed to larger doses.

Most experienced workers in this field would agree that where the total internal and external radiation does not exceed 10% of the maximum permissible level, routine blood examinations may be dispensed with. There is, however, much yet to be learned about this subject, and if such a policy is adopted the precaution should be taken of examining over a long period (10 or 20 years) representative samples of those exposed to low levels of radiation, and in this way detect any long-term effect. For those whose exposure is greater haematological control is generally regarded as advisable. It is as yet too early to pronounce with any finality on the nature and frequency of these blood examinations. It seems probable that a white cell count with a differential count is likely to provide the most important information with the least effort, but more knowledge is required of the significance of these blood changes.

Conclusion

The value of blood examinations in the medical supervision of workers exposed to certain hazards

has been discussed. It is important that facilities for such examinations should be more widely available. Many of the large factories have set up their own haematological laboratories, but when the hazards arise in small factories or in small groups of workers no such outlay can reasonably be expected. These examinations should be undertaken by well-equipped and well-staffed laboratories of the regional hospital boards, or by industrial health laboratories established to do this work. In this way, and in this way only, can the present knowledge of blood changes in industrial disease be used to prevent disease instead of leaving our medical services helpless to deal with the end-results.

I have pleasure in acknowledging the debt I owe to members of my department in Manchester and to many other friends and colleagues for the help and criticism they have given me in preparing this lecture.

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