Table Summarizing Results of Treatment

Case No.	Sex	Clinical Status	Blood Level (Millions)	Lesions	Effective Treatment	Vitamins Ineffective
1	M	Treated 4 months	4.5 +	Glossitis	Pantothenate, oral + i.m.	Nicotinic acid
2	F	Treated 2 years	4.8-5.8	"	Pantothenate, oral	Nicotinic acid (partial effect)
3	M	Treated 1 year	4.3 +	"	Pantothenate, oral	—
4	F	Treated 2 years	4.4 +	"	Pantothenate, (1) i.m., (2) oral	—
5	F	Treated 1 year	3.5-4.0	Glossitis, stomatitis	Nicotinic acid, riboflavin	Nicotinic acid later inadequate
6	F	Untreated	3.4	Glossitis	Folic acid	Pantothenate, nicotinamide, riboflavin
7	F	Treated 5 years	3.41 +	Glossitis, angular stomatitis, vascularization of cornea	Riboflavin	—

instance (Case 5) that different vitamins might be effective at different times against apparently similar lesions.

Discussion

The significance of glossitis in pernicious anaemia is not understood, but it is generally recognized that if sore tongue is a feature before treatment is begun it is usually cured by liver extract. Indeed, so commonly does the glossitis respond to liver extract that it has been said that reappearance of tongue manifestations in patients under treatment is an indication of inadequate therapy (Wintrobe, 1946). This suggests some direct relation between the glossitis and the anaemia. There is, however, evidence to the contrary (Oatway and Middleton, 1932; Brown, 1946).

In the present series glossitis occurred without obvious relation to present or subsequent blood levels (see Cases 1, 2, and 4 especially). The significance of this is not clear, especially in view of the apparent rarity of such an occurrence in the experience of others (Wintrobe, 1946). It seems unlikely from what is known of the individual patients that exceptional dietary inadequacy was by itself responsible. All had good appetites and were taking apparently adequate diets. The possibility of a combination of minor defect of absorption in pernicious anaemia and a sub-optimal post-war dietary cannot be entirely discounted. The question arises whether increased dosage with liver extract would have been effective treatment for the glossitis. No definite answer can be given from these results, which are concerned with the effect of single pure substances, but it should be noted that blood counts were maintained at normal and even high levels (Case 2), and in spite of this the tongue was sore. In addition Case 5 received unusually large doses of liver extract without effect on the tongue.

It would seem possible that the development of a sore tongue in pernicious anaemia reflects a breakdown in a metabolic system similar to that responsible for the megaloblastic marrow and the neurological changes. The fact that in this series the glossitis could be controlled by the administration of synthetic vitamins suggests that the breakdown may involve the availability of the vitamin found effective. Members of the B complex exist in natural foods often in a conjugated and not immediately available form. The suggested breakdown in availability may occur at this stage in assimilation, or later in closer relationship to their final functions as parts of enzyme systems concerned with cellular metabolism. Liver extract contains a factor which in the majority of cases rectifies the defect responsible for the mucosal changes and at the same time corrects those responsible for the marrow and neural disturbances. Vitamin B₁₂, which may be identical with the anti-pernicious-anaemia principle of liver, has been found effective against the anaemia, the neurological changes, and the glossitis. Conceivably this substance may promote the utilization of certain other essential substances, some of which are well-known vitamins of the B complex.

The role of pantothenic acid in human nutrition is not yet fully understood, and the instances described here are

believed to be the first in which this substance has been found to influence symptoms in pernicious anaemia. If this effect represents restoration of an actual deficiency it is difficult to account for the latter except on the basis of a metabolic disturbance secondary to a more fundamental defect such as that already suggested. Pantothenic acid is widespread in Nature, and a deficiency conditioned in such a way seems more probable than one due simply to inadequate intake, especially in persons whose diet is not obviously abnormal.

Summary

Seven patients with Addisonian pernicious anaemia are described each of whom had a sore, red, raw-looking tongue. One also had angular stomatitis and vascularization of the cornea.

In each case it was found possible to control these changes with a single member of the vitamin B complex in pure form. Four cases of glossitis responded to calcium pantothenate, and one each to nicotinic acid and folic acid. One case responded first to nicotinic acid and later to riboflavin. The patient with glossitis, angular stomatitis, and vascularization of the cornea responded to riboflavin.

The significance of these findings is discussed, and it is suggested that the epithelial changes described reflect a breakdown in some metabolic system which may be similar to that responsible for the megaloblastic marrow and the neurological complications of pernicious anaemia.

I wish to thank Professor L. J. Davis for his advice and criticism in the investigations and in the writing of this paper.

REFERENCES

- Brown, A. (1946). *Glasg. med. J.*, 27, 313.
 Hunter, W. (1909). *The Severest Anaemias*. Macmillan, London.
 Oatway, W. H., and Middleton, W. S. (1932). *Arch. intern. Med.*, 49, 860.
 Wintrobe, M. M. (1946). *Clinical Haematology*. Kimpton, London.

UNUSUAL SYMPTOMS IN PETROL-TANK CLEANERS

BY

INDER SINGH, M.B., B.S., M.R.C.P., F.R.F.P.S.

Lieutenant-Colonel, I.A.M.C.

On Sept. 18, 1945, men from a certain labour unit were employed in cleaning a large petrol tank. It had just been drained of its contents, and to overcome the effects of undue exposure to the petrol vapour inside the tank the men were ordered to work in frequent shifts. The air inside the tank was not rendered gas-free, nor were the men given any airline masks or special clothing to wear. After the initial respiratory discomfort and irritation of the eyes the workmen became accustomed to the vapour and some of them stayed in longer.

Two men, whose cases are recorded below, went to the extreme and worked almost continuously for nearly seven hours. No adverse effects during this period prevented them from doing so. Towards the end, however, they

were seized with intense giddiness and they staggered and fell. They were rescued in an unconscious state by other workers. With first-aid measures both came round in about half an hour and complained of severe vertigo, a sense of constriction in the chest, and pains all over the body. They had to be carried to their quarters. The course of their illness was as follows.

Case 1

A man aged 25 was admitted to hospital the day after exposure to petrol vapour. Vertigo was severe and he complained of headache, marked loss of muscular power, soreness of the throat, irritation of the eyes, loss of appetite, and numbness, coldness, and intense pain in the lower limbs; pain in other parts of the body was less acute. Apart from congestion of the throat and eyes there were no abnormal physical signs.

6th Day.—The patient was improving. The calf muscles were, however, acutely tender on pressure. The knee- and ankle-jerks were sluggish. Five multivitamin tablets, each containing vitamin B₁, 1 mg., vitamin B₂, 1 mg., nicotinic acid, 10 mg., and ascorbic acid, 25 mg., were given three times a day.

10th Day.—Improvement was marked. Only slight pain remained in the lower limbs. Next day he was discharged as cured at his own request.

16th Day.—He returned to the hospital with headache, vertigo, and Parkinsonian tremor of both hands and early rigidity. He was irritable and irrational.

26th Day.—Parkinsonian rigidity and tremor were well established, and frequent oculogyric spasms were accompanied by spasms of the muscles of the face and mouth. His face, which was very pale, and his attitude, voluntary movements, and speech, were typical of the disease. Mental and bodily asthenia was profound, and most of the time the patient lay quiet in bed, showing no interest in himself or his surroundings. Rarely he asked for a bed-pan or urinal; mostly he passed his urine and stools in bed. His mood was very changeable, and he often cried without apparent reason. There was progressive loss of weight. The ankle-jerks were very feeble, but the calf muscles were not tender. The knee-jerks were slightly exaggerated and the abdominal reflexes were rather brisk. Heart sounds were very feeble. The pulse was regular, 72 a minute, and of low tension and volume. Blood pressure was 95/70 mm. Hg. Respiration was normal, and the temperature was usually subnormal. Both eyes were slightly icteric (effect of suppressive mepacrine). There was still conjunctivitis of the right eye. Urine showed no albumin, sugar, or abnormal quantities of lead, and deposits were normal. Stools were also normal. A blood count showed: Hb, 120% (Sahli); red cells, 6,830,000 per c.mm.; white cells, 12,600 (polymorphs 68%, lymphocytes 23%, mononuclears 2%, eosinophils 1%, and basophils 6%). There were no malaria parasites in the smear. The bilirubin content of the blood was 0.7 mg. per 100 ml. (icterus index 3.5). Blood urea was 16.6 mg. per 100 ml. Wassermann and Kahn reactions were both negative. The patient weighed 118 lb. (53.52 kg.), having lost 23 lb. (10.43 kg.) since the onset of the disease. He was put on a nutritive high-protein diet of over 4,200 calories. In addition 10 multivitamin tablets were given thrice daily. Suppressant mepacrine was stopped.

36th Day.—For the first time during his stay in hospital the patient had a temperature of 100° F. (37.8° C.) at 6 p.m. Blood smears and thick drops were negative for malaria parasites. Subsequently the temperature was 99° F. (37.2° C.) at 10 p.m., 99.6° F. (37.55° C.) at 2 a.m. next morning, and once again normal at 6 a.m. and after. Between 1 and 10 a.m. he passed four samples of characteristic haemoglobinuric urine, the first very dark, the second and third dark brown, and the fourth considerably lighter. Subsequent samples were progressively normal to the naked eye, although spectroscopic examination showed the presence of oxyhaemoglobin till the next morning. Apart from the transient low fever described above there were no constitutional symptoms and no haemoglobinaemia in a blood sample taken at 10 a.m. Haemoglobin fell from 125 to 120%, and the red cells from 6,830,000 to 6,510,000 per c.mm. The leucocytosis was raised from 12,600 to 14,200, with polymorphs 72%, lymphocytes 20%, mononuclears 2%, eosino-

phils 1%, and basophils 5%. There were no malaria parasites in the smears or thick drop preparations. Spectroscopically, serum collected from blood taken at 10 a.m. with care to prevent haemolysis showed only traces of oxyhaemoglobin, and the icterus index remained at 3.5. There was no appreciable rise in blood urea. The Donath-Landsteiner reaction, the acid-serum test, and the Wassermann and Kahn reactions were negative. Spherocytosis was absent and fragility of red cells was normal. No haemolysins were found *in vitro* in the serum. Urine did not show any evidence of abnormal quantities of lead excretion. Alkalis and fluids were given by mouth, and, on empirical grounds, 20 ml. of concentrated antivenene was injected intramuscularly to prevent further haemolysis.

48th Day.—Improvement set in fairly rapidly. Rigidity and tremor were less pronounced. Headache, giddiness, and oculogyric spasms disappeared. His mood was less changeable and he was taking general interest all around. He was able to stand and to walk slowly by himself, and his weight had begun to rise. Insomnia still persisted.

76th Day.—The patient was now almost completely normal. A noticeable feature was a fall in his erythraemia; the red cells were now 5,200,000 per c.mm., and the Hb was 90%. The blood pressure was 120/80 mm. Hg. Insomnia was less troublesome. Mentally he was still moody and depressed.

96th Day.—He was discharged completely cured.

Case 2

A man aged 23 was admitted on the day after exposure to petrol vapour. His complaints and condition were essentially similar to those of Case 1, but vertigo was very severe and he had considerable pain associated with pins-and-needles in all parts of the body. The throat was very congested and there was conjunctivitis of the right eye. Unlike Case 1 there was no temporary improvement and the patient was completely bedridden.

13th Day.—He developed a Parkinsonian tremor of both hands, at first only when he attempted a voluntary movement, but two days later at rest also, with early rigidity. He was becoming very irrational.

26th Day.—His complaints were identical with those of Case 1, but he was more severely affected. Most of the time he was depressed and cried without any obvious reason. He talked of his family in trouble, which he said would finish without his help. Later he started getting out of bed and running away, and often fell and injured himself. He complained of the sisters and nursing orderlies harassing him, the loss of his pay-book although it was still with him, and a sense of impending death. He said he was guilty, and persistently begged for pardon for all the sins he had committed. There were physical signs of bronchitis at both bases. Heart sounds were very weak. The pulse was regular, 80 a minute, of low tension and volume. The blood pressure was 110/80 mm. Hg. Respiration was normal and the temperature was usually subnormal. Stools were strongly positive for ankylostoma ova. The urine contained no albumin, sugar, or abnormal quantities of lead, and deposits were normal. A blood count showed: Hb, 80%; red cells, 5,630,000 per c.mm.; white cells, 6,800 per c.mm. (polymorphs 62%, lymphocytes 26%, monocytes 4%, eosinophils 0%, and basophils 8%). There were no malaria parasites in the smears or thick drop preparations. The bilirubin content of the blood was 0.4 mg. per 100 ml. (icterus index 2). Blood urea was 53 mg. per 100 ml. Wassermann and Kahn reactions were negative. The patient weighed 130 lb. (58.97 kg.), having lost 28 lb. (12.7 kg.) in 26 days. Similar diet and multivitamin tablets were given as in Case 1.

38th Day.—The patient passed characteristic haemoglobinuric urine; sherry-red in colour, just after midnight. A second sample passed two hours later was lighter, and a third passed in the morning was almost normal. Subsequent samples were macroscopically normal, and before evening there was no spectroscopic evidence of oxyhaemoglobin in the urine. Constitutional symptoms and haemoglobinaemia in a sample of blood taken at 10 a.m. were conspicuous by their absence; the patient did not even have the little fever which occurred in Case 1. Spectroscopic examination of the blood showed only traces of oxyhaemoglobin, and there was no rise in the

icterus index. The blood count was not appreciably changed. The results of other tests as carried out in Case 1 were likewise all negative. Similar treatment was adopted.

48th Day.—The patient had an attack of severe abdominal pain below the umbilicus associated with tenderness in the right iliac fossa, vomiting, fever with rigor, and a leucocytosis of 13,200, with polymorphs 56%, lymphocytes 28%, monocytes 4%, and eosinophils 12%.

60th Day.—There were signs of improvement in the rigidity, tremor, and mental condition.

66th Day.—The patient complained of pain all over the body. He had haemoglobinuria again, and this time it was severer than that of Case 1. After midnight he passed three samples of very dark urine followed by urine of gradually diminishing colour. About twelve hours after the first sample was passed it had cleared considerably, but to the naked eye it was not completely clear until the evening. Once again there were no constitutional symptoms other than the preliminary aches and pains in the body, and no haemoglobinaemia about twelve hours after the first sample of haemoglobinuric urine, and the icterus index did not rise. The haemoglobin fell to 75%, and the red cells to 4,930,000 per c.mm. The white cells numbered 8,400 per c.mm., with polymorphs 68%, lymphocytes 23%, eosinophils 8%, and monocytes 1%. The results of blood smears and other tests carried out previously were all negative. Treatment similar to that in Case 1 was given; 10 ml. of concentrated antivenene was repeated next day also.

By the 80th day the patient had almost completely recovered, and on the 96th day he was discharged as fit.

A follow-up of both cases for twelve months showed that recovery was complete in all respects, and there had been no recurrence of haemoglobinuria.

Discussion

In general petrol is a mixture of hydrocarbons of varying volatility and toxicity, the toxicity decreasing as the boiling-point increases. Octane, which is present in high proportion in some petrols, is very toxic—e.g., *n*-octane is about seven times as toxic as pentane (Lawrence, 1945). Some commercial petrols contain benzene and other aromatic hydrocarbons which are of still greater toxicity. The amount of lead tetra-ethyl is normally too small to be toxic, but, in circumstances to be discussed later, may give rise to lead-poisoning.

The toxic symptoms which arise after the inhalation of petrol vapour depend on the concentration of the vapour and the duration of exposure to it—e.g., Fieldner, Katz, and Kinney (1921) found that 1 part per 1,000 produced drowsiness in men after 15 minutes' exposure, and vertigo, ataxia, and nausea at the end of one hour, but 7 parts per 1,000 produced definite intoxication in five minutes. A very high concentration of the vapour causes almost immediate unconsciousness, and death from respiratory arrest (Rambousek, 1913).

Ordinarily, exposure to low concentration of vapour produces emotional changes simulating those of drunkenness. There may be excitement or euphoric exhilaration. Tolerance may be acquired by repeated exposure, and in such persons tremor of the hands without any emotional changes may alone occur on exposure to low concentrations of the vapour (Hamilton, 1925; Kulkow, 1926). Women may burst into fits of uncontrollable hysterical laughter or crying. Men may become irritable and quarrelsome.

Higher concentrations irritate the eyes, the skin, and the respiratory passages. A sense of constriction in the throat, burning pain in the chest and abdomen, a feeling of pressure over the heart, and irritation of the skin are followed by drowsiness, headache, vertigo, nausea, and muscular weakness. Tonic contractions of flexors of the hands and twitchings of the muscles of the trunk and limbs have been described at this stage by Rudd (1944).

With still higher concentrations the euphoric exhilarative period is very short. The patient becomes rapidly disorientated and abusive. Hallucinations may occur and he may defy rescue and become rapidly delirious and comatose. Convulsions may occur, but may be delayed till he is removed to fresh air for resuscitation (Machle, 1941).

From short exposures recovery is quick and is followed by deep slumber from which he can be roused. After prolonged exposure coma may last several days and end in death from respiratory failure. Recovery from coma may be heralded by muscular twitchings, and is usually associated with severe headache, vomiting, severe abdominal pain, pain in the extremities, extreme restlessness, and bursts of hysterical laughter. Headache, insomnia, loss of appetite, vomiting, pain in the extremities and abdomen, and muscular weakness are the usual immediate after-effects and may last several days. An early erysipelas-like eruption on the skin of the face and the mucous membrane of the mouth and throat followed by necrosis is an early and fatal complication that rarely occurs (Floret, 1927).

Sometimes damage inflicted on the nervous system gives rise after a variable period to symptoms simulating those of disseminated sclerosis or other organic nervous disease (Potts, 1915). The onset of epilepsy has been described by Floret (1927). Peripheral and cranial nerves may be involved, often singly, such as the sciatic (Jansen, 1937), hypoglossal, and optic. Recovery may take place or the nervous disability may be permanent. Lawrence (1945) recorded the occurrence of discomfort and tenderness in the right iliac fossa on the second day after exposure to petrol vapour, lasting till the twelfth day, without any abnormal amount of lead in the urine or faeces.

Lead tetra-ethyl is readily soluble in fats and oils, hence poisoning can occur by its absorption through the intact skin. The chief mode of absorption is, however, through the pulmonary epithelium from inhalation of its vaporized form, the amount absorbed being proportionate to the vapour pressure in the lung alveoli. As much as 5 mg. of lead per litre may be present in air saturated with its vapour, and the symptoms of poisoning are entirely due to this lead content. Owing to the solubility of lead tetra-ethyl in fats, however, the central nervous system is chiefly affected.

The concentration of lead tetra-ethyl in leaded petrol is usually not more than 1 in 3,000 by volume, and in this concentration the occurrence of lead-poisoning is unknown in workmen engaged in its distributive and allied trades, as well as among the general public (Kehoe, Thamann, and Cholak, 1934; Final Report of Departmental Committee, 1930; Lind, 1936). It is unlikely that lead tetra-ethyl plays any part in the symptomatology of acute petrol-vapour poisoning, except when the exposure is prolonged and the concentration of lead in the air is more than the safe limit of 1.5 mg. per 10 m.³ of air (American Public Health Association, 1943). Thus under controlled conditions, which keep the concentration below this limit, poisoning has hardly ever occurred in workmen engaged in the manufacture of the product and its blending with petrol (Kehoe, 1934; Kehoe and Machle, unpublished data, 1936).

No cases have been found in can-fillers and can-washers, although the urine has contained from 0.026 to 0.6 mg. of lead per litre (Cassells and Dodds, 1946).

These authors state that some of the men engaged in underground or semi-underground pump-houses, where the ventilation was poor and the concentration of the vapour naturally higher, however, showed mild symptoms of intoxication and a urinary lead concentration which was as high as 0.275 mg. per litre. Workers in depots built below the level of the surrounding countryside, and hence

with poor natural ventilation, showed a high urinary lead concentration but no symptoms of intoxication. However, 35 cases of poisoning are described in tank-cleaners who overlooked or disobeyed regulations governing the cleaning procedure. Machle (1935) had previously recorded 11 similar cases. In these the poisoning was due to inhalation of lead tetra-ethyl vapour in high concentrations rising out of the sludge or sediment deposited at the bottom of large tanks after storage for some time; these contained in analysed cases as much as 0.044 to 0.84% of organic lead compounds. Symptoms occurred after one to 17 days of exposure. "The classical signs and symptoms of lead-poisoning—namely, abdominal colic, tremors and fibrillary twitchings, myalgia, neuralgia, constipation, pallor, blue line on the gums, paralyzes, stippling of the red blood cells, and punctate basophilia—either did not occur or were a very minor part indeed of the picture" (Cassells and Dodds, 1946), although in fatal cases the various organs showed a high concentration of lead—e.g., brain 0.6 to 0.74 mg., spleen 0.27 to 0.29 mg., liver 2.35 to 2.5 mg., kidneys 0.79 to 1.2 mg., against the normal maximum of brain 0.09 mg., spleen 0.07 mg., liver 0.28 mg., kidneys 0.16 mg. per 100 g. of wet tissue (American Public Health Association, 1943).

The earliest symptom was insomnia, with difficulty in falling asleep, broken sleep, and troubled dreams. Following this, and sometimes preceding it, came a nasty sweet taste in the mouth and halitosis, lack of appetite, nausea, vomiting, and diarrhoea with or without abdominal pain. Next in evidence were irritability, restlessness, nervousness, anxiety, difficulty in passing urine, and possibly tiredness. At this stage the pulse was slow, the temperature subnormal, the blood pressure diminished, and the reflexes increased, with the body weight showing slight loss. When exposure was longer and more severe "the signs and symptoms progressed to increasing tiredness and loss of body weight, tremor, muscular weakness and twitching, oddities of behaviour, and evidence of mental confusion, and then, quite abruptly, came the onset of acute maniacal symptoms with suicidal tendencies, or the occurrence of a convulsion" (Cassells and Dodds, 1946).

Although the classical signs and symptoms of lead-poisoning were absent urine examination showed a lead concentration which was usually above 0.15 mg. per litre. In fact, when the urinary lead concentration was less than 0.1 mg. per litre and symptoms of the above nature were displayed lead tetra-ethyl was considered unlikely to be the cause. The excretion of lead in the urine continued for a long time after exposure ceased, and sometimes the urinary concentration continued to rise in spite of cessation of exposure, to be followed by a progressive and gradual fall.

The clinical symptoms had apparently no relation to the urinary lead concentration—for in one of Cassells and Dodds's cases mental symptoms were present when the urinary lead concentration was 0.215 mg. per litre, but had disappeared later on when it had risen to 0.295 mg. Apparently loss of weight was sometimes very excessive, as shown in another of their cases by a gain in weight of 74 lb. (33.1 kg.) in about three months during the stage of recovery, and by a loss in a further case of between one and two stones (6–12 kg.) in about five weeks during the illness. Although the deep reflexes were usually exaggerated, at times they were diminished; in some cases they were exaggerated, while in others they were diminished—e.g., in one case "all reflexes were exaggerated except the biceps jerk, which was only just elicited." Cerebral symptoms in one case occurred suddenly in the midst of apparent recovery and ended fatally. There were no permanent sequelae: recollection of dreams was all that remained in one case.

Tropical conditions predispose to the occurrence of cases of lead tetra-ethyl poisoning. The two men whose cases are recorded in this paper were engaged, without any provision of airline masks or special clothing, in cleaning a tank which had not been rendered gas-free by ventilation after the petrol had been drained away. They thus faced a dual risk—one from the inhalation of petrol vapour, and the other from the absorption of lead tetra-ethyl by inhalation as well as by direct absorption through the intact skin.

The initial respiratory discomfort and irritation of the eyes were no doubt due to the effects of petrol vapour. It appears that sheer determination to work, associated with a fairly low concentration of the vapour, delayed the onset of giddiness, ataxia, and unconsciousness. To the effects of the same vapour may be ascribed the immediate symptoms, such as vertigo, headache, muscular weakness, anorexia, soreness of the eyes and throat, and pain in the lower limbs.

Symptoms of lead tetra-ethyl poisoning in a petrol-tank cleaner after exposure for a single working day have been described by Cassells and Dodds in one of the cases in their series, mentioned above. It will have to be conceded that these two workmen also absorbed enough lead during the day's exposure to give rise to such symptoms as marked loss of muscular power, muscular tenderness on pressure, and sluggish ankle- and knee-jerks due to its probable neuritic, muscular, spinal, or vasoconstrictor action. The numbness and the coldness of the lower limbs were perhaps due to vasoconstriction and the inability of the blood vessels to relax on account of the action of lead on them. Symptoms such as headache, anorexia, and body pains could be common to both effects.

Among the symptoms tremor, slow pulse, subnormal temperature, increased reflexes, loss of body weight, muscular weakness, and oddities of behaviour have all been described, as recorded above, in lead tetra-ethyl poisoning. It has been said that when symptoms of this nature are displayed lead tetra-ethyl is unlikely to be the cause if the urinary lead is less than 0.1 mg. per litre; yet on account of the similarity of symptoms it must be conceded that in my two cases these were due to lead tetra-ethyl in spite of failure to demonstrate pathological quantities of lead in the urine, and especially as in one of the cases there was no correlation between cerebral symptoms and the urinary lead concentration.

The unusual symptoms appearing in my two cases were:

1. *Acute Parkinsonism*.—As symptoms of organic nervous disorder are known to occur as sequelae of petrol-vapour poisoning it cannot altogether be ruled out that this was the case in these two patients. It is also known, however, that lead, through its vasoconstrictor action, can give rise to temporary blindness, angina pectoris, and gangrene of the extremities. Although localizing signs do not occur in lead encephalopathy, a similar selective action may play a part in the causation of acute Parkinsonism.

2. *Pain Simulating Acute Appendicitis*.—Discomfort and tenderness in the right iliac fossa, starting on the second day after exposure to petrol vapour and lasting until the twelfth day, recorded by Lawrence in one of his cases without any evidence of abnormal amounts of lead in the urine or faeces and apparently without any leucocytosis, bears a strong resemblance to an attack of similar pain in Case 2. However, in this instance it occurred 48 days after the exposure and was associated with a leucocytosis of 13,200 without a relative increase in the polymorphs. Such a leucocytosis is known to be associated with lead colic, and it is not impossible, therefore, that the appendicular reaction in this case was due to lead rather than to delayed effects of petrol vapour or to an incidental appendicitis.

3. *Haemoglobinuria*.—This apparently had all the clinical features of haemoglobinuria of exertion (Whitby and Britton, 1946). Its aetiology is obscure. Regarding the part played by exertion in these cases, all that can be said is that the patients were ambulant the previous day, but not to any great extent. Blood urea remained unraised and urine did not at any time before the onset of haemoglobinuria show evidence of nephritis or necrosing nephrosis due to toxic action of lead, or of haemoglobinuric nephrosis following haemoglobinuria. The possibility that it was caused by an acute haemolytic crisis due to lead cannot be ruled out. It appears that the blood was almost completely cleared of its oxyhaemoglobin content when a sample was taken for examination, whereas the urine collected at the same time was that which had accumulated in the bladder for at least four hours. Subsequent samples of urine had been markedly and progressively clear. The amount of blood destroyed by haemolysis seems to have been small, as shown by the red-cell counts before and after the haemolysis. The first sample of haemoglobinuric urine had been passed from seven to nine hours before the collection of venous blood. Haemolysis had no doubt taken place earlier than this. During this period the haemoglobin in the blood could have been easily cleared by the kidneys. Hence the apparent similarity to haemoglobinuria of exertion.

4. *Erythrocytosis*.—This accompanied the symptoms of acute Parkinsonism very closely. In all probability it was of the same nature as polycythaemia described in encephalitis lethargica and Huntington's chorea by Moehlig and Bates (1933).

5. *Pallor*.—This was not a feature of any of the cases recorded by Cassells and Dodds. Its presence in my two cases was a pointer to its causation by lead.

Summary

Acute Parkinsonism, haemoglobinuria, abdominal pain simulating appendicitis, erythrocytosis, and pallor are recorded in two petrol-tank cleaners. These symptoms were in addition to the usual effects of exposure to petrol vapour and lead tetraethyl.

REFERENCES

- American Public Health Association (1943). Quoted by Cassells and Dodds (1946).
 Cassells, D. A. K., and Dodds, E. C. (1946). *British Medical Journal*, 2, 681.
 Fieldner, A. C., Katz, S. H., and Kinney, S. P. (1921). *Permeation of Oxygen Breathing Apparatus by Gases and Vapours*; technical paper 272, U.S. Dept. of Commerce, Bureau of Mines, Washington.
 Final Report of Departmental Committee on Ethyl Petrol, Ministry of Health, London, 1930.
 Floret (1927). Quoted by Lawrence (1945).
 Hamilton, A. (1925). *Industrial Poisons in the United States*. New York.
 Jansen, H. H. (1937). Quoted by Lawrence (1945).
 Kehoe, R. A. (1934). Quoted by Cassells and Dodds (1946).
 ———, Tamann, F., and Cholak, J. (1934). *J. industr. Hyg.*, 16, 100.
 Kulkow, A. E. (1926). Quoted by Lawrence (1945).
 Lawrence, J. S. (1945). *British Medical Journal*, 1, 871.
 Lind, G. (1936). *J. industr. Hyg.*, 18, 37.
 Machle, W. F. (1935). Quoted by Cassells and Dodds (1946).
 ——— (1941). *J. Amer. med. Ass.*, 117, 1965.
 Moehlig, R. C., and Bates, G. S. (1933). Quoted by Whitby and Britton (1946), p. 410.
 Potts, C. S. (1915). Quoted by Lawrence (1945).
 Rambousek, J. (1913). *Industrial Poisoning from Fumes, Gases and Poisons of Manufacturing Processes*. London.
 Rudd, T. N. (1944). *J. R. Army med. Cps.*, 82, 271.
 Whitby, L. E. H., and Britton, C. J. C. (1946). *Disorders of the Blood*, p. 282. Churchill, London.

Mr. Lawrence B. Hall, sanitary engineer of the U.S. Public Health Service, has gone to Iran to help in that country's fight against malaria. He will continue work in malaria control initiated by another Public Health Service officer, Dr. Justin M. Andrews, and will supervise training of Iranian personnel in carrying out a D.D.T. spraying scheme recommended by Dr. Andrews after a survey a few months ago. Mr. Hall's headquarters will be in Tehran. The Iranian Embassy in Washington requested the services of Mr. Hall under terms of the Smith-Mundt Act, an educational exchange programme through which the U.S.A. gives technical and other services on a reciprocal basis with other nations. Mr. Hall did malaria-control work along the Burma Road in 1941, and also later when he was attached to the China-Burma-India Command of the U.S. Army.

STAPHYLOCOCCI IN THE NEWBORN THEIR COAGULASE PRODUCTION AND RESISTANCE TO PENICILLIN AND STREPTOMYCIN

BY

G. MARTYN, M.R.C.S., L.R.C.P., D.P.H.

(From the Departments of Child Health and Bacteriology,
University of Manchester)

This investigation was undertaken to determine the incidence of staphylococci in the nasopharynx and the faeces of normal infants during the first seven days of life. Potentially pathogenic strains were differentiated by the coagulase method and their sensitivity to penicillin and streptomycin was tested. The results refer to infants born in hospital and may not perhaps be applicable to newborn infants generally. They are, however, a contribution to the study of the oecology of the staphylococcus both with regard to the newborn and in relation to possible effects of antibiotics on staphylococci in the whole community.

Although numerous studies and reviews of the respiratory and faecal flora of normal infants are available there is little information about the incidence of staphylococci during the first week of life.

Torrey and Reese (1945) found carrier rates of haemolytic *Staph. aureus* of 6.6% during the first day, 50% for the second day, 62% for the third day, and 88.8% during the fourth to eighth days. Kneeland (1930) found in 30 normal infants during the first two weeks of life an incidence of 93% of *Staph. albus* and 32% *Staph. aureus*. Todd (1922) cultured dried powdered stools on human blood agar from infants and obtained *Staph. albus* in 53%; *Staph. aureus* was not found. Crowley, Downie, Fulton, and Wilson (1941) found in 57 normal breast-fed infants, 3–23 days of age, that about 50% had *Staph. albus* in the stools; *Staph. aureus* was present only once.

Technique

The infants studied were born in the obstetrical department of St. Mary's Hospital, Manchester, and were in five nurseries each containing a maximum of 12 cots. They were all healthy, full-term, breast-fed, and in contact with their mothers only at feeding-times. None had been treated with penicillin, and so far as could be ascertained none of the mothers had received any. No persons in contact with the children wore masks. Visitors were not allowed in the nurseries. There was no special air-conditioning in the nurseries. The survey was made from August to November, 1948.

Specimens were taken from the nasopharynx by means of per-nasal swabs—i.e., fine cotton-wool swabs on thin flexible iron wire passed via the external nares to the back of the nose. Rectal swabs were taken, using adult-type throat swabs, with special precautions against contamination from the skin surrounding the anus.

The nasal swabs were plated on horse-blood agar within one to two hours of collection and incubated aerobically at 37° C. The rectal swabs were plated on horse-blood agar and MacConkey's bile-salt medium and inoculated into 10% NaCl in Robertson's meat medium as recommended by Maitland and Martyn (1949) for the selective isolation of staphylococci. The culture from the salt-meat medium after incubation aerobically for twenty-four hours at 37° C. was subcultured to horse-blood-agar plates, also incubated for twenty-four hours. It was not necessary to use the selective medium for nasal swabs, as the staphylococci were not mixed with many other bacteria.

When the colonies were uniform in colour on one plate one colony only was subcultured. If there was more than