seeing the patients soon afterwards there was less risk of their forgetting the facts or becoming confused about details.

Results

Of the 60 patients who were treated with an active antihistamine preparation, 47 reported themselves as cured and six as improved. Thus 88% were either cured or improved by the treatment. In the control group, three patients regarded themselves as cured and four as improved, a total of 10%. Table I shows that no case of severe vomiting

TABLE I.—Results of Treatment

Treatment	No. of Cases	No. Cured	No. Improved	No Change
<i>Severe Vomiting</i>				
Antihistamine ..	31	25	2	4
Inert tablet ..	33	—	—	33
<i>Moderate Vomiting</i>				
Antihistamine ..	17	12	3	2
Inert tablet ..	16	2	4	10
<i>Nausea and Heartburn</i>				
Antihistamine ..	12	10	1	1
Inert tablet ..	11	1	—	10

was affected by an inert preparation, and that it was in the cases of moderate vomiting that the inert tablets had most effect.

Most of the patients in the control series were subsequently treated with antihistamines, when they showed a higher proportion of cured and improved (Table II). Thus

TABLE II.—Control Cases Subsequently Treated with Antihistamines

No. of Cases	No. Cured	No. Improved	No Change
50	43	3	4

out of 50 of these patients treated 86% were cured, 6% were improved, and only 8% showed no change. With this group, however, other factors may have affected the results. These patients were being treated at a somewhat later stage in pregnancy, and it was possible that time was effecting a cure. Also, as the antihistamine tablets they subsequently received were of a brighter colour than the inert tablets, they may well have deduced that they were receiving a more potent preparation, and so the factor of suggestion may have influenced the results.

In most cases three days' treatment was insufficient to effect a permanent cure, and it was necessary to continue treatment for at least a fortnight, and sometimes for four weeks. No other treatment was given and no dietary restrictions were imposed. No adverse effects were noted from even a prolonged course, although occasionally some patients complained of drowsiness.

Comment

The causes of nausea and vomiting in pregnancy are not known, and it is therefore a matter of speculation why the antihistamines give relief. Finch (1938) suggested that nausea and vomiting of pregnancy are due to an allergic tendency, and that the patient had become sensitized to some secretion of her own corpus luteum. He carried out intradermal tests with corpus luteum extract and found that the reaction produced was in direct proportion to the degree of nausea and vomiting present. Kapeller-Adler and Adler (1943) have shown that there is an increased histamine production by the body in pregnancy. They suggest that, whereas in normal pregnancies the serum is able to inactivate histamine, in cases of hyperemesis gravidarum and mild pre-eclampsia the serum has lost this power and

in consequence there is an excess of histamine in the body, and it is this excess which is responsible for the disturbed gastric function.

These theories offer some explanation for the mode of action of the antihistamines. On the other hand, it is well recognized that most of the drugs used for their antihistamine properties have some depressant action on the central nervous system, and it is possible that they exert their influence by lowering the sensitivity of the vomiting centre.

Some of the patients who did not respond to treatment improved after the dosage was increased or when a more powerful form of antihistamine such as promethazine hydrochloride, 25 mg. twice daily, was given. This confirms Dougray's experience, although he found it necessary to give a higher dosage.

A number of patients had a recurrence of symptoms in the latter weeks of pregnancy, and these were all successfully treated with antihistamines. It is occasionally taught that vomiting late in pregnancy is of serious significance, but in the absence of any evidence of pre-eclampsia this is not so.

Summary

A number of patients suffering from gastric disturbances in pregnancy were treated with antihistamine preparations and an equal number were given an inert preparation. The results showed that a high proportion of patients obtained relief with the antihistamines and only a small proportion were relieved with the inert preparation.

My thanks are due to Messrs. May and Baker for a generous supply of avomine tablets and for supplying the inert tablets.

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ACUTE NITROBENZENE POISONING WITH TRANSIENT AMINO-ACIDURIA

BY

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AND

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Many cases of nitrobenzene poisoning have been recorded. The majority of these have been due to accidental ingestion, contact, or inhalation, especially in industry. The case reported here was the result of a deliberate attempt at suicide and showed the usual characteristic manifestations of methaemoglobinaemia. There was also a marked transient amino-aciduria.

Case Report

A married woman aged 24, living apart from her husband and 4-year-old son, became depressed and decided to commit suicide. At 11 a.m. she swallowed "about half a bottle" of a bee mixture, which was clearly labelled as a poison. So far as could be ascertained later, she drank about 1 oz. (28 ml.) of this mixture, which contains nitrobenzene (or oil of mirbane) 2 parts, safrol oil 1 part, and petrol 2 parts. Therefore she may have swallowed almost 200 minims (12 ml.) of nitrobenzene.

She found the taste of the mixture most unpleasant and noted a burning sensation in her mouth. Half an hour

later she vomited twice and felt dizzy and had to be helped to her bed. After a further half-hour she was seen to be deeply cyanosed. Her relatives became alarmed, and with some difficulty persuaded her to go to hospital. She was admitted in the early afternoon of December 13, 1951.

On admission she was hysterical and strongly resented having her stomach washed out with sodium bicarbonate. Her breath and the odour of the gastric residue were suggestive of floor polish. There was an intense blue-grey cyanosis, especially of the lips and face and beneath the finger-nails. She soon became more rational, although apprehensive, and told us that she had swallowed the bee mixture in an attempt to end her life. This preparation is popular with bee-keepers, and we had no difficulty in discovering that nitrobenzene was the active ingredient.

Examination revealed that the pulse was of poor volume but regular at 120 beats a minute. Her blood pressure was 120/70. There was no gross peripheral circulatory failure. She was given 1/30 gr. (2 mg.) of strychnine sulphate by hypodermic injection. An intravenous drip was begun soon after admission. Normal saline was given at first, but when we concluded that the cyanosis was due to methaemoglobinaemia, 2 ml. of 10% methylene blue was injected into the drip tubing. Immediately afterwards the intravenous saline was replaced by blood and the patient was placed in an oxygen tent. There was no immediate change in colour, but approximately 20 minutes after the injection of methylene blue her colour reverted to normal. In view of this and as she was not obviously anaemic, the blood transfusion was discontinued after 350 ml. of blood had been given. For the next 24 hours 5% glucose by slow intravenous drip was given. Ascorbic acid, 1 g., was added to each pint (570 ml.). Two hours after admission the pulse rate was 88 and the blood pressure 110/70. The respirations had been rapid on admission, but soon became normal as the patient became more composed. A sample of blood which had been taken as the intravenous drip was started revealed methaemoglobin spectroscopically. A specimen of urine obtained later did not contain albumin or sugar.

The following day the blue-grey cyanosis was again intense and the patient complained of a severe headache, dizziness, and a bad taste in her mouth. The urine contained methaemoglobin and methylene blue in large amounts. Intravenous therapy was abandoned and the following oral regime begun: 16 gr. (1 g.) of methylene blue a day in divided doses and 200 mg. of ascorbic acid thrice daily.

On December 15 the intense cyanosis remained but she felt fairly well. The next day she complained of nausea and low back pain. On December 17 blood examination showed: haemoglobin, 85% (Haldane), or 12.6 g. per 100 ml.; red cells, 4,220,000; white cells, 6,650 (neutrophils 42%, eosinophils 3%, lymphocytes 45%, monocytes 10%). There was no punctate basophilia. The patient remained cyanosed but was free from symptoms.

On December 18 urinary chromatography, using the "rack tank" technique of Datta, Dent, and Harris (1950), revealed alanine, glutamine, serine, glycine, taurine, tyrosine, glutamic acid, and β -aminoisobutyric acid, all present in concentrations markedly in excess of the normal. Two days later the cyanosis finally disappeared and the patient felt well, but on December 24 she became dizzy when she was out of bed. Blood examination revealed: haemoglobin, 66% (Haldane), or 9.7 g. per 100 ml.; red cells, 2,860,000; colour index, 1.12; white cells, 12,750 (metamyelocytes 4%, neutrophils 54%, eosinophils 6%, lymphocytes 34%, monocytes 2%); corrected E.S.R., zero; P.C.V., 28%; M.C.V., 98 μ^3 ; M.C.H.C., 34%. A blood film showed polychromasia and anisocytosis with slight macrocytosis.

On December 27 the patient complained of nausea, but her appetite was good. Haemoglobin was 63% (Haldane), or 9.3 g. per 100 ml.; red cells, 2,890,000; colour index, 1.07; corrected E.S.R., zero; P.C.V., 30%; M.C.V., 103 μ^3 ; M.C.H.C., 31%; white cells, 11,050 (neutrophils 58%,

eosinophils 8%, lymphocytes 32%, monocytes 2%). On January 5, 1952, the haemoglobin was 65% (Haldane), or 9.6 g. per 100 ml.; red cells, 3,260,000; colour index, 0.98; corrected E.S.R., zero; P.C.V., 31%; M.C.V., 94 μ^3 ; M.C.H.C., 32%; white cells, 7,900. Although the blood picture was slowly reverting to normal the patient was given 2 pints (1,140 ml.) of blood by intravenous drip, to expedite recovery.

Blood examination on January 12 showed: haemoglobin, 85% (Haldane), or 12.6 g. per 100 ml.; red cells, 3,950,000; colour index, 1.06; corrected E.S.R., 7 mm. in one hour; P.C.V., 38%; M.C.V., 94 μ^3 ; M.C.H.C., 33%; white cells, 9,200; reticulocytes, 2.5%. On January 12, and again on February 8, the urinary chromatogram was normal.

The patient remained afebrile throughout her stay in hospital and was never jaundiced.

Discussion

This case differs from cases of nitrobenzene poisoning reported by Chapman and Fox (1945) and Nabarro (1948) in that cyanosis was noted one hour after the ingestion of the nitrobenzene, which was much sooner than in their cases. The odour of nitrobenzene is quite distinctive and has been likened to that of essence of bitter almonds by Nabarro.

Hamblin and Mangelsdorff (1938) found methaemoglobin in the blood of all cases of nitrobenzene poisoning, whereas Loeb, Bock, and Fitz (1921) were unable to detect it and suggested the formation of a nitrobenzene haemoglobin compound. In our case the spectrum for methaemoglobin was obtained, although with considerable difficulty, in spite of the intense degree of cyanosis. Nabarro (1948) suggested that if methylene blue was given transfusion might not be necessary, and our case confirmed this, as the blood picture was definitely improving spontaneously before the second blood transfusion. It is unfortunate that the effect of methylene blue seems to be transient. Its mode of action has been discussed fully by Gibson (1948).

In view of the results obtained by Deeny, Murdock, and Rogan (1943) in the treatment of congenital methaemoglobinaemia with ascorbic acid we gave the patient large doses of this vitamin, although Shiels and Goldwater (1949) concluded that the beneficial effect of ascorbic acid in experimental and human benzene poisoning was not convincing.

Wirtschafter and Wolpaw (1944) have recorded a case of nitrobenzene poisoning in which there was a low total plasma protein content, a decrease in cholesterol esters, and slight but significant bromsulphthalein retention. It is probable that in their case, as in ours, there was an acute zonal hepatic necrosis. The condition must have been quite transient in our case, as subsequent urinary chromatography and extensive liver and kidney function tests did not reveal any abnormality. Uzman and Denny-Brown (1948) reported persistent amino-aciduria in early cases of hepato-lenticular degeneration (Wilson's disease) before liver-function tests showed any abnormality, and this has been confirmed in a similar case in this hospital. Himsworth (1950) considered that urinary chromatography was the best means of demonstrating amino-acids in the urine in cases of acute liver atrophy, and he suggested that their presence in this condition signified not only that liver cells had been killed but that few survived.

Wirtschafter and Wolpaw recommended glucose to fortify the liver and saline to replace that lost by vomiting. They dismissed replacement blood transfusion as unnecessary, but thought that the inhalation of oxygen in high concentration helped to prevent the formation of methaemoglobin, and they concluded that nitrobenzene affects the circulatory, respiratory, and central nervous systems both directly by toxic action and indirectly by the formation of methaemoglobin, with resultant anaemia. They thought that the hepatic and haemopoietic systems were damaged by direct toxic action.

Summary

A case of acute nitrobenzene poisoning is recorded in which there was methaemoglobinaemia and aminoaciduria. Urinary chromatography revealed a transient gross excess of all the normal amino-acids. The literature on the symptomatology and treatment of the condition is reviewed briefly. The patient made a rapid recovery.

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ACUTE TETRACHLORETHANE POISONING

A REPORT ON TWO FATAL CASES

BY

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Cases of acute tetrachlorethane poisoning, following its ingestion by mouth, are unusual. Only three such cases are reported in the English literature (Hepple, 1927; Elliott, 1933; Forbes, 1943). Acute tetrachlorethane poisoning is generally suicidal, its distinctive odour rendering its accidental ingestion unlikely. One case of acute accidental poisoning has, however, been recorded (Hauser, 1939). There is no record of tetrachlorethane having been used as a homicidal agent.

Tetrachlorethane is a colourless, non-inflammable, oily liquid, boiling at 146.3° C., and with a specific gravity of 1.600 at 20° C. It is soluble in fats, oils, resins, and waxes, miscible with alcohol, and soluble in water to the extent of 1 part in 5,000. It has a sweetish smell and taste, somewhat resembling trichlorethylene, carbon tetrachloride, and chloroform, but quite distinct to those who are familiar with it. The commercial preparations have a yellow tinge. As a solvent, tetrachlorethane has many applications in industry, but, owing to its intensely poisonous properties, being the most toxic of the halogenated hydrocarbons (Hamilton, 1934; Browning, 1937), it is falling into disuse. At one time it was issued to the Army as "silk cleansing fluid," and two of the three acute cases recorded in the English literature occurred in soldiers. Its widest application outside industry is in horticulture—as an effective insecticide against white fly. In the two cases described below, the tetrachlorethane was originally purchased as an insecticide.

Chronic tetrachlorethane poisoning has been described and reviewed by a number of authors (Willcox, 1915; Minot and Smith, 1921; Legge, 1934; van Oettingen,

1937; Forbes, 1943). Methods for the early detection of chronic tetrachlorethane poisoning by examination of the blood and urine have been described by Minot and Smith (1921), and Gurney (1943). Toxic jaundice due to tetrachlorethane poisoning became compulsorily notifiable in this country after January 1, 1916, as the result of cases occurring amongst aircraft workers, who used it as "dope" for the treatment of fuselage. Twenty-six cases, five of which were fatal, were notified in 1916, but no further cases were notified until a fatal case occurred in 1929. Although chronic tetrachlorethane poisoning is becoming virtually unknown in this country, cases are still occurring abroad. Seven such cases, one of which was fatal, have been recorded by Coyer (1944).

When taken in large quantities by mouth, tetrachlorethane kills by its narcotic action before recognizable changes can take place in the liver and other organs. Consciousness is rapidly lost, and this is followed by a gradual depression of the vital centres, death occurring some 10 to 20 hours after ingestion. In these cases, except for the presence and smell of tetrachlorethane, the necropsy findings are those of narcotic poisoning, with changes in the gastric mucosa depending on the quantity taken and the presence or otherwise of food. In the two cases to be described the tetrachlorethane had been deliberately taken by mouth.

Case 1

A gardener aged 57 had become depressed because the estate on which he had been employed for thirty years was about to change hands. He left home one day as usual at 7 a.m., taking his sandwiches with him. As his mother, with whom he lived, was often in bed before he returned home in the evening, he was not missed until the next morning. At about 10 a.m. on that day he was found dead on the floor of his potting-shed; an uncorked bottle of tetrachlorethane lay by his side and a short farewell note was found scrawled in chalk across his work-bench.

Necropsy was carried out the next morning. A strong smell of tetrachlorethane was apparent on entering the mortuary. The body was that of a well-nourished man. There was an intense cyanosis of the post-mortem livid stains. Anoxic haemorrhages were present in the scalp.

There was no corrosion of the mouth, lips, or tongue. The lower third of the oesophagus was congested, and early superficial necrosis of the mucosa was present. At the cardiac end of the stomach extreme congestion of the entire gastric mucosa was found, with superficial necrosis and frank erosion. At the pyloric end of the stomach the exposed ridges of the rugae were principally affected. From the stomach and the first half of the duodenum 15 oz. (425 ml.) of tetrachlorethane was recovered. The tetrachlorethane had not passed beyond this point. The stomach also contained a further 5 oz. (142 ml.) of fluid consisting mainly of mucus. Food was not present.

Numerous anoxic haemorrhages were scattered throughout the brain, and there was early basal collapse of both lungs. No material natural disease was present in other organs.

Case 2

A carpenter aged 20, recently discharged from the R.A.F., was depressed over an error he had made at work. On the day before his death he returned home as usual for lunch. He had a good meal and left the house at 1.20 p.m. to return to work. At 2.30 p.m. it was noticed that his bicycle was still in the garden, and almost immediately afterwards he was found unconscious in a wheel-barrow which was standing close to a greenhouse. Later a medicine bottle which contained tetrachlorethane was found in the greenhouse, with approximately 1 to 2 oz. (28 to 57 ml.) missing.