The patient was first seen at Addenbrooke's Hospital on February 26, 1953, when there was no clinical evidence of recurrence and the liver was not palpable. An x-ray film of the chest showed multiple small opacities at the base of the left lung, and examination of the urine at the same time showed melanogens to be present, and he was accordingly regarded as having pulmonary metastases. The presence of melanogens in this urine was shown by the ferric chloride in hydrochloric acid test, and by Thormählen's nitroprusside reaction (Harrison, 1947). No treatment was given.

Re-examination on July 8 showed disappearance of the pulmonary metastases and no melanogens in the urine. Since then repeated clinical and radiological examinations have shown no evidence of recurrence, and melanogens have not been present in the urine.

Discussion

Melanogen, the colourless chromogen of melanin, is excreted in the urine when there are extensive secondary deposits of malignant melanoma. Urine containing melanogen reduces sodium nitroprusside to ferric ferrocyanide (Thormählen's reaction) and reduces ferric chloride to ferrous chloride. Haden and Orr (1924) and Peters (1923) describe cases with apparent melanogenuria with no malignant melanoma in the body, but it seems doubtful if melanogen was really present in the urine in these cases. von Jaksch (1905) claims that a positive Thormählen reaction may be obtained in urine free from melanogen and has seen it in children suffering from chronic constipation; he says an abundance of melanogen occurs in the urine of wasted patients. Harrison (1947) states that he has tested many pathological urines and has never obtained a positive Thormählen reaction except in melanogenuria, and he concludes that if both the ferric chloride test and the nitroprusside reaction are positive it is safe to diagnose melanogenuria. In the case reported here it is considered that, as the choroidal tumour removed was a proved malignant melanoma, the pulmonary opacities were metastases and responsible for the presence of melanogens in the urine.

Spontaneous disappearance of a malignant tumour is a rare phenomenon of considerable interest, and several theories regarding the aetiology have been put forward. Rohdenburgh and Bullock (1918) collected 302 cases in which temporary or permanent regression of a malignant growth occurred. In this series the greatest number of spontaneous regressions followed incomplete surgical removal of the tumour or acute infections with prolonged pyrexia such as erysipelas, and a smaller number were associated with a profound upset of the patients' metabolism such as the menopause. He considered it probable that these conditions act by depressing the proliferative energy of the malignant cell until the defensive forces of the body are able to accomplish its final destruction. Ewing (1940) says the only explanation of many cases of spontaneous cure of highly malignant tumours is a local or general immunity. It is recognized that necrosis, probably starting because the tumour outgrows its blood supply, is a prominent feature of choroidal melanoma, and out of 106 tumours described by Samuels (1934) 24 were completely necrotic. Reese (1951) saw spontaneous necrosis occur in a malignant melanoma of the iris.

In the case reported here there was no obvious cause for the regression of the metastases such as an acute infection. As necrosis can bring about regression and apparent cure of the primary choroidal tumour, it is thought probable that this is the cause in this case rather than the other theories discussed.

Summary

A case of spontaneous regression of pulmonary metastases from a malignant melanoma of the choroid is described. Several theories concerning the aetiology are discussed, necrosis due to the tumour outgrowing its blood supply being considered the most probable.

I am grateful to Professor J. S. Mitchell for permission to publish details of this case and for his help, to Dr. N. R. Lawrie for assistance with the biochemical details, and to Dr. N. Ashton for supplying me with the pathology report.

REFERENCES

- Bennett, W. H. (1899). *Lancet*, 1, 3.
 Ewing, J. (1940). *Neoplastic Diseases*, p. 45. Saunders, Philadelphia.
 Gould, A. P. (1906). *Arch. Midx Hosp.*, 9, 7.
 Haden, R. L., and Orr, T. G. (1924). *Johns Hopk. Hosp. Bull.*, 35, 58.
 Harrison, G. A. (1947). *Chemical Methods in Clinical Medicine*, p. 221. Churchill, London.
 von Jaksch, R. (1905). *Clinical Diagnosis*, translated and edited by A. E. Garrod, p. 396. Griffin, London.
 Mathews, F. S. (1915). *Ann. Surg.*, 62, 115.
 Peters, J. P. (1923). *Arch. intern. Med.*, 32, 709.
 Reese, A. B. (1951). *Tumours of the Eye*, p. 224. Hoeber, New York.
 Rohdenburgh, G. L., and Bullock, F. D. (1918). *J. Cancer Res.*, 3, 193.
 Samuels, B. (1934). *Arch. Ophthal. (Chicago)*, 11, 998.
 Willis, R. A. (1953). *Pathology of Tumours*, p. 908. Butterworth, London.

THERAPY IN EXPERIMENTAL HEPATIC FAILURE

BY

P. C. REYNELL, D.M., M.R.C.P.

Medical Tutor, Radcliffe Infirmary, Oxford

It is difficult to assess the effect of any drug in the treatment of acute hepatic failure in man. A few patients will recover spontaneously, and any method of treatment used will then be given credit for the successful outcome. No satisfactory therapeutic trial comparing similar groups of treated and untreated cases has ever been carried out, and the difficulties in the way of such a trial are formidable, for the condition is uncommon and may be due to a variety of causes.

A controlled trial of the efficacy of some of the measures advocated for the treatment of acute hepatic failure in man has therefore been carried out on rats in which the syndrome has been reproduced experimentally.

Methods

It has been shown that the injection of 0.02 to 0.04 ml. of carbon tetrachloride into the mesenteric vein of the rat will reproduce many of the clinical and pathological features of the syndrome of acute liver failure seen in man (Reynell, 1953). A large proportion of the rats so treated will die within 48 hours. The procedure was designed to produce severe hepatic necrosis without damaging other tissues. Adult male rats of the Wistar strain (200–400 g. body weight) and free of Bartonella infection were used in these experiments.

Experiment I: Vitamin Supplements by Mouth.—Thirty-four rats reared on stock diet were each given 10 g. of a synthetic diet daily for two days before the injection of carbon tetrachloride into the mesenteric vein. The diet was made up as follows: cornstarch, 71 parts; casein, 26 parts; and salt mixture, 3 parts. During the three days after operation each rat was offered 5 g. a day of the same diet, although even this reduced amount was not always consumed. Half the rats were given the following vitamin supplement, which was mixed with the diet: 2 mg. of nicotinic acid, 1 mg. of thiamine, 1 mg. of riboflavin, 1.5 mg. of tocopherol, and 30 mg. of choline chloride per rat daily. This supplement resembles the parenteral vitamin mixture advocated by Latner (1950) for the treatment of hepatic failure.

Experiment II: Large Doses of Parenteral Liver Extract.—Of 24 rats fed on stock diet and subjected to the injection of carbon tetrachloride into the mesenteric vein, 12 were given 0.25 ml. of commercial liver extract daily by subcutaneous injection for two days after operation.

Experiment III: Sodium Gluconate.—Of 28 rats fed on stock diet and subjected to the injection of carbon tetrachloride into the mesenteric vein, half were given 50 mg. of the monosodium salt of glutamic acid eight-hourly by subcutaneous injection for 48 hours after operation.

Experiment IV: Cortisone.—Of 40 rats fed on stock diet and subjected to injection of carbon tetrachloride into the mesenteric vein, 20 were given 2 mg. of cortisone per 100 g. body weight twice a day by intramuscular injection for two days after operation.

Results of Treatment

Treatment	Treated Animals		Controls	
	Surviving	Dead	Surviving	Dead
Vitamin supplements ..	10	7	11	6
Liver extract ..	5	7	4	8
Sodium glutamate ..	4	10	5	9
Cortisone ..	6	14	7	13

Results

In none of these experiments was there any significant difference between the mortality of the treated rats and that of the controls (see Table). Vitamin supplements by mouth, large doses of liver extract parenterally, sodium glutamate, and cortisone all separately failed to improve the chances of survival of rats with experimentally induced hepatic failure.

Discussion

Polyvitamin therapy (Latner, 1950), large doses of liver extract (Snell and Butt, 1941), glutamic acid (Walshe, 1953), and cortisone (Ducci and Katz, 1952) have all been advocated for widely differing reasons in the treatment of hepatic failure. Though these measures may sometimes be followed by symptomatic improvement, claims that they increase the patient's chances of survival should be examined critically. Although there are possible dangers in applying the results of animal experiment to man, no adequately controlled human therapeutic trial has been done, and one is obliged to draw conclusions from human observations which are relevant but inconclusive and from animal experiments which are conclusive but of uncertain relevance.

The clinician faced with a patient suffering from acute liver failure has to deal with a liver which is already severely damaged, and treatment is probably effective only in so far as it will protect the organism against the effects of liver damage until regeneration can occur. Since the metabolic effects of liver injury are so extensive, it is unlikely that any single chemical substance will do this completely, and, as in acute renal failure, the object of treatment must be to maintain chemical homoeostasis until spontaneous recovery occurs. There is a need for more fundamental knowledge of the biochemistry of liver failure in order to plan rational therapy.

Summary

Acute hepatic failure has been produced in rats by the injection of small quantities of carbon tetrachloride into the mesenteric vein.

Vitamin supplements, large doses of liver extract, sodium glutamate, and cortisone all failed to reduce mortality in this type of experimental liver failure.

I am grateful to Miss Shirley Thomas for technical assistance and to Professor L. J. Witts, in whose department this work was done.

REFERENCES

- Ducci, H., and Katz, R. (1952). *Gastroenterology*, 21, 357.
 Latner, A. L. (1950). *British Medical Journal*, 2, 748.
 Reynell, P. C. (1953). *J. Path. Bact.*, 66, 47.
 Snell, A. M., and Butt, H. R. (1941). *Trans. Ass. Amer. Phys.*, 56, 321.
 Walshe, J. M. (1953). *Lancet*, 1, 1075.

SURGICAL EMPHYSEMA AS A COMPLICATION OF ANAESTHESIA

BY

J. OZINSKY, M.B., Ch.B.

AND

A. B. BULL, M.B., Ch.B., D.A.

(From the Department of Anaesthesia, University of
Capetown)

Surgical emphysema is that condition in which gas is present in the tissues. This gas may be air or, during anaesthesia, any of the gases used in induction. The first case of surgical emphysema occurring as a complication of anaesthesia was reported by Woolsey in 1912. Thereafter sporadic reports of cases have been published.

Two factors are concerned in the aetiology: (a) the presence of gas under pressure, and (b) some form of trauma permitting entry into the tissues. During anaesthesia, trauma may be produced on any portion of the surface lining of the respiratory tract, including the nose and pharynx, and is usually due to instrumentation (Barrett and Thomas, 1944; Gordon, 1950). Laceration of the mucosa permits gases in the lumen of the respiratory tract to gain access to the submucosal connective tissue and to spread from there.

Gas under pressure in the lumen of the respiratory tract may itself produce the trauma and spread in the connective tissue. Normally the weakest point of the respiratory tract is the alveolar wall, and raised pressure will cause trauma here. In man, a case has been reported in which an intrabronchial pressure of only 12 mm. Hg caused emphysema (Heidrick *et al.*, 1940; Marcotte *et al.*, 1940), and a pressure above 80 mm. Hg will almost always rupture the alveolar walls and their contained vessels, causing air embolism (Haldane and Priestley, 1935). This excess pressure may be exerted by the anaesthetist with his machinery easily enough nowadays, when controlled respiration is so commonplace. Tuffier (1906) showed that a pressure of 6 mm. Hg was enough to maintain distension of the lungs, and 15 mm. Hg has been advocated as the maximum pressure that should be employed in controlled respiration (Thornton *et al.*, 1944). The patient may himself raise the intrabronchial pressure, as by coughing or straining (Hamman, 1945).

The mechanism involved is (Macklin, 1937): The alveolar wall ruptures and gas passes perivascularly along the vessels to the hilum and mediastinum, producing mediastinal emphysema, which becomes the focal point for the further spread of the gas. The gases may (a) spread with the large vessels up to the neck and present as subcutaneous emphysema, (b) spread with the vessels down into the retroperitoneum, or (c) rupture the mediastinal pleura, thus producing pneumothorax. The important point is that pneumothorax does not result directly from rupture of the alveolus.

Clinical signs and symptoms depend on the site and the amount of gas present. Mediastinal emphysema (Hamman, 1945) causes obstruction to the return of blood to the heart and thus lowers the cardiac output, showing clinically as dyspnoea, cyanosis, engorged veins, obliteration of the cardiac dullness, and crackling sounds