one of these is clearly shown in fig. 3a. Serum bilirubin and SGPT levels were normal and alkaline phosphatase was only slightly raised at 125 IU/l. No further evidence of metastatic disease was obtained from a brain scan, bone scan, or bone marrow biopsy. Combination chemotherapy was administered monthly consisting of cyclophosphamide 1 g, vincristine 1.5 mg, and methotrexate 200 mg, the latter infused over 48 hours, and was followed by a course of folinic acid. His cough was relieved by treatment and chest x-ray pictures showed no detectable increase in the small right-sided hilar shadow over a three-month period. After three months the liver had become palpably enlarged but liver function test results were normal. An ultrasonogram at the same parasagittal level as before (fig. 3b) showed that the metastasis had doubled in size and that the overall size of the liver had increased. Repeat ultrasonograms four and five months after the start of chemotherapy (figs. 3c and d) showed a progressive increase in the tumour size until most of the liver substance was replaced and gross hepatomegaly was apparent. Enlarging cold areas were now apparent in serial liver scintigrams. Six courses of chemotherapy were given, during which time there was a gradual decline in the patient's health. The liver continued to enlarge, right hypochondrial pain occurred, and the patient lost weight and developed spinal metastases. He died seven and a half months after the start of treatment, but permission for necropsy was refused.

Discussion

The ability to detect early metastases in liver has important implications for the surgeon considering a radical excision of malignancy as well as for the doctor considering the use of radiotherapy or chemotherapy. Physical examination is a time-honoured method of attempting to assess metastasis in the liver but, as shown by our second case, this may be extensive before any clinical enlargement is apparent. Liver function test results were significantly abnormal only when gross disease was present.

In Case 2 the use of ultrasound allowed us to measure precisely the size of the lesion as well as the overall size of the liver, estimated from the distance between the superior and inferior borders. Liver volume can be estimated by ultrasound by integrating multiple cross-sectional areas (Rasmussen, 1973),

but since this requires a computer it is simpler to assess liver size by the method mentioned above.

In case 1 both ultrasound and scintigraphy allowed detection of metastases before they were clinically apparent, but a formal comparison of the methods has shown that ultrasound is more reliable in the detection of early lesions (Taylor *et al.*, 1974). Moreover, it is more reliable than scintigraphy for monitoring the response of the lesion to radiotherapy (Taylor, 1974). Spurious cold areas may be seen on scintigrams after such treatment since local phagocytic activity of Kupffer cells, on which isotope uptake depends, is depressed.

Fine structure of liver cannot be displayed with most commercially available ultrasound scanners, which are suited only to urogenital and obstetric investigations. The scanner we used was developed on the principles used by Kossoff (1972) for detailed obstetric examinations, and its application to cancer diagnosis allows detection of hepatic lesions of less than 1 cm in diameter (Taylor *et al.*, 1973). Taylor *et al.* (1973) also described dramatic changes in the appearance of tumours after radiotherapy, and similar changes occurred after chemotherapy. Successful treatment in case 1 resulted in a change from a black homogeneous tumor area to more highly reflective areas with normal liver architecture. Unsuccessful treatment, as in case 2, was indicated by both the continued growth of the metastasis and the absence of any change in consistency.

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MEDICAL MEMORANDA

Usefulness of ^{99m}Tc-Technetium Pertechnetate in Periarthritis Nodosa

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Radioisotopes have a wide range of applications in the clinical investigation of many organs. Muscle diseases are an exception in this expanding field. We report here a case of periarthritis nodosa in which unusual scintigraphic images were obtained with ^{99m}Tc-pertechnetate. The kinetics of this isotope and the scintigraphic changes were followed during treatment and found to be useful clinical tools.

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Case Report

A 58-year-old butcher was admitted to hospital because of fever of unknown origin. The illness had started 10 days previously and had become progressively more severe. It was characterized by bouts of fever, generalized muscle ache, profuse sweating, and headache. The muscle aches were severe and more or less migratory though the musculi sternocleidomastoidii, masseteri, quadriceps femori, and solei were the most affected. There were few other symptoms and none which could suggest infection and the patient had taken no drugs before the onset of symptoms.

Three years previously an artificial anus had been constructed after a 60-cm colectomy performed for a glandular epithelioma. At that time and during follow-up the prognosis was considered good.

On admission the patient was fully conscious and did not look ill. The physical examination showed only a slight degree of pyrexia and extremely tender muscles. There was a discreet motor deficiency of the muscles of the thighs but no other neuromuscular abnormality.

Many clinical investigations were carried out. Bacterial, viral, and parasitic infections were ruled out using cultures of blood, urine, sputum, and faeces on various media as well as antibody characterization. The results of classical rheumatic tests were normal as were the creatine phosphokinase and aldolase serum levels. There was no anaemia but the W.B.C. was 20,700/mm³ with 94% granulocytes. The erythrocyte sedimentation rate (E.S.R.) was 75 mm in 1 hr (Westergren) and reached 125 mm in 1 hr three days later. The fibrinogen was 1,380 mg/100 ml

(normal 150-300 mg/100 ml), the α -2 globulins were raised, and the total complement was nil (normal 300-660 mU/100 ml).

On the fifth day in hospital painful nodules were felt in the lateral aspect of the left thigh. Biopsy showed lymphocytic and histiocytic infiltrations of the arterial walls. A probable diagnosis of connective tissue disease was made and prednisolone therapy was begun.

Examination of the biopsy specimen after inclusion and staining confirmed the diagnosis. The lesion was described as being typical of necrosing arteritis, the muscles themselves being devoid of lesions.

Because of the probable collagenosis a joint scan using ^{99m}Tc -pertechnetate was performed. The joints seemed undamaged but an unusual patchy distribution of the isotope in various muscles was seen.

The patient reacted favourably to the prednisolone therapy though daily doses of 100 mg were necessary at the beginning. His fever subsided and the biological values returned to normal. The patient left the hospital after two months. He was told to take 12.5 mg prednisolone a day and was followed in the outpatient department. One month later the only abnormality was a E.S.R. of 30 mm in 1 hr.

A second muscle biopsy specimen obtained in the fifth week was normal.

The first scans were obtained on the patient's 10th day in hospital and dynamic studies were performed on days 21, 35, and 86.

RADIOISOTOPIC INVESTIGATIONS

A total of 10 mCi of ^{99m}Tc -pertechnetate was injected intravenously. The first scintigrams were obtained on a conventional γ -camera (Pho-Gamma III, Nuclear, Chicago). The joints were free of isotope concentration while there was an intense patchy distribution of the tracer in the muscles above and below the joints (fig. 1).

FIG. 1—Scintigram of region of right knee showing intense and irregular distribution of ^{99m}Tc -pertechnetate in muscles.

The dynamic studies were performed afterwards as follows: the γ -camera was connected to a computer (Varian) equipped with a magnetic tape recorder and an electrostatic printer (Statos). The radioactivity was continuously recorded and stored on an incremental basis over half an hour. Regions of interest were selected on the electrostatic image in such a way that they could be reinvestigated with accuracy on later occasions. The evolution of the radioactivity in each region was easily seen.

The variation of the radioactivity during 30 minutes in one region of interest at days 21, 35, and 86 is shown in fig. 2. A plateau was reached after about 22 minutes, 16 minutes, and seven minutes respectively. Curves obtained in six normal men showed that the plateau was reached between the sixth and eighth minute. The same pattern was observed for other regions. The height of

FIG. 2—Kinetics of ^{99m}Tc -pertechnetate in same region of thigh on days 21, 35, and 86. Arrows indicate time at which plateau was reached.

FIG. 3—Scintigram of calves at day 86 showing less intense and more uniform distribution of tracer.

the plateau depends on the experimental conditions; it has no meaning as far as comparison of the curves is concerned.

Polaroid images were also obtained during these follow-up investigations, and patchy distribution of the tracer was confirmed, though the uneven distribution became less intense with time (fig. 3).

Comment

Mintz *et al.* (1970) mentioned that radioiodinated serum albumin showed a patchy distribution in muscles affected with periarteritis nodosa and concluded that isotopes were simple and promising tools for the study of connective tissue disease and muscle physiology and disease.

Nobody so far has studied the kinetics of a radioisotope-labelled material in periarteritis nodosa.

Technetium-99m-labelled pertechnetate is 90% bound to intravascular proteins and diffuses readily to extravascular spaces (Hays and Green, 1972). In normal subjects an equilibrium is reached in muscles 6-8 minutes between intravascular and extravascular pertechnetate. This time was more than doubled in our patient at the beginning of the disease, most probably because of the inflammatory processes involved in the angiitis, but it returned to normal under treatment.

Furthermore, the scintigraphic changes correlated well with the clinical state and the changes in the biological values. The scan pattern and the delay in the equilibrium of the curve were still abnormal when the second biopsy was normal though one could infer from the clinical state and the E.S.R. that the disease was still active. After 13 weeks the only abnormalities were a raised E.S.R. and the scan pattern.

Whether the appearance of the scan is pathognomic for periarthritis nodosa, as stated by Mintz *et al.* (1970), remains to be proved, but we feel that the combination of dynamic studies and scintigraphy provided a valuable and objective means of evaluating the extent of this disease and its response to treatment. The possibilities offered by this simple method in other collagen and muscle diseases are under investigation.

We thank Mr. A. Dobbeleer for technical help and Professor S. Orloff for referring normal controls.

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Termination of Pregnancy with Utus Paste: Report of a Fatal Case

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Termination of a mid-trimester pregnancy when the uterus is already scarred from a previous hysterotomy has until recently posed a problem of management. If a second hysterotomy is performed subsequent pregnancies may require delivery by caesarean section to avoid a risk of the uterus rupturing during labour. Hence pharmacological methods of termination have been used instead of a second hysterotomy. One such abortifacient agent which has been available for a number of years is Utus paste and many reports of its efficacy have appeared.

Utus paste is a proprietary preparation consisting of a semi-solid soap mixed with potassium iodide and astringents. It is administered after warming to 37°C by injection through a sterile metal cannula which has previously been introduced through the uterine cervix. Expulsion of the uterine contents usually occurs within 24 hours and should be complete. If uterine evacuation is incomplete or if it is followed by persistent bleeding curettage is performed.

Reports of serious and sometimes fatal reactions to the use of intrauterine pastes have appeared in the literature during the past 30 years. We report such a case which occurred immediately before the prostaglandins became available.

Case Report

The patient, aged 19 years, was undergoing therapeutic termination of a pregnancy of 14 weeks' gestation for social reasons. Three years previously she had undergone a hysterotomy for the termination of a pregnancy of 20 weeks' gestation. On the present occasion the uterus was thought to be too large to allow suction termination and it was therefore decided to use Utus paste. Preoperatively her haemoglobin was 13.4 g/100 ml and there was no previous history of serious illness or allergies. She was not taking any medication.

Premedication with papaveretum 15 mg and atropine 0.6 mg was given about one hour preoperatively. Anaesthesia was induced with 70 mg methohexitone intravenously and maintained with 70%

nitrous oxide, 30% oxygen, and 0.5% halothane. The cannula was introduced into the uterus and 25 ml of Utus paste was injected.

Anaesthesia was discontinued and the patient opened her eyes almost immediately. She was lifted on to a trolley and turned to the right lateral position. Within seconds she became apnoeic, cyanosed, and pulseless. She was intubated immediately and ventilated with 100% oxygen and external cardiac massage was begun. A catheter was passed to the right side of the heart and aspiration of blood from the catheter showed no obvious evidence of air embolism. Atropine 0.6 mg, isoprenaline 0.1 mg, and sodium bicarbonate 200 mEq were infused through the catheter. E.C.G. showed asystole but injection of 1 ml of adrenaline 1/1,000 and 10 ml of 20% calcium chloride produced ventricular fibrillation. This was converted to sinus rhythm by external defibrillation and the peripheral pulses were found to be regular and of good volume. Cyanosis persisted however, though the lungs were easy to inflate, and after two or three minutes ventricular fibrillation recurred. External cardiac massage was resumed, mannitol infusion was begun, and a urinary catheter was inserted into the bladder. Uniformly blood-stained urine was obtained and because of the possibility of haemolysis blood samples were sent for full haematological analysis. About 45 minutes after the initial cardiac arrest the patient's colour improved and she reverted to sinus rhythm spontaneously. She was then transferred to the intensive care unit.

The chest x-ray picture was normal. The whole blood haemoglobin was 13.2 g/100 ml but 1.1 g of this was accounted for by the plasma haemoglobin. Also the urine was positive for haemoglobin. Intravascular haemolysis was diagnosed from this evidence. The peripheral blood film showed entirely normal red cell morphology. Because of the severe degree of red cell breakdown the serum potassium was estimated and found to be 4.1 mEq/l. (normal). A diagnosis of "defibrination" syndrome appeared to be confirmed by the following results of test performed on the appropriate serum and citrated blood samples: thrombin clotting time 40 seconds (normal control value 14 seconds), corrected by the addition of equal parts of normal plasma to 15 seconds; fibrinogen titre 1 in 4 (normal value 1 in 128 or greater); and fibrin-fibrinogen degradation products (latex agglutination kit; Diagen) a normal level of less than 8 µm/ml. These results were interpreted as showing severe consumption coagulopathy without evidence of enhanced fibrinolytic activity.

In view of this diagnosis anticoagulant therapy was instituted. Heparin was administered by constant intravenous infusion at a rate of 1,600 units/hour in an attempt to prevent progression of the consumption coagulopathy. About six hours later the patient's condition deteriorated and despite intermittent positive-pressure ventilation, blood transfusions, mannitol, and dexamethasone she died 13 hours after her initial cardiac arrest.

Necropsy showed evidence of massive haemolysis, the blood being almost completely fluid throughout the circulatory system. There were extensive subcutaneous haemorrhages, subdural haemorrhages, and a retroperitoneal haemorrhage. No pulmonary embolism was evident though the lungs were oedematous and showed extensive intrapulmonary haemorrhage. There was also haemorrhage into the myometrium and broad ligament but no evidence of uterine trauma and the uterine membranes were intact.

Comment

This patient developed three complications immediately after

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