The chromosome aberrations—for example, gaps, breaks, and fragments—present in our patient's second bone-marrow examination, taken in remission, and in the stimulated lymphocyte culture are of uncertain significance; the bone-marrow changes may have been due to the rubidomycin, but the lymphocyte changes could well be due to the lysergide. Thus we have found that similar abnormalities in bone-marrow chromosomes occur after a course of rubidomycin therapy (unpublished observations). Nevertheless, as only a few hours had elapsed between the administration of the first injection of rubidomycin and the preparation of the lymphocyte culture, it may be that the aberrations detected in the lymphocytes are a lysergide effect.

On the basis of the findings reported in this and other communications it is suggested that cases of leukaemia that follow administration of lysergide be reported, preferably with cytogenetic studies, as this may allow an appraisal of the possible relationship between lysergide and leukaemogenesis.

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Diagnosis of Deep-vein Thrombosis with an Ultrasonic Doppler Technique

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Summary: An ultrasonic technique has been used to diagnose deep-vein thrombosis, the venous system being examined from the calf to the inferior vena cava. The method is quick, simple, and repeatable, and the results compare favourably with those from phlebography.

Introduction

The clinical diagnosis of deep-vein thrombosis in the early stages when there is a risk of massive pulmonary embolism is notoriously difficult and inaccurate. Currently the methods available for confirmation of a suspected diagnosis are phlebography and in some centres isotopic studies. Strandness *et al.* (1967) and Sigel *et al.* (1968) reported experience with an ultrasonic method incorporating the Doppler principle for the diagnosis of peripheral thrombosis, which promised to be simple, inexpensive, and reliable. We have further extended this use and now report our early experience based on this principle.

Technique

Apparatus.—A portable battery-run Sonicaid machine independent of mains supply operating at 2 megahertz (MHz) was used. This consisted of a power generator and amplifier con-

nected by a lead to a transducer containing two piezoelectric crystals. A controlled squeeze was applied to the calf by means of a cuff which could be rapidly inflated. If in addition to the audible signal permanent visual recordings were required a standard two-channel recording machine was used.

Principle.—The transducer containing two piezoelectric crystals were applied to the skin overlying the vessel to be examined, olive oil being used as a coupling medium. One crystal acted as a source of ultrasound and the other as a receiver. When the transducer was applied over a vein a faint noise was heard from the amplifier, due to sound reflected from the blood passing along the vein. If the velocity of blood flow in the vein was accelerated more blood passed through the ultrasonic beam and caused a change of frequency and amplitude of the sound to be picked up by the receiving crystal. In a normal leg augmentation of velocity of flow by squeezing the thigh or calf produced an easily audible roar from the amplifier. With a recent venous occlusion there was either little or no augmentation of venous return and no corresponding response from the ultrasonic detector.

The ultrasonic response to increased venous flow has been termed the "A" wave by Sigel.

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Method

Patients with suspected deep-vein thrombosis were first clinically assessed. The girth of the legs, leg temperatures, local calf tenderness, tenderness along the axis of the vein, or filling of the superficial veins were assessed, and the diagnosis of deep-vein thrombosis based on the interpretation of these signs.

The patients were then subjected to ultrasonic investigation at the bedside and were examined sitting at 45° with the legs straight out in front and the ankles supported to allow good filling of the calf veins (see Fig. 1).

FIG. 1.—Ultrasonic investigation. The transducer is applied to the groin. The patient sits at 45° with the legs straight and the feet supported to allow filling of calf veins. A cuff is applied to the calf and is rapidly inflated to accelerate the velocity of deep venous flow.

The transducer of the Sonicaid machine was placed on the groin and the femoral artery first audibly detected. The transducer was then moved medially for "½" in. (1.3 cm.) to be sited over the common femoral vein. The thigh of the patient was gently squeezed over the line of the superficial femoral vein, and a controlled pressure squeeze was then applied to the calf. The results were heard and recorded to produce a Dopplergram.

In those subjects with normal limbs Dopplergrams showing A waves from the thigh and calf were recorded. In those with obstruction the presence of A waves depended on the site of occlusion. If the popliteal vein was obstructed A waves would be detected only from the thigh, while if in addition the superficial femoral vein was occluded no A waves would be present (see Figs. 2 and 3). By siting the transducer operating at 2 MHz over the external iliac vein and inferior vena cava it was possible to detect the presence or absence of A waves from the thigh. Five minutes was sufficient time for examination by this method.

FIG. 2.—Dopplergrams of right and left legs. In the right leg normal A waves are present on compression of the upper, mid, and lower thigh and calf. In the left leg they are absent, indicating obstruction.

Patients with clinical suspicion of deep-vein thrombosis were then subjected to either bilateral peripheral phlebography or ^{125}I -labelled fibrinogen studies and the results compared. The correlation between ^{125}I -labelled fibrinogen and phlebography has previously been established by Flanc *et al.* (1968) and Negus *et al.* (1968).

Results

Thirty normal people were subjected to Dopplergrams. A waves were present on standard calf squeeze in all 60 legs.

Nineteen patients with possible deep-vein thrombosis were then examined. In these 19 patients 19 legs were thought clinically to be the site of deep-vein thrombosis and 19 to be clinically normal. In the former category ultrasonic investigation showed that in eight A waves were absent (see Table I), while in 11 the results were normal. On x-ray or isotopic examination 10 of the 19 legs showed evidence of thrombosis whereas nine were found to be normal. The two which were normal on ultrasonic investigation were found on venography to have minor calf thrombosis.

In the latter category two legs which appeared to be clinically normal had obstruction on ultrasonic examination (see Table II), while on venography three were abnormal. Of these

FIG. 3.—Peripheral venogram of left leg of patient illustrated in Fig. 2. There is total obstruction of the popliteal and superficial femoral vein.

two had obstruction of the popliteal vein or above and one had minor calf thrombosis. This latter one was missed on ultrasonic examination.

TABLE I.—*Comparison of Ultrasonic and X-ray or Isotopic Studies in 19 Legs with Clinical Deep-vein Thrombosis. The Two Legs Which Were Normal on Ultrasonic Examination had Very Minor Calf Thrombosis on Venography*

	Ultrasonic Dopplergram	X-ray or Isotope Examination
Positive	8	10
Negative	11	9

TABLE II.—*Comparison of Results of Ultrasonic and X-ray or Isotopic Studies in 19 Clinically Normal Legs. The One Patient Not Diagnosed by Ultrasound had Minor Calf Thrombosis on Venography*

	Ultrasonic Dopplergram	X-ray or Isotope Examination
Positive	2	3
Negative	17	16

By varying the site of the squeeze applied to the leg it was possible to indicate accurately the upper limit of the thrombosis in the affected veins if the occlusion was in the popliteal vein or above. The correlation between Dopplergrams and venograms was accurate. One patient had incomplete occlusion of his popliteal vein on venography, and Dopplergrams again showed the upper limit of the thrombus. In the 25 legs which were normal on venographic or isotopic survey no false positives were obtained by Dopplergrams.

Discussion

In this preliminary report ultrasonic investigation was far superior to clinical examination. Clinical assessment was accurate in only about half of the cases in this series where the diagnosis of deep-vein thrombosis was made. More important possibly was the fact that three legs thought clinically to be normal proved to have thrombosis. In two of these the process was extensive.

Ultrasonic investigation was performed after clinical examination and before the results of the ancillary tests were known. The correlation between ultrasonic and venographic or isotopic

studies in this small series was 92%. On ultrasonic investigation thrombosis was diagnosed in 10 legs whereas with venography or isotopic tests thrombosis was found in 13 of the 38 legs examined. The three legs not diagnosed by ultrasound were found to have thrombosis in one group of calf veins only.

Five per cent. of all hospital deaths result from massive pulmonary embolism, and of these patients just over half would have returned to a normal mode of life but for the fatal incident. As most of the emboli originate from the deep veins of the leg the need for a method which is simple, quick, accurate, easily repeatable, and without discomfort to the patient is obvious. An individual can be rapidly trained to use such a method, and it appears that ultrasound will prove to be a useful test for regular screening of a patient at risk of massive deep-vein thrombosis, especially as Dopplergrams can be performed at the bedside with the minimum of discomfort to the patient.

As tissue penetration with ultrasound is inversely related to the frequency it has been found that, operating at 2 MHz, it is possible to scan the venous system from the calves to the inferior vena cava.

Potential hazards from the ultrasound appear to be negligible as the entry output is 10 milliwatts/sq. cm. Many thousands of obstetrical cases have been monitored for lengthy periods at a similar energy output by means of the same instrument without any reported ill effects.

Further investigations into the problem of diagnosing deep-vein thrombosis are in hand, and the results will be presented in a more extensive future communication.

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Medical Memoranda

Severe Muscle Cramp due to Acute Hypomagnesaemia in Haemodialysis

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Attention has recently been drawn to the complications of hypermagnesaemia induced by haemodialysis for chronic renal failure (Govan *et al.*, 1968). We report here a case of severe muscle cramp due to acute hypomagnesaemia occurring in chronic intermittent haemodialysis. Wacker and Parisi (1968) extensively reviewed abnormalities of magnesium metabolism in man; there is no reported evidence for acute hypomagnesaemia related to dialysis.

CASE REPORT

The patient, a 38-year-old white South African with advanced chronic glomerulonephritis, was started on regular twice-weekly haemodialysis early in 1968, a Kolff kidney with twin coil 145 being used for nine hours per dialysis. After about four months he began to develop severe muscle cramps in both legs and to a lesser degree in both arms. These involved the smaller muscles in particular and usually came on about six to seven hours after the start of dialysis, gradually fading in the 12 hours after the end of dialysis. The blood pressure and pulse remained normal throughout, and no excessive loss of weight was noted. Both oral quinine and intravenous saline were given without any effect on the cramp.

Physical examination failed to show any abnormal signs beyond the muscle spasm. Both Chvostek and Trousseau signs were