Death in this series was due similarly either to recurrent coronary thrombosis with myocardial infarction (6 cases), congestive heart (5 cases), or to extracardiac causes (3 cases). Upon comparison the mortality rate mainly from cardiac cause in the control series was 30% as against 12% for the choline treated patients.

Discussion. Previous clinical and experimental observations on the action of choline in preventing or mitigating experimental atherosclerosis have suggested that this lipotropic agent like that of its fellow members of the vitamin B complex inositol,(5) pyridoxine, (8) and methionine,(5) appears to prevent arterial atheromatous deposition or to exert a decholesterolizing effect on the atheromatous deposits in the vascular walls of experimental animals,(3,4,5) and in man.(6)

Summary. Over a 3-year period the lipotropic agent choline was effective in significantly reducing the mortality rate due to recurrent coronary thrombosis with myocardial infarction in a series of 115 patients with proven coronary atherosclerosis.

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Portal Blood in Collateral Veins of Patients with Cirrhosis. Acetylation by the Intestine. (17567)

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Few direct studies on absorption from the gastro-intestinal tract have been carried out in humans because of the inaccessibility of the portal vein. The use of the London angiostomy technique(1) for obtaining portal vein blood shed considerable light on the absorption process in animals, but due to the difficulty of the procedure the studies were limited. Furthermore, the applicability of these studies to humans is uncertain. Sherlock and Walsh(2) made the interesting observation that a large superficial collateral vein over the abdomen of a patient with cirrhosis of the liver could be shown to contain portal blood. Their observations were restricted, however, because the vessel became thrombosed after the injection of radio-opaque dye. Three other patients with cirrhosis failed to show evidence of portal blood in their abdominal veins. The present investigation was undertaken to ascertain the incidence of superficial abdominal veins carrying portal blood in patients with cirrhosis of the liver and to devise a simple method for detecting such channels. A large proportion of patients with cirrhosis were found to show abdominal portal collaterals. Two simple techniques for their detection are described, together with preliminary physiological studies using the proven portal collaterals. After this work was completed, Billings and DePree(3) reported observations on glucose absorption in abdominal veins of patients with cirrhosis. They also found a high incidence of portal collaterals.

The dynamics of the absorption process as revealed in portal (abdominal collateral vein) and peripheral (antecubital vein) blood are illustrated in Fig. 1. A patient with cirrhosis and ascites was given 2.5 g of sulfadiazine orally and the concentration of the total drug in the blood was determined by the method of Bratton and Marshall.(4) The level in the

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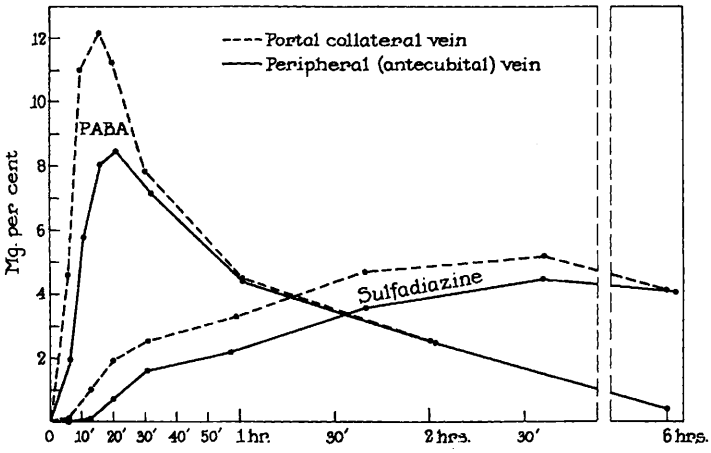

FIG. 1.

Portal (collateral vein) and peripheral (antecubital vein) blood levels after feeding 2.5 g of sulfadiazine and 2.5 g of PABA on separate days.

portal blood rose to 1 mg% before any significant amount of drug appeared in the peripheral blood. The level was consistently higher in the portal blood until after the peak of absorption, when the levels in the two systems became equal. The same patient on another occasion was fed 2.5 g of p-aminobenzoic acid. Because of the more rapid absorption of this drug, there were wider differences between the levels in portal and peripheral blood until the peak of absorption was reached. Following this, the level in the portal blood began to fall, while that in the peripheral blood was still rising. Both levels then dropped to reach the same concentration, and remaining equal, fell further as the drug was eliminated rapidly from the blood stream.

Since the determination of sulfonamides is tedious and time consuming, substances that could be measured more easily were used to demonstrate portal blood. Fig. 2A shows the levels of thiocyanate in the peripheral and portal blood after an oral dose of 1 g of sodium thiocyanate. Thiocyanate is rapidly and simply determined by the method of Crandall and Anderson(5) modified for use of only 1 cc of serum. The determination of fluorescein is even simpler and requires only a fraction of a cc of blood. After feeding 0.25 g of sodium fluorescein (Fig. 2B), 0.1 cc of serum was diluted in 10 cc of weak base and the level read directly in the photofluorometer. In the fasting state thiocyanate and fluorescein are almost completely absorbed within 45 to 60 minutes. Fifteen minutes after ingestion the level in the portal blood is approximately twice that in the peripheral blood. An additional determination at 25-30 minutes may be used to confirm the wide difference in levels diagnostic of the portal

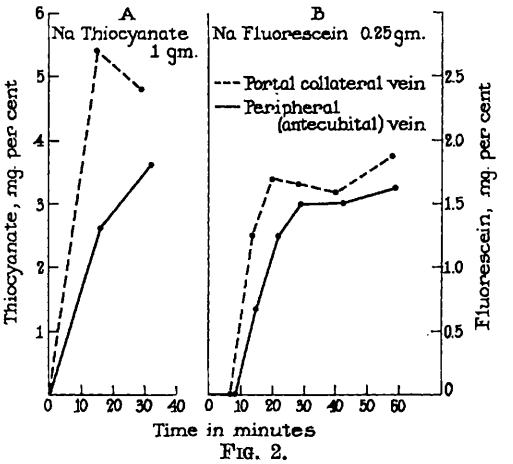

FIG. 2.

Portal (collateral vein) and peripheral (antecubital vein) blood levels after feeding of thiocyanate and fluorescein in different patients.

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TABLE I.
Acetylated and "Free" PABA Levels in Portal and Peripheral Blood after Oral Administration.

Dose in tablets	Time of samples, min.		Acetyl-PABA, mg %		"Free" PABA, mg %	
	Portal	Peripheral	Portal	Peripheral	Portal	Peripheral
0.5 g PABA	16.5	21	0	0	0	0
	23.5	26.5	.05	0	0	0
	32	37	.09	.05	.07	0
	47	49.5	.14	.08	.09	0
	82	84.5	.20	.17	.06	0
	119	125.5	.21	.23	.15	0
	164	169	.28	.25	.29	06
2.5 g PABA	7.5	9	0	0	0	0
	12.5	14	.22	0	0	0
	21.5	24	.29	.17	0	0
	72.5	74	.37	.37	1.23	.62

origin of abdomnal vein blood. Glucose and other substances with high initial levels may also be used to demonstrate portal blood. They require much larger oral doses than do foreign substances to raise the blood levels significantly.

These rapid procedures for the diagnosis of portal collateral channels were applied to 12 patients with proven esophageal varices and other signs of portal hypertension resulting from cirrhosis of the liver. Of 8 patients with ascites, portal collaterals were demonstrated in 6. Two of these patients showed portal blood in more than one collateral vein. Abdominal veins in the region of the epigastrium tended to be the most likely sources of portal blood. Of 4 patients without well marked ascites, only one gave a positive test. The level of the test materials in the patients classified as negative was either the same or lower in the abdominal veins than in the antecubital veins. The reason for negative results in cases with proven portal hypertension has not been determined. While significantly higher levels of test drug in an abdominal than in an antecubital vein definitely indicate portal origin, identical or lower values apparently do not disprove portal origin.

All substances absorbed through the portal system that were tested were found in higher concentration in the abdominal than in the peripheral veins of these patients. These include sodium, sulfapyridine, glucose, and amino acids, as well as the various drugs discussed above. Evidence was obtained that blood from widely separated areas of the portal bed may drain into the same collateral vein. After PABA was given by mouth and thiocyanate by rectum, both drugs were found in higher concentrations in the abdominal vein tested than in peripheral blood.

In the course of studying PABA absorption evidence for acetylation by the intestine was found. PABA was fed as compressed sugar coated tablets, so that absorption was slowed. Table I shows the results in 2 patients in whom portal blood contained only acetylated PABA, without any "free"† PABA, at a time when neither compound had yet entered the peripheral circulation. The acetylation was apparently accomplished by the intestinal tract. After the first appearance of acetylated PABA in the portal system, subsequent samplings showed higher portal than peripheral levels. This phenomenon of higher portal than peripheral levels of acetyl-PABA was demonstrated again in both of these patients on repeating the experiment; it also occurred in 2 other patients tested. When PABA was absorbed slowly, the portal blood contained chiefly acetylated PABA and very little of the "free" drug was present and available for acetylation by the liver. However, in other experiments where PABA was fed as a rapidly absorbed solution, a large amount of "free" PABA appeared in the portal blood which was then acetylated principally by the

† "Free" refers to unacetylated PABA; it includes a fraction conjugated with other radicals.

liver. As a result of this evidence it appears that under the circumstances where small amounts of material are slowly absorbed, intestinal acetylation assumes relative importance.

Summary. 1. Portal origin of blood in abdominal collateral veins of patients with portal hypertension may be demonstrated simply and rapidly by feeding fluorescein or thiocyanate and finding higher concentrations in the abdominal veins than in the antecubital veins.

2. Seven out of 12 patients with cirrhosis gave positive tests for the portal origin of abdominal collateral vein blood. Patients with acites are more likely to give positive results than those without ascites.

3. Evidence is presented for the acetylation of PABA by the human intestinal tract.

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Effect of Inhibitors on Phosphate Uptake in Excised Gills of the Mussel (*Mytilus edulis*). (17568)

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The factors limiting the rate of penetration of phosphate into the ciliated epithelium constituting the molluscan branchial tissue have been discussed.(1) The present study is a survey of the effects of some commonly-used metabolic inhibitors (cyanide, azide, sulfide, fluoride, iodoacetate, and cysteine) upon the phosphate uptake process.

Materials and methods. Excised fragments of the gills of *Mytilus edulis* L., a pelecypod mollusk, were obtained as previously described and placed in a shallow glass irrigation cell equipped with a thin cover glass.(1) Immediately above this was a counting tube of a Geiger-Müller circuit. The tissue was irrigated with an artificial sea water (ASW) containing 5 micromols of phosphate per liter, of which a minute fraction was labelled with radioactive phosphorus (P^{32}). The radioactivity of the tissue was estimated at intervals of about 10 minutes. When sufficient information had been obtained to describe the uptake of the isotope under these conditions, the flow of irrigant was stopped, and a new fluid was introduced containing, in addition to the other components mentioned, an inhibiting agent in 0.001 M concentration. Readings were then continued until sufficient information was obtained pertaining to the new conditions. At the conclusion of observations the tissue was removed from the glass cell and examined with the compound microscope to observe the ciliary activity. All experiments were performed at 15°C.

Results. Phosphate content of the gill fragment was expressed as a percentage of the tissue radioactivity at the time of addition of the inhibitor. Fig. 1 shows the results of plotting the data so adjusted. The heavy broken lines connect the averages obtained with each inhibitor. The lighter smooth curves, identical in each graph, show the expected phosphate uptake, based on 22 previous experiments,(1) in which the value of k, the phosphate saturation constant, was found to be 0.0050 $min.^{-1}$ The administration of cyanide, sulfide, or iodoacetate resulted in a phosphate uptake less than expected, while addition of azide or fluoride was without pronounced effect. An apparent stimulating effect of cysteine is shown in the last curve.

Rigorous statistical treatment of the data was impractical for several reasons, but an idea of the significance of the observed differences may be obtained by comparing the relative value of radioactivity obtained at a

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