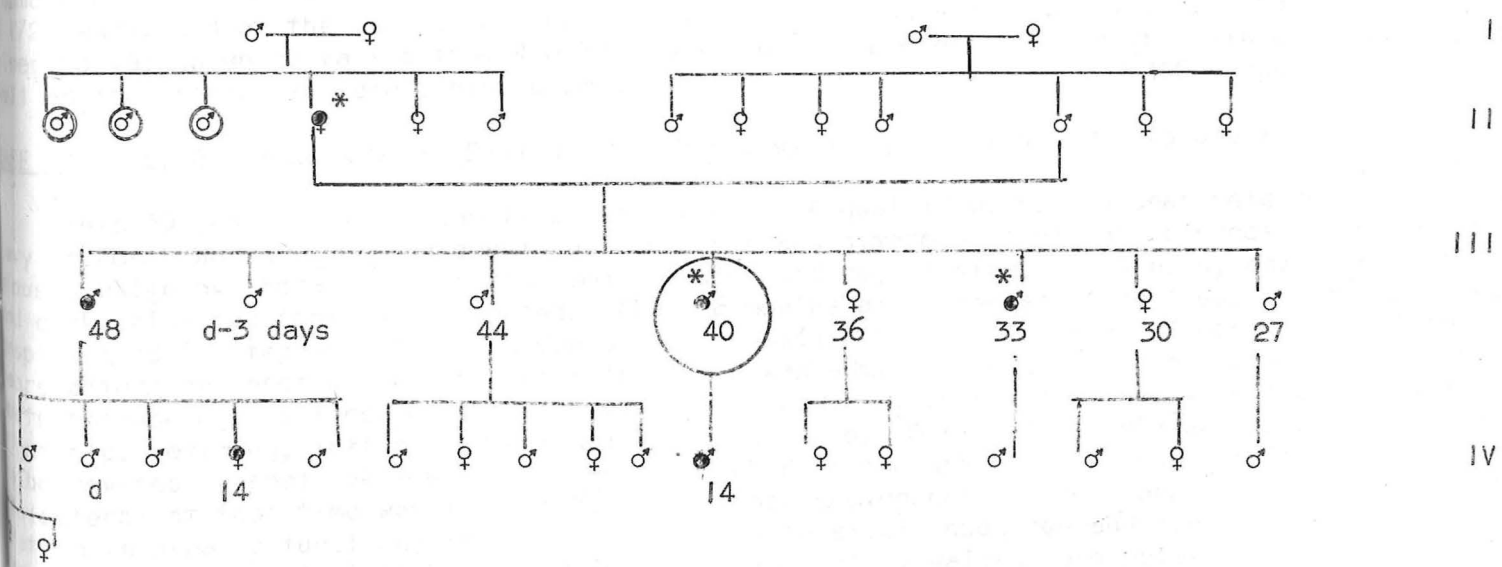
November 1, 1962

XANTHOMATOSIS

CASE 1. [redacted] - Essential Hypercholesterolemia.

This 40 year old [redacted] man first noted the appearance of thickening of the achilles tendons, arcus senilis, and bilateral xanthelasma at about the age of 34. At approximately the same time he noted the onset of an intermittent "racing" of the heart. He was diagnosed at that time as having essential hypercholesterolemia and was subsequently treated with MER-29, nicotinic acid, and a low fat diet. Two years ago he began to have attacks of angina on exertion. On [redacted], 1962 he developed tachycardia, followed by severe chest pain and unrelieved by nitroglycerin. He was subsequently admitted to a local osteopathic hospital where he was diagnosed as having an acute myocardial infarction. The convalesence was complicated initially by shock which responded to 48 hours of continuous vasopressor administration and 10 days later by a pulmonary infarct and a second episode of shock. He was subsequently discharged on pronestyl, thrombolysin, and tromexan; after a week at home on complete bed rest he had another episode of chest pain following an episode of tachycardia, and he was readmitted to the osteopathic hospital where he was told that he had had an extension of the infarct. He was subsequently referred to the [redacted] tion [redacted] The family history is given below:



KEY: ◉ = hypercholesterolemia (> 300 in adults, > 250 in children)

* = xanthomatosis

◯ = propositus

⊙ = heart disease, deceased, cholesterol level unknown

at the time of his admission revealed a man who appeared much older than his age. He had a BP 90/60, grey hair, bilateral arcus senilis, xanthelasma, a xanthomatous placque over the right iliac crest, a xanthoma tuberosum over the right elbow, and thickened achilles tendons. EKG revealed ST and T wave changes suggestive of posterior ischemia. The routine laboratory studies were normal. Blood cholesterol was 550. He was kept on anticoagulants (coumadin), slowly rehabilitated, and placed on an unsaturated fat diet supplement with 100 gm corn oil per day, and on bronestyl.

Since his initial discharge in [redacted] he has had two readmissions because of a paroxysmal supraventricular tachycardia culminating in severe angina. At the present time he is on a regimen of coumadin, peritrate, corn oil milkshakes, digitalis, quinidine, and nitroglycerin; he is able to work 2-3 hours a day. His blood cholesterol on [redacted] was 200 mgm%.

ASE 2. [redacted] - Essential Hypercholesterolemia.

6 years PTA,

This 42 year old man noted the appearance of nodules over his elbows / becoming progressively larger over the ensuing years. He was placed on a low fat diet for six years and in addition treated with thyroid (1 grain/day for 5 years). In 1957 he was referred to Dr. Siperstein. His family history was entirely negative. Physical examination revealed multiple yellow macules and papules over both elbows. There was no xanthelasma or xanthoma tendinosum. EKG, Chest x-ray, CBC, and urinalysis were within normal limits. The following lipid values were obtained:

Cholesterol	419 mg% (67% esterified) N < 300
Total fatty acids	3100/μm/100 ml N 700-2000 μm/100 ml
Phospholipids	491/μm/100 ml N 200-450 μm/100 ml

e was placed on a high unsaturated fat diet with Mazola oil supplements. On this regimen his cholesterol fell promptly and was maintained at levels which varied from 150-250 mgm%; the xanthomata markedly improved, those on the left virtually disappearing. He moved to Formosa for 1 1/2 years, and at the time of his return, despite adherence to his diet, his cholesterol had risen to values which varied from 416-579 mgm%. At the present time on choloxin and nicalex, as well as the unsaturated diet, his serum cholesterols are back to the 200-300 range.

ASE 3. [redacted] - Billiary Cirrhosis with Hypercholesterolemia and Xanthomatosis.

This 39 year old woman was first seen here in [redacted] 1960, having been referred by Dr. Louis evy of [redacted]. She had developed the signs and symptoms of biliary cirrhosis 6 years previously while on thorazine, and the symptoms of jaundice, itching, drowsiness, nausea and vomiting, nd dark urine had continued unabated. About 6 months after the start of these symptoms she was ospitalized in Stephenville and given an unsuccessful therapeutic trial of cortisone. Three ears after the onset of her present illness she was admitted to [redacted] because of the first of many pathological fractures, eventually involving the left pelvis, ght hip, left leg, left arm, and finally the left hip. During this 1957 admission she was noted be covered by small yellow macules which erupted in one area only to subside in another. Her olesterol at that time was 1800 mgm%. During her subsequent course - and despite a slow deterioration in hepatic function, the eruptive xanthomata slowly subsided and finally disappeared. At e time of her first visit here, the following laboratory values were obtained:

Cholesterol	279 mg% (45% esterified) N = < 300
Phospholipids	302 mg% N = 150-350 mg%
Triglyceride	250 mg% N = 0-400 mg%

e serum cholesterol remained within normal limits until her death in the [redacted] of 1962. The topsy confirmed the diagnosis of biliary cirrhosis.

CLINICAL CLASSIFICATION OF THE DISEASE STATES IN WHICH XANTHOMATA MAY BE A PROMINENT FEATURE
(after Thannhauser)

Type	Disease	Types of Xanthomata	Familial Occurrence	Blood Findings
Hypercholesterolemic xanthomatosis	Essential hypercholesterolemia	Xanthelasma Tendon xanthoma Xanthoma tuberosum	Usual	Cholesterol ↑↑ Phospholipid ↑↑ Triglycerides ↑ or N
	Liver Disease: 1. Biliary cirrhosis 2. Extrahepatic biliary obstruction 3. Congenital dysplasia of bile duct	Eruptive xanthomata - particularly around eyes, elbows, knees, buttocks, and creases of the hand. No tendon xanthomata	Rare	Cholesterol ↑↑ Phospholipid ↑↑ Triglycerides N
Hyperlipemic xanthomatosis	Idiopathic familial hyperlipemia	Eruptive xanthomata - occasionally tuberous and tendon xanthoma	Usual	Cholesterol ↑ Phospholipid ↑ Triglycerides ↑↑
	Secondary To: Untreated diabetes Glycogen storage disease Nephrotic syndrome	Eruptive xanthomata similar to those in idiopathic hyperlipemia	Variable	Cholesterol ↑ Phospholipids ↑ Triglycerides ↑↑
Normocholesterolemic xanthomatosis	Hand-Schuller-Christian Disease and Eosinophilic granuloma of bone	Skin xanthomata predominant around neck, face, and trunk (axillae, bends of knees and elbows)-H.S.C. Granulomas eventually undergo xanthomatous infiltration	Rare	All serum lipids normal
	Essential xanthomatosis	May be disseminated or tuberous	Rare	All serum lipids normal
	Juvenile xanthomata	Wart-like papular lesions appearing during the first year of life resembling eruptive xanthoma	Rare	All serum lipids normal
	Xanthomatous degeneration of inflammatory and malignant lesions	May occur in almost any type of lesion	Rare	All normal

COMPARISON OF VARIOUS XANTHOMATA

Descriptive Term	Clinical Features	Histological Features	Association with Clinical Syndromes
Xanthelasma	Flat or slightly raised and outlined yellow placques on the lids. Occasionally red, brown, or grayish-white	Isolated and coalescent foci of lipid histiocytes or foam cells. No giant cells	1. Normal individuals (50%) 2. Essential hypercholesterolemia
Xanthoma Tendinosum	Lumpy, irregular thickening of the large tendons with predilection for the achilles tendons	Infiltration by lipid histiocytes into the tendon, the tendon sheath, and the periosteum. Fibrosis develops early. Touton giant cells rare; foreign body giant cells more common	Essential hypercholesterolemia
Xanthoma Tuberosum	Oval, circular, irregular, discrete, and coalescent placques, nodules or tuberositus; some pedunculated with a predilection for the extensor surfaces of extremities	Rows and clumps of lipid filled histiocytes with few giant cells of either touton or foreign body type; fibrosis and mononuclear cells variable. Cholesterol crystals frequently seen	Essential hypercholesterolemia
Eruptive xanthomata	Firm purplish-red papule with yellowish centers and surrounded by inflammatory area, appearing in large clusters on the palms, soles, extensor surfaces, and trunk		1. Idiopathic hyperlipemia 2. Untreated diabetes, glycogen storage disease, and nephrotic syndrome 3. Liver disease
Xanthoma disseminata (rare)	Papules, nodules, and placques with a predilection for flexor surfaces of extremities. Mucous membranes may be involved		1. Hand-Schuller-Christian Disease 2. Essential xanthomatosis

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