There is considerable controversy on what actually constitutes the 'early lesion', on whether all lesions begin in the same way and whether all develop into fibro-fatty plaques. This introduction outlines the morphology and histochemistry of lesions regarded as 'early' in terms of chronology and the general pathology of atherosclerosis (Movat et al., 1959; Haust, 1971a; Geer and Haust, 1972).

Fatty Dots and Streaks

The first of these presents itself on gross examination as a yellow (fatty) dot or streak; microscopically the changes vary from a stage considered to be early to somewhat more advanced. In the early yellow dot, fat droplets are present in the native smooth muscle cells (Geer et al., 1961; Haust et al., More, 1963) of a focal area. As the lesion grows in size, the number of fat droplets in a given smooth muscle cell as well as the number of these cells involved in the change increases. When much of the cytoplasm is occupied by fat, the cell acquires the appearance of a foam cell. By electron microscopy it is often possible to recognize the foam cell derived from the smooth muscle cell ("myogenic" foam cell) (Balis et al., 1964) and distinguish it from that which appears only in advanced fatty streaks and is of histiocytic origin (Balis et al., 1964). In the advanced fatty streaks there is also extracellular fat. Much of it resembles by light microscopy the finely distributed fat "dust" present in small amounts along the elastic lamellae of normal intima. By electron microscopy, in addition to these small osmiophilic bodies, fat may present itself in the form of myelin figures and droplets resembling those of intracellular fat (Haust et al., 1967). Cellular necrosis progresses with advancement of the lesion, but possibly these 'developed' fatty streaks should no longer be regarded as early lesions. Using the fluorescent and ferritin antibody techniques, in small fatty dots there appears to be no definite increase in albumin or in $\alpha$- or $\beta$-lipoproteins, and fibrin appears to be absent, but in the larger raised fatty streaks there appears to be an increase in all the plasma proteins, and fibrin can be demonstrated (Wyllie et al., 1964; Cho et al., 1966; Haust, 1968).

'Normal' Diffuse Intimal Thickening. In all human subjects there is a progressive age-related thickening of the intima in both the aorta and the coronary arteries (Movat et al., 1958; More and Haust, 1968) which probably should not be regarded as part of the atherosclerotic process, but which must be used as the baseline for assessing the changes in 'early lesions' in any age group.
'Gelatinous Elevations'. These translucent thickenings are not very conspicuous on gross inspection, particularly in young subjects, but become larger and more prominent in the 4th - 6th decades. They appear as focal swellings of the intima reminiscent of a blister, or a gelatinous elevation (Movat et al., 1959; Haust, 1971). Microscopically, it shows an intimal area in which the extracellularly formed connective tissue components are either "wiped" out, or distorted, fragmented, separated and swollen. There is a decrease or absence of metachromasia indicating either a change in the physico-chemical state, or "disappearance" of the acid mucopolysaccharides of the ground substance. The picture is that of serous insudation, but often, fibrin may be found in the insudate. The presence of fibrin in such areas may be easily confirmed on electron microscopic examination. Often, fibrin concentrates around the smooth cells — a feature noticed long ago but not explored in depth. The cellular elements of the lesion may be entirely free of change (Haust, 1971a; Haust, 1971b) but there may be some extracellular fat. Occasionally, particularly when on gross examination there is a slight yellow tint to the lesions, the smooth muscle cells contain fat droplets (not unlike those in fatty streaks), so that the lesion has features both of the fatty streak and gelatinous elevation (Haust, 1971a). With fluorescent antibody techniques (Haust et al., 1964; Wyllie et al., 1964; Cho et al., 1966; Haust, 1968) one may demonstrate the presence of fibrin and low-density lipoproteins, and increased amounts of albumin and high density lipoproteins.

Mural Microthrombi

The third early lesion is seldom, if ever, seen by naked eye and is often found on microscopic examination by chance. It represents a microthrombus which may be observed in various stages. Most often it is composed largely of fibrin, but microthrombi with a considerable core of platelets or predominantly consisting of platelets may be also found. Some of such microthrombi are covered by endothelium and may be in various stages of "contraction" of their fibrin mass and organization. Microthrombi may extend over somewhat larger area of the intima, but most commonly are focal. They may be found at all ages, even in small children, and over microscopically unaltered intima (Haust and More, 1960). Microthrombi consisting predominantly of platelets resemble closely those produced experimentally by various means.

It has been reasonably well established that the above three lesions occur in man. However, even investigators who consider these to be the "forerunners" of the atherosclerotic plaques and thus to represent early atherosclerotic lesions, do admit that at present it is not known how often each of the three occurs in relation to the other two, and how often each progresses to the atherosclerotic plaque, becomes arrested or regresses. Moreover, it is not known whether there is an interdependence of the three lesions in their steps of evolution to the atherosclerotic lesion. All these problems are not easily solved in man and must be approached through the co-ordinating and collaborative efforts of many investigators.

MODIFICATION OF LESIONS BY LOCATIONAL FACTORS

D. Sinapius

In cerebral arteries fatty streaks occur as well as in the aorta and in the coronaries. But I suppose that they are less common in this region. On the contrary mural thrombi seem to play an important role in cerebral arteries, microthrombi as well as thicker ones. I have never seen typical intime edema in cerebral arteries such as is well known in the aorta.