

PROBLEM SOLVING EXERCISES – ATHEROSCLEROSIS & A PROBLEM PIG**PSE: PART 1: ATHEROSCLEROSIS****AIM**

To understand the nature and factors influencing development and progression of atherosclerosis.

ATHEROSCLEROSIS: INTRODUCTION

One of the most common causes of death in the Western world is due to the consequences of coronary artery disease including myocardial ischaemia and myocardial infarction. This most often results from atherosclerosis in the coronary arteries. The process of atherosclerosis leads to formation of atherosclerotic **plaques**, which have a **fibrous cap** overlying a soft centre, composed of lipid and necrotic material (**lipid pool**). Atherosclerotic plaques may rupture, stimulating the development of thrombus. A large thrombus on the surface of a ruptured plaque can cause obstruction of the lumen of the artery – and this is the commonest cause of myocardial infarction. Spasm of the coronary arteries and emboli in the coronary arteries are occasionally involved, but less frequently. To prevent atherosclerosis, it is important to understand the underlying processes (see diagram below) and the relevant risk factors. **Risk factors for atherosclerosis include: 4 major risk factors - smoking, hypertension, diabetes mellitus, hyperlipidaemia**, and several minor risk factors - increasing age, male sex (hormonal effects on blood lipid levels), family history, obesity, & certain ethnic origins.

The **AORTA** and larger arteries are **elastic** arteries. Arteries have 3 layers: tunica intima (inner layer in contact with blood in the lumen), tunica media (middle layer containing smooth muscle cells), and tunica adventitia (outer layer composed of supporting fibroconnective tissue with capillaries and nerves). The 3 layers are separated by 2 elastic laminae. In H&E sections, the elastic laminae appear pink and usually have a wavy appearance. The **intima** is the innermost layer and lies between the innermost elastic lamina and the endothelium. At birth the intima consists solely of the endothelium with its basement membrane. Within the arterial system including the aorta and the coronary arteries, there is uniform thickening by smooth muscle cells and fibrous tissue, to form so-called **diffuse intimal thickening (DIT)**.

ATHEROSCLEROSIS: PROBLEM-SOLVING EXERCISE

First, look at the photographs of macroscopic specimens of normal aorta (P22.1) and atherosclerotic aorta (P22.2), then examine the photomicrographs of microscope slides of normal aorta (P22.3) and an

atherosclerotic plaque (22.4) taken from atherosclerotic aorta. Proceed to the diagram of atherogenesis and answer the problem-solving questions about this pathological process.

PHOTOGRAPHS: MACROSCOPIC SPECIMENS:

P22.1 Normal Aorta

Catalogue Number	Small Image	Image Map	Large Image
N_CR_AO_17.jpg	Normal Aorta		Normal Aorta

P22.2 Atherosclerotic Aorta

Catalogue Number	Small Image	Image Map	Large Image
A_VA_AZ_AO_41.jpg	Atherosclerotic aorta		Atherosclerotic aorta

PHOTOMICROGRAPHS:

P22.3 Elastic artery: normal aorta

Catalogue Number	Small Image	Image Map	Large Image
N_CR_AO_18.jpg	Elastic artery – normal aorta		Elastic artery – normal aorta

This aorta was from an 18-year-old girl killed in a road traffic accident.

P22.4 Aorta: atherosclerosis complicated by thrombosis

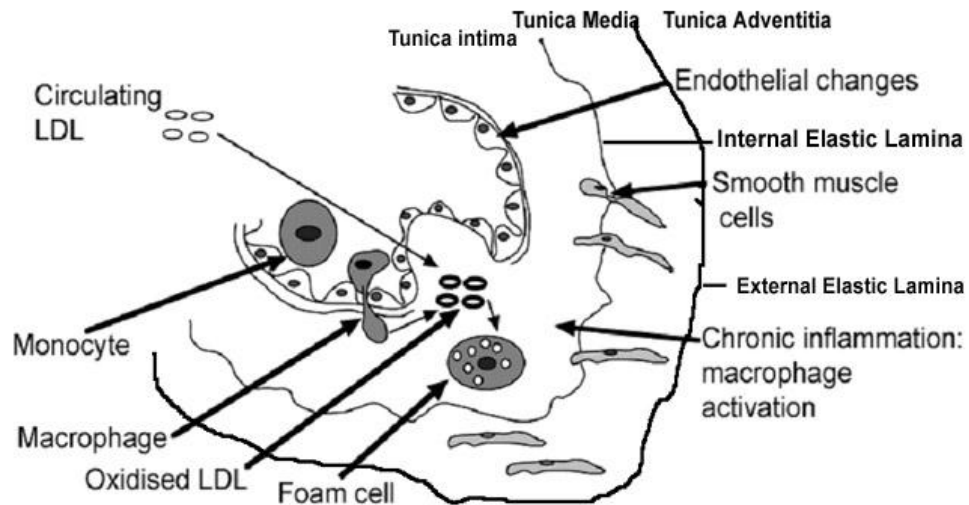
Catalogue Number	Small Image	Image Map	Large Image
A_VA_AZ_AO_42.jpg	Aorta : atherosclerosis		Aorta : atherosclerosis

This aortic tissue is from an 80-year-old man who had thrombosis over plaques in his abdominal aorta.

Thrombus has formed over the **ruptured surface** of an atherosclerotic plaque containing abundant lipid. Within the plaque, there are clear central areas which originally contained **necrotic tissue** and **lipid**, (the latter dissolved out during the processing of the tissue), covered **by a fibrous cap**. In fresh tissue, the necrotic centre of these lesions is very soft with a fancied resemblance to porridge, hence the lesion is called **atheroma** (from the Greek word, athera = gruel). The central necrotic material contains many **cholesterol clefts** (crystal-like formations of cholesterol that dissolve out during tissue processing).

Macrophages are present within the plaque, whose cytoplasm is filled with many lipid-laden vacuoles. These appear after tissue processing as clusters of clear bubbles, hence the descriptive term “foam cells”.

This DIAGRAM OF ATHEROGENESIS shows the major components important in the formation of an atherosclerotic plaque and its progression.



Monocytes (in blood) enter the Tunica Intima becoming macrophages and these take up the LDLs and lipid to become Foam cells/Foamy macrophages.

ATHEROSCLEROSIS: PROBLEM-SOLVING QUESTIONS:

QA. At the earliest stages of plaque development, what influences lipid circulating in the blood, in the form of Low Density Lipoprotein (LDL), to enter the tunica intima of the artery wall?

QB. What stimulates blood monocytes to enter the arterial wall (becoming tissue macrophages) at the same site as the LDL?

QC. If the macrophages can phagocytose LDL forming “foam cells” (containing intracellular lipid), how does the extracellular lipid pool form and grow larger? (seen as cholesterol crystals and lipid gruel in your section).

QD. What triggers the smooth muscle cells in the tunica media to migrate to the tunica intima, proliferate and secrete extracellular matrix?

QE. Can you assign the four major risk factors (smoking, hypertension, diabetes mellitus & hyperlipidaemia) to pathogenic events in atherosclerosis?

QF. What makes an atherosclerotic plaque rupture? Why is this an important event?

PART II: A PROBLEM PIG

A country vet was called to a small local abattoir to advise on the suitability for butchery of a recently slaughtered pig. The post-mortem appearance of the left ventricle and aortic valve are shown in figure A and of the lung in B.

Q1. Describe these appearances, using accurate, professionally appropriate terminology, and interpret the relationship between A and B.

Catalogue Number	Small Image	Image Map	Large Image
A_VA_TI_HT_01.jpg	Figure A		Figure A
A_CI_OE_LU_02.jpg	Figure B		Figure B

The vet took two samples from the aortic valve for histology and bacteriological culture. The cultures grew *Erysipelothrix rhusiopathiae*. The histology from the two sites is shown at low power magnification in figures C and D.

Catalogue Number	Small Image	Image Map	Large Image
A_IN_BI_HT_01.jpg	Figure C		Figure C
A_VA_TG_HT_01.jpg	Figure D		Figure D

Q2. What is the relationship between the bacteriological and histological findings?

Q3. What would you expect to see on higher power examination of the regions marked 3.1, 3.2 and 3.3? (Explain why).

The vet inquired about the origin of the sick pig. It turned out to be a farm he had visited only a few days before. The farmer had not impressed him, as he was rearing his pigs in an overcrowded concrete-floored barn with little other than the floor straw to keep them occupied. The farmer had noticed one pig had badly chewed ears, but for poorly-explained reasons had not called the vet for several days. The vet had thought the pig was listless compared with the others in the barn and had taken a blood sample to check the haemoglobin content. At that time he had advised the farmer to avoid overcrowding but had intended to revisit once he had the haemoglobin value. The pig undergoing postmortem also had bitten ears, and he recognised it as the same animal he had been called to see. He phoned the practice and heard

that the haemoglobin value had been 5g/dL (normal 10-15g/dL), the film showing a mild reticulocytosis.

Q4. In a flow diagram, show the relationships between as many of the features in the story as possible. How might the postmortem appearance in small intestine (Figure E) and myocardium (Figure F) fit into this diagram?

Q5. What would his advice about butchering have been?

Catalogue Number	Small Image	Image Map	Large Image
A_VA_ET_VT_01.jpg	Figure E		Figure E
A_VA_PY_HT_01.jpg	Figure F		Figure F

Similar cardiac pathology is sometimes found in cattle shortly after calving, but the lesions are usually found in the right side of the heart.

Q6. Explain why these animals should be susceptible, and why the right side of the heart should be particularly vulnerable? What sort of organisms might be cultured on this occasion? This condition is difficult to treat, even in human beings. Can you suggest why?