ON THE SELECTION OF ANIMAL SPECIES AS MODELS FOR ATHEROSCLEROSIS RESEARCH, WITH PARTICULAR REFERENCE TO THE COMMON MARMOSET (CALLITHRIX JACCHUS)

M. John Chapman, Patricia Forgez, Sonia Goldstein and Fergus McTaggart
Unit 35, Groupe de Recherches sur le Métabolisme des Lipides, Institut National de la Santé et de la Recherche Médicale, Hôpital Henri Mondor, 94010 CRETEIL, France, and *Pharmaceutical Division, Imperial Chemical Industries Ltd., Alderley Park, MACCLESFIELD, Cheshire SK10 4TG, U.K.

Much has been written in recent years of the complex and multiple processes implicated in the development of atherosclerosis. Despite such intense activity in this field however, it is evident from the present Conference that controversy still surrounds many aspects of this insidious disease. One may especially cite questions surrounding the nature and relative importance of the various factors which may contribute to the initiation of the atherogenic process itself, as well as those relevant to its regression.

As a consequence of several extensive epidemiological surveys in human populations, such as that performed over a period of years in Framingham, Massachusetts, (Kannel et al., 1971), we have come to recognise the importance of elevated serum lipid (and particularly cholesterol) levels as major risk factors for vascular disease. The intractability and undesirability of humans as subjects for detailed study of the disease process has tended however to restrict researchers to use of post-mortem tissue. Such limitations thus prompted the search for alternative species as experimental models for study of the dynamic facets of lesion development.

The earliest use of an animal species for atherosclerosis research was perhaps that of the rabbit by Anitschkow in the 1920's.
Indeed his studies in rabbits fed cholesterol-supplemented diets provided a major stimulus for subsequent investigations of the pathogenesis of the disease in a wide variety of animals rendered hypercholesterolemic by dietary means.

To date, members of almost all the major classes of vertebrates have been the subject of atherosclerosis-related study. Among them, representations of the fishes (salmon, Oncorhynchus sp.; rainbow trout, Salmo gairdnerii), birds (pigeon, Columba sp.; chicken, Gallus domesticus; turkey, Meleagris galapavo) and mammals (rat, Rattus norvegicus; rabbit, Oryctolagus cuniculus; dog, Canis familiaris; pig, Sus domesticus) have been the subject of most attention. To these species may be added the non-human primates (especially Old and New World monkeys), which as a group, account for possibly the largest number of experimental studies within the past decade; many of these have emanated from the Primate Research Centers in the United States (for reviews, see Clarkson et al., 1976, Wissler, 1979 and Malinow, 1980).

Unlike Western man, in which atherosclerotic disease is apparently indigenous, the vast majority of animal species only rarely appear to present with spontaneous lesions in their natural habitat. This has led to the inbreeding of some species, such as certain strains of quail (Chapman et al., 1976), pigeons (Clarkson et al., 1976), mice (Roberts and Thompson, 1976) and monkeys (Clarkson et al., 1976), in order to derive animals with increased susceptibility to experimental atherosclerosis. Nonetheless, the induction of arterial lesions in such inbred strains still suffers from the same drawback as their random-bred counterparts, i.e. relatively drastic measures, usually involving administration of massive amounts of cholesterol and saturated fat, must be employed in order to induce arterial lesion formation within a comparatively short time period.

If we accept the thesis that diet-induced hypercholesterolemia has been the most common means of producing experimental atherosclerosis in animals, then it would appear reasonable to assume that some fundamental relationship exists between the nature of the circulating cholesterol-transporting molecules, in this case the serum lipoproteins, and the nature and anatomical distribution of the arterial lesions. Furthermore, since the hypercholesterolemic animal species which have been studied have been assumed to represent valid models for the evaluation of the disease process as it supposedly occurs in man, then it has to be further assumed that their...