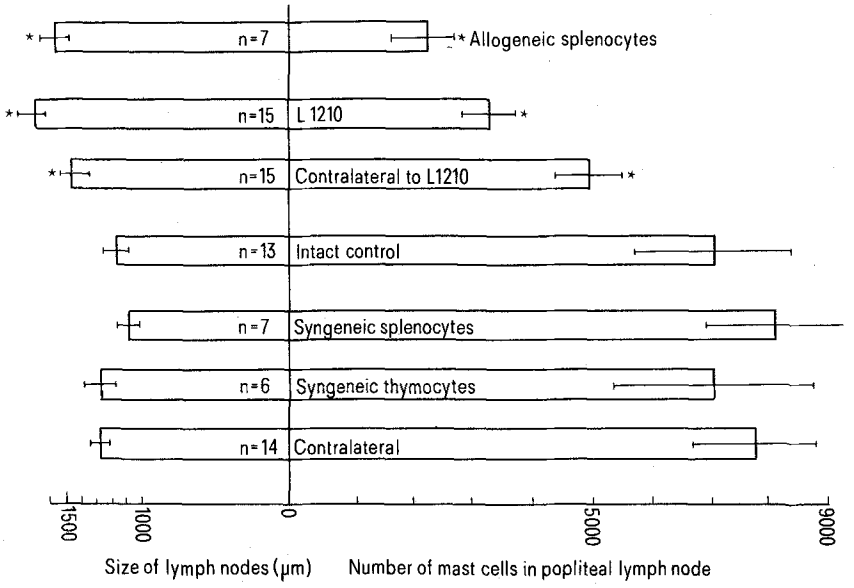

Changes of mast cell number and lymph node size in response to allogeneic antigens and semisyngeneic tumor antigens. Each bar represents the mean number ± SE of mast cells (to the right of the line) and mean diameter and SE of lymph node stimulated by antigens indicated (to the left of the line). The number of specimens is given in each bar. Asterisks indicate the values different from that of intact control at $p < 0.05$.

Normal syngeneic cells did not cause any decrease in the number of MC in regional lymph nodes. Decrease in the number of MC following the injection of allogeneic lymphocytes or semisyngeneic leukaemic cells was accompanied by an enlargement of the stimulated lymph nodes ($p < 0.05$), clearly indicating that the reduction of MC was not due to a decline of lymph node cellularity.

Decrease of MC number is a very sensitive response of the regional lymph node against antigenically alien cells as it is observed as a consequence of injection of both allogeneic cells as well as semisyngeneic leukaemic cells. Thus, this decrease is sensitive enough to detect tumor-specific antigens. It is worth mentioning that the number of MC in the stroma of human squamous cell cancer was 2–30 times lower than in the stroma of normal squamous epithelium or in the connective tissue distant from neoplastic epithelium[13].

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An H-2-associated difference in murine serum cholesterol levels

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Summary. We describe, in mice, a difference in serum cholesterol and adrenal weight associated with an H-2^a/H-2^b haplotype difference.

Genes of the major histocompatibility complex play an important role in determining patterns of immune response in both animals and man. Recent interest in immunological models of cardiovascular disease[1] has prompted a number of studies on the relationship between ischaemic heart disease and the presence of various histocompatibility antigens. Mathews[2] found a significant correlation between national death rates for ischaemic heart disease and population frequency of histocompatibility antigen HLA-8. However, other investigators, examining patients who had sustained a myocardial infarction, could find no significant increase in HLA-8 or any other histocompatibility antigen in this group[3,4]. In neither of these patient studies were results stratified by serum cholesterol levels. In another study[5], which suggested a link between BW38 and premature coronary artery disease, the patient population was chosen to exclude hypercholesterolaemia.

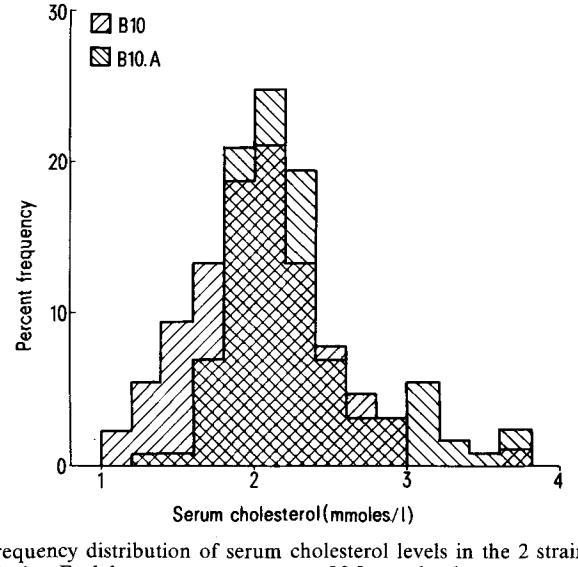
Although heredity is known to exert a major influence on the development of hypercholesterolaemia, there has been done little work on the relationship of serum cholesterol levels and the major histocompatibility complex. Mathews, though observing a correlation between the geographical distribution of HLA-8 and higher population cholesterol levels, could not find a similar association with HLA-8 when investigating individual patients with hypercholesterolaemia[6].

The mouse strains C57BL/10.ScSn (B10) and C57BL/10.A (B10.A) are genetically identical except in the major histo-

compatibility region where the B10 strain is haplotype H-2^b, and the B10. A strain haplotype H-2^a. Thus inherited differences between these 2 strains are likely to be determined, directly or indirectly, by genes in the major histocompatibility complex. We observed that the mean serum cholesterol level of female B10.A mice in our colony was significantly higher than that of female B10 mice. A similar result was noted in mice purchased from Olac Laboratories. The results described here are pooled results from mice of both colonies.

Mice were caged under identical conditions in the same room and fed the same diet (CRM diet, Labsure) for at least 1 month prior to death. To minimize age related differences in serum cholesterol, in every experiment a B10 mouse was paired with a B10.A mouse of the same age in weeks. No mouse tested was younger than 8, or older than 16 weeks. Mice were killed by rapid asphyxia with CO_2. Blood was removed by cardiac puncture, serum separated, and cholesterol determined, using an enzymatic oxidation method[7] by Mrs S. Duff and Miss K. Rowan of our clinical chemistry group.

Mean serum cholesterol of 128 female B10 mice was 1.96 mmoles/l; of 129 female B10.A mice 2.22 mmoles/l. Median values were 1.94 mmoles/l and 2.09 mmoles/l. The mode of the 2 groups was similar. The difference in mean serum cholesterol levels arose largely because the B10.A population distribution was significantly skewed (coefficient of skewness = 1.12). There were a disproportionate number of high serum cholesterol levels in the B10.A population. Since there was a significant deviation from the normal distribution, a non-parametric test (the Mann-Whitney test) was used to compare populations. Using this test, the difference in serum cholesterol levels was very highly significant ($p < 0.0001$). The figure shows a histogram of this data.



Frequency distribution of serum cholesterol levels in the 2 strains of mice. Each bar represents a range of 0.2 mmoles/l.

The effect of strain difference on serum cholesterol levels was confined to female mice. Male mice had considerably higher serum cholesterol levels than female but there was no difference between the B10 and B10.A strains (mean values 2.85 mmoles/l and 2.76 mmoles/l respectively).

Changes in blood levels of sex hormones, or changes in adrenal cortex function, can both affect cholesterol levels. The strains B10 and B10.A do show significant differences in both plasma testosterone levels and testosterone binding capacity[8], however we observed a significant difference in serum cholesterol levels only in female and not in male mice. Differences in cortisol binding protein associated with the H-2^a/H-2^b haplotype difference have also been reported[9], and in our study adrenal weights were higher in the B10.A strain, both in females and in males, though the difference was larger in the female sex. Mean values of weight of each adrenal pair were; in our B10 females 3.29 mg (SE = 0.07 mg), in our B10.A females 3.62 mg (SE = 0.07 mg). Statistically, this difference was highly significant. Adrenal weight distributions were sufficiently close to the normal distribution to use an unpaired t test, which gave $p < 0.001$.

Our results suggest that it may be worthwhile to include serum cholesterol measurements in clinical studies of the relationship between HLA type and coronary artery disease.

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Action of ACTH, cAMP and cytochalasin B on steroid production by Y-1 mouse adrenal tumor cells in culture[1,2]

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Summary. Continued incubation of Y-1 mouse adrenal tumor cells with adrenocorticotrophic hormone (ACTH) or with dibutyryl-3′,5′-cyclic adenosine monophosphate (dbcAMP) resulted in an initial increase and a subsequent decrease in steroidogenesis. ACTH- or dbcAMP-stimulated steroidogenesis was inhibited by cytochalasin B (CB) to approximately the same extent during the entire period of incubation; CB inhibition of the ACTH response was reversible.

Recently, Nolin[4] suggested that rat adrenal steroidogenesis may be stimulated when ACTH is internalized. Gonadotropins are internalized by an endocytotic[5] process which may require microfilament activity[6]. Both endocytosis and microfilament function have been reported to be inhibited by CB[6-8]. Since ACTH-controlled steroid synthesis involves changes in the thin filaments[9] and is inhibited by CB[10-14], it was suggested that CB may prevent thin filaments from