平 成 ２４ 年 度

（医学部医学科　後期日程）

問 題 冊 子

教　　科　　等	ページ数
小 論 文 Ⅰ	3

試験開始の合図があるまで、問題冊子を開かないこと。

解答の書き方

1. 解答は、すべて別紙解答用紙の所定欄に、はっきりと記入すること。
2. 解答を訂正する場合は、きれいに消してから記入すること。
3. 解答用紙には、解答と受験番号のほかは、いっさい記入しないこと。

注 意 事 項

1. 試験開始の合図の後、解答用紙に受験番号を必ず書くこと。
2. 下書き用紙は、片面だけ使用すること。
3. 問題の内容についての質問には、いっさい応じないが、その他の用事があるときは、だまって手をあげて、監督者の指示を受けること。
4. 試験終了時には、解答用紙を必ずページ順に重ね、机上の右側に置くこと。
5. 試験終了後、問題冊子及び下書き用紙は持ち帰ること。

問題　次の文章を読み、問に答えなさい。

The long-standing controversy over the validity of the lipid hypothesis of atherosclerosis[1] has been settled. In several large-scale, 5-year trials[2], statins[3] have reduced coronary heart disease (CHD)[4] morbidity and mortality[5] by ≈30%, and the magnitude of the protective effect mirrored the magnitude of the low-density lipoprotein (LDL)[6] lowering. However, as has been quite correctly pointed out, some 70% of those expected to have an event[7] (based on the number of events in the control group[8]) went on to have one during the 5 years of the trial despite statin therapy. For example, in the Scandinavian Simvastatin Survival Study, 502 events occurred in the untreated group and 353 in the statin-treated group. The number of events prevented (n=149), as a percentage of the number expected, was 29.7% (149/502×100); the number of events in the statin group that were not prevented (353) amounts to 70.3% (353/502×100). Looked at this way, the results are admittedly not quite so impressive. In fact, some investigators are now taking the position that we can expect to achieve higher salvage rates[9] only if we supplement LDL-lowering therapies[10] with alternative interventions such as the use of antiinflammatory agents[11] or immunotherapy[12]. This may turn out to be true. However, it is much too early to reach that conclusion for reasons we discuss here. The search for alternative or supplementary therapies is already in full swing and should continue. We are confident that one day these additional therapies will take their place alongside cholesterol-lowering agents in our armamentarium[13]. However, we believe that the results of the statin trials to date considerably underestimate the full potential of cholesterol-lowering strategies. It would be unfortunate if efforts to fully exploit that potential faltered because of a misplaced pessimism based on the statin results to date. Our current approaches may be a case of "too little, too late." How much further can we expect to decrease risk by treating dyslipidemia[14] (ie, lowering LDL levels and/or raising high-density lipoprotein levels[15])?

One important line of evidence comes from a consideration of the Japanese experience. In 1952, mortality from CHD among Japanese men 55 to 64 years of age was <10% of what it was in the United States. Their total cholesterol levels at the time averaged ≈160 mg/dL (estimated LDL, ≈80 mg/dL). It is noteworthy that the Japanese enjoyed this relative

immunity to CHD despite the fact that the prevalence of one of the major risk factors—cigarette smoking—was much higher in Japan than in Western countries, and another —- hypertension[16] — was just as high. Even the diabetic population in Japan fares better than the diabetic[17] population in Western countries. In 1985, almost 30% of British male diabetics but only ≈15% of the Japanese male diabetics had CHD. The implication is that if blood cholesterol levels are sufficiently low, the other dominant risk factors[18], including cigarette smoking, hypertension, and diabetes mellitus[19], constitute much less of a threat.

(A) Are these large differences in incidence between Japan and Western countries based primarily on genetic factors[20]? No. Two cleverly designed epidemiological[22] studies showed that the Japanese who had migrated[21] and taken up permanent residence in Hawaii had higher blood cholesterol levels and a higher incidence of CHD than those who remained on the home island. For those who migrated even further, on to California, the differences were even more striking. This and other migration studies showed that the differences in CHD risk among different populations are certainly not entirely genetic. (B)Which environmental factors[23] are at play?

(*Circulation*, Volume 118, p672, 2008 より)

（注）

1) lipid hypothesis of atherosclerosis：脂質代謝異常による動脈硬化発症説

2) large-scale, 5-year trials：5 年間の大規模臨床研究

3) statins：コレステロールを低下させる薬物の総称

4) coronary heart disease (CHD)：心筋梗塞などの冠動脈疾患

5) morbidity and mortality：罹患率と死亡率

6) low-density lipoprotein (LDL)：低比重リポプロティン（悪玉コレステロール）

7) event：心事故（冠動脈疾患の発症）

8) control group：対照群

9) salvage rates：救助率

10) LDL-lowering therapies：悪玉コレステロールを低下させることで動脈硬化を改善する治療法

11) antiinflammatory agents：抗炎症薬（炎症を抑えて動脈硬化を治療）

12) immunotherapy：免疫療法

13) armamentarium：治療手段

14) dyslipidemia：脂質代謝異常

15) high-density lipoprotein：高比重リポプロティン（善玉コレステロール）

16) hypertension：高血圧症

17) diabetic：糖尿病の

18) dominant risk factors：動脈硬化の主要なリスクファクター

19) diabetes mellitus：糖尿病

20) genetic factors：遺伝的要因

21) migrated：移住した

22) epidemiological：疫学的

23) environmental factors：生活環境因子

問１　この文章に適切な英語のタイトルをつけなさい。

問２　１９５２年頃の日本では CHD 発症率が米国に比べて低いのかを危険因子の側面から 150 字以内で述べなさい。

問３　下線（A）のように述べられている根拠を 150 字以内で説明しなさい。

問４　下線（B）の問いに対してあなたの見解を 300 字以内で述べなさい。