Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Lymphopenia in SARS

Sir—A common observation in patients with severe acute respiratory syndrome (SARS) has been pronounced lymphopenia with reported prevalence of 69·6%[1] and 54%.[2] Glucocorticoids have a profound effect on circulating T lymphocytes,[3] which may involve their movement out of the intravascular compartment.[4] Glucocorticoids are also used therapeutically in lymphoproliferative diseases, because of their cytolethal actions. In the study by Lee and colleagues,[1] use of steroids may account for the decreasing trend in lymphocyte count over the 7 days of treatment. Booth and colleagues[2] only used steroids in 40% of the patients, less than half of whom received them during the first 48 h. Therefore, some of the lymphopenia reported by Booth and colleagues[2] may be associated with use of steroids, but it does not account for all the patients, and certainly not for the lymphopenia at the initial presentation.

Any critical illness is accompanied by the activation of the hypothalamic-pituitary-adrenal axis resulting in increased adrenocorticotropic hormone (ACTH) and cortisol to maintain the integrity of the vasculature and modulate the actions of proinflammatory and anti-inflammatory cytokines.[5] In a healthy person under severe stress, pituitary ACTH can easily cause the adrenal cortex to release 225–440 mg per day of cortisol,[5] which is equivalent to the dosage of methylprednisolone used by Lee and colleagues[1] that can drive T lymphocytes out of the peripheral circulation. Therefore, is the lymphopenia seen in some of the SARS patients an indication of the integrity of the status of the hypothalamic-pituitary-adrenal axis? More importantly, are the patients without lymphopenia, adrenal insufficient?

The answers to these questions need to be addressed urgently, because they may have a bearing on whether to use glucocorticoids in the treatment of SARS. Thompson[5] has provided a helpful review of glucocorticoids and acute lung injury.

Nirmal S Panesar

Department of Chemical Pathology, Chinese University of Hong Kong, Shatin, New Territories, Hong Kong Special Administration Region, People's Republic of China
(e-mail: nspanesar@cuhk.edu.hk)

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5 Thompson BT. Glucocorticoids and acute lung injury. *Crit Care Med* 2003; **31:** S253–57.

ASCOT-LLA: questions about the benefits of atorvastatin

Sir—We have no doubts about the benefit of lipid-lowering drugs on cardiovascular morbidity and mortality. However, we dispute the conclusions of Peter Sever and colleagues (April 5, p 1149)[1] about the beneficial effects of atorvastatin as presented in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA). As Lars Lindholm and Ola Samuelsson report in the accompanying Commentary (p 1144),[2] the additional benefit of lipid-lowering treatment upon antihypertensive treatment was rather low in ASCOT-LLA.

The benefit of atorvastatin was not significant in patients with diabetes, left-ventricular hypertrophy, and previous vascular disease. Among women, placebo even had non-significantly better results than atorvastatin. The positive results for atorvastatin were not significant in patients aged 60 years or younger, those without renal dysfunction, and in those who had metabolic syndrome.

The disappointing results among women accord with the findings of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT),[3] in which pravastatin did not reduce all-cause mortality, myocardial infarction, or fatal coronary heart disease. One explanation for this finding could be that in ALLHAT-LLT, almost 50% of the participants were women and a high proportion of patients in the control group used statins. The ASCOT investigators argue that the number of events among women and participants with diabetes was too small, because of the inadequate power of the study. However, we doubt the usefulness of lipid-lowering treatment in a population of women with such a low incidence of cardiovascular events (36 for almost 6500 patient-years).

The finding that atorvastatin had no effect on total mortality accords with the results of previous primary prevention studies. However, an effect on cardiovascular mortality would be expected in view of the high number of risk factors among ASCOT-LLA participants.

Why was ASCOT-LLA stopped prematurely after 3·3 years when no significant reduction in mortality could be shown? During the first 3 years of the study, there was no decreasing trend in mortality. In addition, there was even a non-significant trend towards a disadvantage with atorvastatin for fatal and non-fatal heart failure, peripheral arterial disease, and development of diabetes mellitus or renal impairment.

The reason why atorvastatin did not show a similar beneficial effect to simvastatin or pravastatin might be found in the low dose of atorvastatin used in ASCOT-LLA. A higher dose might have shown better results. But there is also a substantial difference in the biochemical structure of the different statins. Lovastatin and pravastatin are natural statins of fungal origin, whereas simvastatin is a semisynthetic derivative of lovastatin. Atorvastatin and fluvastatin are fully synthetic statins.[4] In addition, Cromwell and Ziajka[5] found that the long-term use of atorvastatin led to tachyphylaxis (a decreasing response to a physiologically active agent), which resulted in an increase of LDL cholesterol over time despite optimum treatment. By contrast, all other statins showed no evidence of tachyphylaxis.[5]

Atorvastatin offers no additional benefit above antihypertensive treatment for the reduction of fatal and non-fatal cardiovascular events in women, patients with diabetes, and those with left-ventricular hypertrophy or previous vascular disease—and all this without affecting mortality.

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