on mortality from all causes can lead to serious errors: examples include the use of high titre measles vaccine (which resulted in a higher mortality than standard titre vaccine in girls),[4] failure to investigate the role of polysaccharide pneumococcal vaccine in children in high mortality areas (because of poor antibody responses and poor protection against otitis media in children in developed countries),[8] and failure to appreciate the possibility of substantial non-specific effects from measles, BCG, and DPT vaccines.

The Guinea-Bissau investigators speculate that BCG and measles vaccines may have beneficial non-specific effects because they stimulate Th1 immunity and that DPT vaccine may have adverse non-specific effects because the aluminium adjuvant stimulates Th2 immunity.[2] It has been suggested that reduced exposure to BCG and other microbes combined with increased exposure to aluminium, DPT vaccine, and other Th2 adjuvants may have contributed to the apparent increase in allergic disease in developed countries.[9 10]

Some will argue that the Guinea-Bissau data should not have been published, because publication might damage immunisation programmes. However, it would be inappropriate to suppress this evidence—just as it would be inappropriate to withhold DPT vaccine on the basis of these preliminary results. The appropriate response is to extract as much information as we can from this important study, to perform similar cohort studies in other high mortality areas, and to ensure that new vaccines are introduced into developing countries only after randomised trials of their effect on mortality from all causes. We need accurate information about the effect of the vaccines in the Expanded Programme on Immunisation on mortality from all causes in children in developing countries, and we need it soon.

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Does physical activity prevent cancer?

Evidence suggests protection against colon cancer and probably breast cancer

Physical activity has marked effects on several functions of the human body that may influence cancer risk. These effects vary according to the mode, duration, frequency, and intensity of the activity and include changes in cardiovascular and pulmonary capacity, bowel motility, endogenous hormones, energy balance, immune function, antioxidant defence, and DNA repair. Although a role for energy balance in cancer causation was advanced almost three centuries ago, it is mainly in the past decade that over 200 population based studies have linked work, leisure, and household physical activities to cancer risk. The most researched cancers are those of the bowel, breast, endometrium, prostate, testes, and lung.

Cancer of the large bowel is the most commonly investigated cancer in relation to physical activity.[1–4] Meta-analysis[1] and systematic reviews[2 3] show an inverse dose-response association between activity and colon cancer such that physically active men and women experience around half the risk of their sedentary counterparts. This observation is seen across populations and study methods, with little indication of publication bias.[1] Plausible mechanisms of protection include the favourable effect of physical exertion on insulin, prostaglandin, and bile acid levels, all of which influence the growth and proliferation of colonic cells. Moreover, physical activity reduces bowel transit time and thereby the duration of contact between faecal carcinogens and colonic mucosa, which may explain its inverse association with colon cancer risk and the absence of a relation with cancer at the rectum.

Endogenous sex hormones are strongly implicated in the development of breast and endometrial cancer. Physical activity may modulate the production, metabolism, and excretion of these hormones, so an association with these cancers is biologically possible. Physical activity may also reduce the risk of cancer through its normalising effect on body weight and composition. Evidence from population based studies suggests that occupational, leisure, and household activities are associated with about a 30% reduction in breast cancer rates,[5] with a dose-response relation reported.[3 6 7] Findings are, however, less consistent than for colon cancer, and the sizes of the reported associations are generally lower. This may reflect a genuinely weaker relation or the fact that the strength of the association may vary across the life course as it does for more established markers of risk such as reproductive factors and body mass index. Those studies that have explored the link between physical exertion and the risk of endometrial cancer suggest a negative association.[1 3]

The observation that athletes show lower levels of circulating testosterone than non-athletes, and that

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testosterone influences the development of prostate cancer, has led to the hypothesis that physical activity may protect against this cancer.[3] Though most studies suggest an inverse association between activity and prostate cancer, null and positive associations have also been shown.[3] These inconsistent findings may be explained by a variation in the detection of latent disease. Data are similarly discrepant for testicular cancer.[8 9]

Although physical activity improves pulmonary ventilation and perfusion, which may reduce both the concentration of carcinogenic agents in the airways and the duration of agent-airway interaction, the association of activity with lung cancer has received relatively little attention. Findings from most, but not all, studies suggest a negative relation,[1 3] with those of strongest design—prospective cohort studies relating repeated assessments of physical activity to subsequent lung cancer[10 11]—showing an inverse, dose-response association in men.

In the absence of randomised trials, confounding could be an alternative explanation for the apparent protective effect of activity. Individuals who are physically active may be different from their sedentary counterparts in genetic predisposition, dietary habits, and tobacco and alcohol use. Although several investigators report inverse associations between activity and cancer that are robust to statistical adjustment for these potential confounders, genetic predisposition has been little studied and dietary characteristics have been inadequately assessed. Furthermore, physical activity itself is often measured crudely, so misclassification, albeit non-differential, is likely to result.

In addition to the apparent role of physical activity in the primary prevention of some cancers, there is growing interest in its use in the treatment and rehabilitation of patients with cancer.[12 13] Physical activity may reduce the likelihood of recurrence and enhance survival through its capacity for improving bodily movement, reducing fatigue, and enhancing immune function. Studies are, however, hampered by small sample sizes, short follow up, selection bias, and variations in the stage of cancer at study induction. Thus, although initial results are promising, clearer conclusions depend on larger and better designed studies.

How can the clinician interpret these data on physical activity and site-specific cancers? Overall the evidence supports a potentially important protective effect of activity against colon cancer and probably breast cancer, with no association with cancer of the rectum. Notably, physical exertion does not appear consistently to increase the risk of any cancer. Further data relating activity to cancers of the endometrium, prostate, testes, and lung and to haematopoietic cancer[14] are required. The optimal permutation of mode, intensity, duration, and frequency of physical activity, and its association with cancer at different stages of life, is unclear. In the meantime, in light of the decreasing population prevalence of total physical activity, doctors should advocate moderate endurance-type activity, such as walking and cycling. As well as reducing the risk of chronic diseases such as coronary heart disease and non-insulin dependent diabetes, such physical activity does seem to protect against some cancers.

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Age related macular degeneration

New hope for a common problem comes from photodynamic therapy

Age related macular degeneration is the commonest cause of severe loss of central vision in people aged over 50 in the Western world.[1] The vision loss results from loss of function of the macula, the centre of the retina, which is responsible for central visual tasks such as reading, driving, and recognising faces. Macular degeneration has until recently been untreatable, but laser treatments have become available within the past few years that can halt progression of the disease and the consequent loss of vision in some patients.

The early stages of macular degeneration (usually without significant vision loss) include the formation of drusen,[2] which can be seen with the direct ophthlamoscope (after dilatation of the pupil) as small yellow deposits in the centre of the retina. Drusen are

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