When taken into consideration, the role of asbestos fibres within the lung tissues. If these eight cases with high amphibole concentrations are deducted, the rate of mesothelioma becomes 1.6 per million a year which is very close to the generally estimated background rate.

Greenberg seems to be unaware that high aspect ratio amphibole fibres have been found in the pleura. By contrast with animal studies, which rely on the administration of enormous doses and overload of the respiratory defences, human studies have been remarkably consistent in showing a strong association between amphibole exposure and mesothelioma whereas chrysotile it has been weak or non-existent. Even in chrysotile miners and millers, in whom there have been few mesotheliomas, the evidence indicates that they were related to taconite rather than chrysotile exposure.

To the best of our knowledge the forthcoming review of chrysotile by the International Programme on Chemical Safety will not present any new evidence although it might give a different opinion. Other reviews conclude that amphiboles have a much greater potency than chrysotile for producing mesothelioma.

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4 McDonald JC, McDonald AD. Chrysotile, tremolite and mesothelioma. Science 1995;267:


Biomarkers of exposure to low concentrations of benzene: a field assessment

Editor—Ong et al* present data on the relation between concentration of benzene in ambient air and urinary muconic acid concentration. With the formula they provided in figure 3, the urinary concentration of muconic acid (mg/g creatinine) at concentration exposure to 1 part per million (ppm) is 144-4 or 128-6 ng/mg creatinine, depending on whether log or to the base 10 or natural log is used, respectively. This number seems to be very low compared with that given in many studies which are usually in the range of >100 ng/mg creatinine. It will be helpful if Ong et al could provide some explanation for this apparent discrepancy.

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Author's reply—The overall objective of our article was to evaluate the usefulness of five commonly used biomarkers (a 0.25 ppm exposure to 0.25 ppm) exposure to benzene and as stipulated in the conclusion all the biomarkers were unable to provide sufficient specificity for biomonitoring at the low concentration range. All data suggests that they are not to be used for estimation of exposure to low level environmental exposure to benzene, particularly <0.25 ppm. Our earlier data showed that the level of trans,cis-muconic acid could be useful for environmental exposure to benzene >0.5 ppm; with a calculated exposure to 1 ppm benzene, about 0.9-1.7 mg/g creatinine would be expected at the end of eight hours of exposure.

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Offspring sex ratios and reproductive hazards


8 James WH. Evidence that mammalian sex ratios at birth are partially controlled by parental hormone levels at the time of conception. J Theor Biol 1996;180:271-86.

(2) Under some models, coital rate would determine the time of fertilisation within the cycle.

(3) Distribution of the sexes within litters of several mammalian species suggest that Fm/m (the probability that a zygote is male) will vary from one zygote to another within litters.

Interpretation of the data is not established, but it seems likely that the variation of sex ratio across the female cycle is partially controlled by the varying female hormone concentrations across that time. In particular such an interpretation can be confirmed to explain Weijin and Olsen's report of a significant decline of offspring sex ratio with waiting time to pregnancy. This confirms the data of Renkonen et al and may be caused by the different mean times of fertilisation within the cycle associated with different coital rates (which decline very rapidly during the first year of marriage*).

If I am right, the sexes of mammalian (including human) offspring are partially controlled by the hormone concentrations of both parents. An adverse exposure to a hormone prior to sexual differentiation may have a profound effect on offspring sex ratio. Such environmental agents which are endocrine disruptors may show themselves in biased offspring sex ratios. It thus may be expected that offspring sex ratios should be commonly used as indicators of adverse occupational exposures to men and women.

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8 James WH. Evidence that mammalian sex ratios at birth are partially controlled by parental hormone levels at the time of conception. J Theor Biol 1996;180:271-86.

BOOK REVIEWS

Book review editor: R L Maynard

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be made by cheque in sterling drawn on a UK bank, or by credit card (MasterCard, VISA, or American Express) stating card number, expiry date, and your full name. (The price and availability are occasionally subject to revision by the Publishers.)


One of the aims of this handbook, declared by the editors in its preface, is to chart a new medical specialty: Stress Medicine. Cooper qualified in psychology and business studies in California and now holds the chair of organisational psychology at Manchester Utding's Institute of Science Technology. He is coeditor of the journal Stress Medicine, and is well known for his many publications in this field.

The book constitutes a gold mine of reference for anyone wishing to chart the development of the stress concept, from the early work of the physicians who noted that diverse physical challenges (such as noise, cold, heat, pain, toxins, blood loss, x ray films, etc) caused certain physiological disturbances in common. Hans Selye borrowed "stress" from engineering usage to denote these shared, non-specific distortions of normal functioning. This was an unfortunate choice, which has caused much confusion: to an engineer, it is the limit is exceeded, after which irreversible changes and breakage occur. In other words, as Selye himself later acknowledged, "strain" would have been the right term. Nevertheless stress has persisted, albeit as something of a chameleon with shifting definitions towards pressures of a more psychological kind and stress has become a vague word.

Most of the 19 chapters which comprise the book are by psychologists, although some chapters are written by other fields is also included. Detailed chapters are devoted to a variety of adverse conditions which can exert stressful pressures: cancer, ischemic heart disease, HIV/AIDS, and other chronic illnesses. These, as described above, may cause strain, well, bring their burdens of anxiety and depression, which worsen further the quality of life. There is detailed consideration of the need for social support and techniques for coping.

It is much more difficult to show the reverse process: the ability of stress to produce organic disease. What is clear is that emotional factors may also play some part in the onset and course of many medical conditions. However, the most convincing evidence that stress may be a significant aetiological factor for a specific illness concerns the acute myocardial infarction and psychological variables. Some of the authors who contribute to this book casually include other conditions (such as essential hypertension) for which, on the basis of much less adequate evidence, emotional factors have been claimed to be important primary causes. This book does not always provide adequate critical assessments of the evidence which it presents: instead, the mission of the authors seems (with some encouraging exceptions) to be to accumulate everything which can be traced in the scientific literature in support of the claimed aetiological relation, to add to their case. It would be unfair to liken the approach to that of the current advocates of psychosomatic medicine between 1930 and 1950, who produced an immense, tendentious literature supporting the case for the alleged emotional origins of essential hypertension, rheumatoid arthritis, thyrotoxicosis, peptic ulcer, ulcerative colitis, neurodermatitis, and asthma. But it is unfortunate that some of the literature on stress reviewed in this handbook has not been presented with more rigorous criticism.

The book offers few practical tips to occupational physicians who advise companies on personnel policies aimed at reducing the adverse effects of restructuring and "downsizing", without jeopardising economic objectives. Professional advisers are only too aware of the reality of stress in organisations which are undergoing such changes. Uncertainties about job security, workload, roles, and self esteem give rise to anxiety and depression, and today general practitioners increasingly certify that stress is the cause of the resulting problems. Those to whom senior managers and personnel secretaries must answer are concerned above all with financial viability, but many are also responsive to practical, cost neutral proposals for preserving the morale of the workforce.

Although the handbook contains little direct practical guidance, some of the academic work which it reviews can nevertheless be interpreted in helpful terms for this purpose. An example will illustrate this. An employee's performance generally increases, up to a point, as pressure of work goes up: but a critical point is reached beyond which increasing pressure produces maximum output, and may damage performance irreversibly. Again, there is an engineering analogy: increasing tension in a metal sample produces reversible stretching until the elastic limit is exceeded, after which irreversible changes and breakage occur. In employees, the critical point differs from person to person. The changes underway in many companies involve people whose critical point is too easily reached. But there are alternatives: for example it is now clear that, if people are allowed some control over how they do their jobs, they are less at risk from the stressful pressures, and are imposed with little flexibility or empowerment.

D. DIGOLE


Goodman and Gilman (G and G) was described many years ago as the "Blue Bible of Pharmacology"—this edition is black but still the best textbook of pharmacology and therapeutics available. Occupational physiologists wishing to understand toxicological and pharmacological principles and needing a reference source for information on drugs and chemicals, will find this edition an excellent addition to their libraries.

The editors acknowledge that this is the first edition not to be edited by a Goodman or a Gilman. The editors, preserved the best features of earlier editions while adding many excellent new features. These include several new chapters (including one on gene therapy), synopses at the opening of each chapter, and a prospectus setting out likely future advances at the end of each chapter. This latter introduction has expanded: not only is G and G now up to date, but it also provides the information which you may need next year.

In reviewing this book I have looked closely at their famous group of chapters on the autonomic (ANS) and central nervous systems (CNS). This has been a challenging experience, especially with regard to the CNS. The group of chapters starts with an account of neurotransmitters (the foldout diagram of the ANS remains) which is splendidly up to date but which still includes adequate accounts of the historical development of the field. This has always been a feature of G and G and it is good to see that it has not been lost. The diagrams explaining neurotransmission have been improved and now involve a modest use of colour. This is helpful and attractive. Details of such esoteric subjects as structure of the "docking complex" for neurotransmitters (do you know neuroexin and syntaxin?) are rapidly assimilated from the excellent diagrams. As one would expect, nicotinic and musolinic receptors are discussed in detail. The referencing of this chapter is as up to date as one could hope in a book of this size: references from 1994 and one from 1898 are included.

The chapter on anticolinesterase (AChE) agents has been an old friend for 15 years. Palmer Taylor has taken over the authorship of this chapter from Koelle, and has improved on the valuable series of diagrams illustrating the interaction between the AChE molecule and the anti-AChE molecule. A useful note on Alzheimer's disease and the possible value of AChE blockers has been added. The bibliography of the chapter has been shortened and it is odd that Koelle's masterpiece (Handbuche der Experimential Pharmakologie, 1963) and Ballantine and Marts' more recent volume (in many ways the successor to Koelle's work) do not figure more prominently.

To other chapters: those in the treatment of gastrointestinal ischaemia seem uniformly excellent as is that on the management of asthma. The latter stresses asthma as a predominantly inflammatory disorder and provides a concise review of the inflammatory mediators which may be involved in its pathogenesis. The prospectus is brief, perhaps disappointing so. As well as being a textbook of pharmacology, G and G has always been a textbook of toxicology. This edition maintains that tradition with a chapter on heavy metals and one on nonmetalllic environmental toxicants by Klaassen. The reviews, on a compound by compound basis, are short but the coverage is good and although the bibliography looks just a little dated (no Schwartz, Pope, or Dockery on particles), there are some references to works published in 1994. The book concludes with 79 chapters and tables of pharmacokinetic data dealing with about 360 drugs. This is a unique source of information.

Goodman and Gilman is a large book and this review, although long, does not do it justice. That such a book can be priced at £65 is nothing short of amazing. No doctor, pharmacist or toxicologist, or even medical student could spend £65 or many hours better than by buying this book. For those who have entered the computer age there is even a version available on CD Rom.

R.L. MAYNARD