

dipitously just before the Alsabti story broke⁴; and I should also acknowledge that Dr Peter Green gave me the Tom Lehrer quote.

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- ¹ Halmos PR. *Sci Am* 1957;196:88-99.
² Gaston J. *Minerva* 1971;9:472-92.
³ Hagstom WO. *Am Social Rev* 1974;39:1-18.
⁴ Garfield E. *Current Contents (Clinical Practice)* 1980; 8 (23):5-9.

Ear syringing

SIR,—I read with interest the letter by Dr E R Seiler (24 May, p 1273) concerning the Water Pik for syringing ears. We introduced the Water Pik at this clinic five years ago. We suggested an essential improvement—that is, incorporation of a foot switch instead of the manual one in the instrument. This is most important. It leaves both hands free and the accuracy of the syringing (correct direction of the stream, regulation of the pressure, etc) is greatly enhanced. With the foot switch the procedure is altogether easier and we strongly recommend it. It is surprising how many people use almost prehistoric and clumsy instruments for such an important procedure as syringing ears.

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Retroperitoneal fibrosis associated with atenolol

SIR,—The chemical theories put forward by Dr D W Bullimore in his letter (5 July, p 59) are misconceived and his conclusion therefore does not stand up to critical examination. Figures from the Committee on Safety of Medicines have been quoted, but not in their entirety.

The fact of the matter is that retroperitoneal fibrosis has been listed by the CSM against beta-blockers other than the three that Dr Bullimore places under scrutiny (practolol, oxprenolol, and atenolol). These other beta-blockers do not possess the chemical configuration suggested as important. The figures listed by the CSM (February 1980) are: atenolol 2, metoprolol 1, oxprenolol 3, pindolol 1, practolol 2, and propranolol 3. Atenolol, oxprenolol, and propranolol now comprise about 80% of beta-blocker prescriptions. This is obviously important in evaluating the figures given above. It is also important to note that retroperitoneal fibrosis is listed by the CSM in association with other antihypertensive drugs, including diuretics; for example, bendrofluazide 1, bethanidine 1, chlorthalidone 1, guanethidine 1, and methyl dopa 1.

A drug that can undoubtedly cause retroperitoneal fibrosis is methysergide (an ergot alkaloid). In one publication¹ 61 cases were reported. This is to be contrasted with the two unvalidated published cases associating atenolol with retroperitoneal fibrosis.²⁻⁵ It may be worth stressing yet again the fact that there are 16 patients formerly treated with practolol who developed the fibrosing oculomucocutaneous syndrome causally related to this drug and who were transferred to treatment with atenolol. Now, after six years, none has shown any fibrotic type of response to atenolol (F J Zadiarias, personal communication).

We have no knowledge about exposure to oxprenolol, but for practolol the two unvalidated retroperitoneal fibrosis reports must be related to 250 000 patient years' exposure to the drug in the UK. There were about 1500 cases of practolol-induced oculomucocutaneous syndrome, including about 200 involving the visceral peritoneum. This fibrotic process, when practolol induced, is specific and easily recognised and is different from the fibrotic process in retroperitoneal fibrosis. Atenolol has now had a greater exposure than practolol (350 000 patient years in the UK). So it is hardly surprising, in the light of the figures just given, that two cases should be coincidentally reported in association with atenolol after so great an exposure. This would also apply to the three cases listed against propranolol, which has an exposure of around three million patient years in the UK.

So, six years after the advent of the "practolol syndrome," how do matters stand on beta-blockers and fibrotic reactions? It is reasonable to conclude that beta-blockers other than practolol are not causally associated with the oculomucocutaneous syndrome. We also feel that beta-blockers are no more likely than other antihypertensive agents to be associated with retroperitoneal fibrosis. While continued vigilance is required, the letter by Dr Bullimore serves only to cause apprehension around the world, whereas the evidence to date is reassuring.

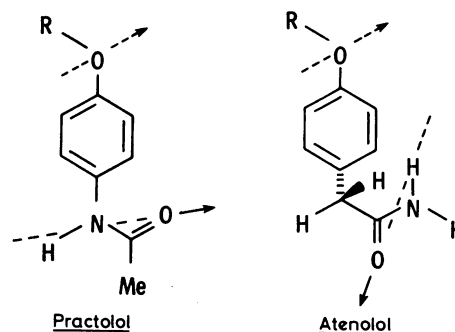
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- ¹ Graham JR, Suby HI, Le Compte PR, Sadovsky NL. *N Engl J Med* 1966;274:359-68.
² Docherty CC, McGeown MG, Donaldson RA. *Br Med J* 1978;ii:1786.
³ Johnson JN, McFarland J. *Br Med J* 1980;280:864.
⁴ Asbury MJ. *Br Med J* 1979;ii:492.
⁵ Gavin MJ, Castle WM, Cruickshank JM, Waycott JA. *Br Med J* 1980;280:1227.

SIR,—In his letter (5 July, p 59) commenting on the alleged association of fibrosing syndromes with certain β -adrenergic blocking agents, Dr D W Bullimore has sought to explain comparative effects on the basis of chemical structure. In doing so, however, he appears to have used concepts long since discarded as having meaningful significance in medicinal chemistry, or for that matter in chemistry itself. For example, the molecular mass of a drug substituent group (except in strictly homologous series) bears no accurately definable relationship to either its biological or its chemical properties. Otherwise, nitro (46 daltons) compounds would closely resemble carboxylic acids (45 daltons) and methoxyl (31 daltons) would confer similar properties to those of hydroxylamino (32 daltons) compounds, and so on. Indeed, it was on this erroneous basis that William Perkin set out in 1856 to synthesise quinine and discovered instead the first aniline dye. In no way, then, can practolol, oxprenolol, and atenolol be grouped together as suggested.

Nor is it permissible to play fast and loose with double bonds and the nebulous concept of associated "electron clouds." These, in so far as they can be defined, possess dipoles, which may be weak or strong; and dipoles have directionality. The strong carbonyl (C=O) dipoles of practolol and atenolol face different ways (see arrows on the diagram), so giving these molecules overall, opposing



electronic configurations. Further, the chemical and physical properties induced by a carbonyl group differ entirely from those of an ethylene residue such as that ($-\text{OCH}_2\text{CH}=\text{CH}_2$) in oxprenolol. In fact, the effect on partition coefficient (the important π factor determining biological activity in Hansch linear free energy functions) of the latter is almost identical to that of the saturated methoxyethyl side chain in metoprolol.¹

Finally, the suggestion—ignoring fine structural detail—that the side chains of practolol and atenolol are "essentially identical" because they both derive from acetamide would implicate all peptides and proteins in the same way. They too derive from acetamide. No, practolol is an anilide, and as such would be expected to show a very different pattern of behaviour from a simple primary amide like atenolol, and this is seen in the results from detailed metabolic studies.^{2,3} The only beta-blocker, other than practolol, which is an anilide is acebutolol.

It seems regrettable that naive and ill-digested chemical concepts should have been used in such a speculative manner, and at a level of scientific rigour far below current practice in discussing biological structure-activity relationships.

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- ¹ Cruickshank JM. *Am Heart J* (in press).
² Reeves PR, McAinsh J, McIntosh DAD, Winrow MJ. *Xenobiotica* 1978;8:313-20.
³ Reeves PR, Case DE, Jepson HT, et al. *J Pharm Exptl Ther* 1978;205:489-98.

Reactive arthritis

SIR,—Your leading article (17 May, p 1196) focused on several important features of reactive arthritis and Reiter's syndrome and did well to stress that "Sex and reactive arthritis may have become too closely associated in the minds of physicians." As you say, before the link can be considered immutable, data from controlled studies are required.

Referring to prognosis, your article states that "a prolonged and stormy course is more likely in individuals with certain histocompatibility antigens, particularly HLA-B27." However, the reference quoted¹ is a symposium consisting of several papers, many with conflicting opinions. For example, Willkens and colleagues (p 10) found little difference between B27-positive and B27-negative patients, and Masi et al (p 49) suggested that the disease may be more persistent in those without the antigen. The contrasting view was presented by Keat and others (p 52). Elsewhere we have found comparable disease

activity (p 29; Fox *et al.*²), a finding not consistent with the data of McClusky's *et al.*³

Thus there is no consensus regarding the relationship between the presence or absence of HLA-B27 and disease severity in Reiter's syndrome. This is an important issue since it would appear that knowledge of HLA status does not provide the physician with useful prognostic information, a topic discussed more fully elsewhere.⁴

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¹ Bitter T, ed. *Ann Rheum Dis* 1979;38,suppl.

² Fox R, Calin A, Gerber RC, Gibson D. *Ann Intern Med* 1979;91:190-3.

³ McClusky OE, Lordon RE, Arnett FC. *J Rheumatol* 1974;1:263-8.

⁴ Calin A. *Ann Intern Med* 1980;92:208-11.

Risk to health and pocket

SIR,—I would be grateful of the opportunity, through your columns, to alert as many people as possible to the possible risks of over-the-counter medicines obtainable by holiday-makers in Spain.

A patient of mine consulted me with a productive cough shortly before going on holiday to Spain. Bacteriological examination of the sputum revealed no infection amenable to antibiotic treatment. She duly went away but was still troubled by her cough and, having been told that the local doctor spoke no English, consulted a pharmacist. She was persuaded to accept a course of tablets which cost her £12 and consisted of 16 tablets of rifampicin. These were handed over without reference to any medically qualified person. Needless to say this expensive remedy had no effect on the symptom, but I suppose at least one should be grateful it was not chloramphenicol.

Perhaps all general practitioners should warn travellers about the potential risks of obtaining medication from pharmacists abroad, the risk being to both their health and their pocket.

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"Batch" or "on-line" for child health

SIR,—Dr Colin H M Walker's review "Batch" or "on-line" for child health" (5 July, p 90) serves only to obscure the issues involved. A proper reply would be too lengthy for your correspondence pages. There are three main issues.

The first is to decide where child health computing lies in the overall context of primary care computing. What is the system trying to do, and how well does it succeed and at what cost? Does it allow for expansion of facilities? Can it be changed easily to cope with changing needs? Comparisons between the child health and Exeter systems are meaningless, particularly when done by someone with so little understanding of the facilities and the degree of flexibility of the Exeter system.

The second issue is to decide how computer technology can most effectively be used in order to achieve the aims of the system and it is in this area that Dr Walker is on even more insecure ground. Batch processing of the type that he espouses is labour intensive, increasingly expensive, inefficient, and difficult to implement. The price of modern computers is such that for £25 000 enough computer hardware could be

bought to run locally all the child health computer systems for an area with a population of, say, one million. The programs that run the Exeter system could with very little modification be used to run the child health system. Such a system would cost a lot less to run, even though it would be "on-line," than the charges currently being applied by some regional health authorities to the national standard system. It should then be considered whether such local processing should be amalgamated in the future with FPC systems. Real-time systems will become cheaper and are easier to implement, and it is easier to maintain the quality of the operational system and the quality of the information. The computer would be under the control of the staff of the area medical officer and the local medical committee could be asked about such questions as release of data.

The third issue and the most difficult is the question of to what extent information should be shared between individuals with varying levels of responsibility to the patient. It is too easy when too much information is bandied around about a patient for other health care agencies to bypass the general practitioner and deal with the patient directly, so that the GP has no knowledge or no say in what is happening to the patient. This is not simply a question of general practitioners feeling insecure but is mainly a question of organisational clarity—so that the patient does not feel that the health service is a gaggle of separate organisations scrapping over his symptoms. It is in our view a prime tenet of health service organisation that the general practitioner is the organiser of resources in the health service for the patient, and that any diminution of his role in this respect will lead to confusion in the patient's mind, as well as the GP's, and inferior use of health service resources.

We think it fair to say that doctors do not know what patients feel about the confidentiality of their records. Until work has been done to establish what patients feel then the proper attitude in this situation is to treat patients' records with greater respect rather than lesser respect. Keeping information confidential will never lessen the patient's respect for the doctor. A discovery by the patient that information has been revealed that he did not want revealed could damage a doctor-patient relationship for ever. It may be that general practitioners are more sensitive on this subject as the patients are to a much greater extent "theirs."

A system designed for general practitioners must respond to individual needs. If we at Ottery St Mary felt that the needs of the patient were better served by a greater release of data then we could release it. However, the decision is ours and is a decision that was carried forward from the manual system when the envelopes containing patient records were released to the community nurses only on an individual basis.

Primary care computing is at a crossroads with systems being separately developed, with no co-ordination, for child health, for the family practitioner committee, for general practitioners, and for the Prescription Pricing Authority. Systems such as the child health system which lead up a technological blind alley should be brought into line with those systems which will provide services for those members of the primary care team who provide most care for the patient. They should not detract from efforts that need to be spent working out overall systems that eventually should assist in all aspects of primary care.

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The Flowers Report and the Institute of Dermatology

SIR,—Dr Andrew Warin is absolutely right about the threat to the Institute of Dermatology. The key phrase in his letter is "critical mass." Were the functions of the institute to be fragmented and dispersed to other departments—even if we suppose that this were possible or indeed likely—the temperature would inevitably fall below that needed for creativity. I know what I am talking about, having struggled unsuccessfully with this very problem of critical mass related to dermatological progress. If the institute is closed dermatology in Britain will go off the boil. To me that would be a self-evident disaster; but, unfortunately for dermatology, it would not be evident to all. There are many in the medical profession who think that it would matter little if at all. Certainly if it meant that important things—their own specialties, for example—were more likely to survive, they would be ready enough to shed a few crocodile tears over the demise of dermatological progress.

For some reason that I have never understood, dermatology is regarded in Britain as trivial, second-rate, a minor specialty, although this is not so in other countries. Yet it concerns the largest organ in the body, which is placed at the interface between the external world and the body, so that a knowledge of both environments is necessary—a far larger field of inquiry than is faced by any other specialty. Disease can be seen actually happening in the skin, while in the internal organs it can be seen only by invasive or indirect methods. Consequently, dermatology is the best subject for teaching about disease in general, though few physicians use it for that purpose. "I don't know a damned thing about rashes, old boy," says the physician who asks for help; but you, the dermatologist, have to have a working knowledge of his specialty, whichever organ or system he may favour. There is really no excuse for the widespread ignorance of dermatology among physicians, particularly since dermatologists require such a good general knowledge of medicine, in its widest sense, in order to be able to practise their specialty intelligently.

Perhaps we need a plague of generalised pustular psoriasis, mycosis fungoides, severe atopic dermatitis, and total alopecia among our administrators and legislators to drive home to them the misery of skin disease. Were that to happen there would be no question of closing the institute: As it is, while these disasters happen only to other people, the closure may seem a thoroughly rational procedure. But I know that it would be a sin against suffering humanity, as well as a betrayal of those who have worked for the advance of dermatology, and whose work is beginning to bear fruit.

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A threat to dispensing doctors and small chemists

SIR,—From June 1980 the majority of chemist wholesalers are to change their pricing policy for both dispensing doctors and chemists, increasing the prices of many drugs from drug tariff or MIMS prices to "notional" prices.

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