

also hope to convey our enthusiasm for experimental and clinical pathology and to train students individually in research methods, to the benefit of both student and department. Our goal is to motivate these students with a view, in many cases, to the possible fulfilment of their promise in a clinical academic career.

From 1968 to 1985, 67 students graduated BMedBiol in pathology. We wish to dispel the notion that intercalated degrees have no research output and are therefore not the responsibility of the Medical Research Council (MRC). Table I shows the number of refereed publications, emanating directly from their research projects, of the 24 students in 1980-5. Fifty six per cent of all students completed research which provided the basis of at least one publication.

TABLE I—Publications in refereed journals by Aberdeen intercalated BMedBiol students in pathology 1980-5: number of papers in which individual students appear as coauthors*

Total No of papers†:	0	1	2	3	4	5
No of students (n=24)‡:	11	6	2	2	3	1

* Journals include: *Agents Actions*, *Bibl Anat*, *Biochem Pharmacol*, *Biol Neonate*, *Br J Exp Pathol*, *Br J Obstet Gynaecol*, *Br Med J*, *Cancer Immunol Immunother*, *Clin Exp Immunol*, *Cytobios*, *Exp Cell Res*, *Immunol Lett*, *J Reprod Immunol*, *J Pathol*, *Lancet*, *Oncodev Biol Med*, *Scott Med J*, *Toxicol Lett*, *Transplantation*, *Virchows Arch*.

† Two students appear on one paper.

‡ In 11 papers the students were first author, in 14 second, and in 8 third.

After completing their BMedBiol 41% of our students graduated MB, ChB with either honours or commendation. Of our 67 students, 55 are now fully registered and we know the career choices of 46 (table II). These figures are broadly in accord with those of Dr Wyllie and Professor Currie, although slightly fewer of our students are pathologists or clinical academics while more specialise in general medicine.

TABLE II—Careers of 46 of the 55 fully registered doctors who did BMedBiol degrees in pathology*

General practice	9
Hospital practice	37
General medicine	16
Histopathology	5
Haematology	2
Clinical chemistry	1
Psychiatry	3
Surgery	3
Anaesthetics	2
Paediatrics	2
Others	3

* Fourteen out of 42 of these students are known to be in academic posts.

Do we attain our stated aims? All our students perform research projects and most publish their work, some commendably, in several papers. We have encouraged students to present findings at national meetings of learned societies. Our students do apparently enhance their enthusiasm for the subject and do well in the pathology degree examinations, winning 25 of the 42 first class certificates awarded in pathology between 1969 and 1985. We would be delighted if more of our former students followed academic careers; at present, many are junior doctors who may yet move to academic posts.

Training intercalated degree students is undoubtedly costly in staff time and materials, but if we assess these costs objectively—by papers produced and in terms of benefit to students, departments, universities, and national research—we believe it is an invaluable degree. The

possibility of withdrawal of MRC support for intercalated years on a point of financial expediency (21 June, p 1619) is unacceptable and would clearly stifle the expression of research potential at an impressionable stage in the career of the medical graduate.

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SIR,—The title of Dr Richard Smith's leading article (21 June, p 1619) could not have been more apposite.

Only students with the highest academic achievements are enrolled on the course for the intercalated year in Manchester Medical School. Since 1976, 47 students have obtained BSc(Hons) in the department of anatomy. Not surprisingly, in view of their high academic standard, 19 were awarded first class honours, 22 second class honours (division 1), and 6 second class honours (division 2). Students invariably comment that they find the intercalated year the most rewarding in their undergraduate training and that their basic attitudes to medicine are changed by their experience. This department has always insisted that the year is devoted entirely to a substantial research project. The student receives a thorough grounding in the research milieu, and the project is written up fully and presented as a bound thesis.

Among our 47 intercalated students six have opted to study for higher degrees, either PhD or MD, four within the department, one in an MRC unit, and one in a cancer research unit. Three students decided to register for a PhD immediately after their BSc course. All have or will complete their medical course. Many of the students have obtained higher clinical qualifications, including FRCS, MRCP, FFARCS, and MRCOG and are pursuing careers in academic departments.

If the MRC is forced to abandon sponsorship of the intercalated BSc year it will be one of the most retrogressive decisions yet taken. It will be stifling what has been one of the more fruitful areas for the seeding of research and one which has contributed to the general enrichment of the practice of medicine. The MRC should in fact be allocated more money by the government for the specific purpose of increasing this particular sphere of their activity.

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SIR,—What a tragedy would be the loss of the intercalated degree (Dr Richard Smith, 21 June, p 1619). We have surveyed the students at Nottingham (where all students do an honours BMedSci) who did their degree in community health since the inception of the medical school in 1968. Of 98 respondents, 90 reported the year as very or fairly valuable, 81 reported specific gains in skills (interpersonal as well as research), and 57 reported changes in attitude, usually in the direction of an increased awareness of the need for critical evaluation. Fully 86 were glad they had done the year.¹ Half the students in recent years have published or presented their research findings (research which, because it requires few funds and addresses local practical problems, is not "rated" by the GMC). I see no reason why similar results would not apply to students who pursued other subjects at Nottingham and feel that the honours year—one year of education compared with four of mere learning—is

very worth while. Let us have a fuller and longer term evaluation by all means, but to reduce the proportion of new medical graduates who have a sound scientific training will only add to the difficulties of keeping the health services effective.

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1 Elwood JM, Pearson JCG, Madeley RJ, *et al*. Research in epidemiology and community health in the medical curriculum: students' opinions of the Nottingham experience. *J Epidemiol Community Health* (in press).

SIR,—I was surprised that you found it necessary to carry a leading article about the threat to the intercalated honours degree in science. Students who are inclined to go in for the science degree are likely to be those who would normally and naturally follow a more scientific course at the end of their medical studies. I do not see how it would be any loss to them to avoid having to do an extra year during their medical careers. It certainly puts them at an advantage and they seem to me to form part of an elite.

Dr Richard Smith seems to suggest that a system that has produced someone like him must be a good one. Many of us are inspired by medicine without the need of an extra year at university.

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Non-steroidal anti-inflammatory drugs and the kidney

SIR,—There is increasing awareness of the renal side effects of non-steroidal anti-inflammatory drugs,¹ and Professor M L'E Orme has emphasised that particular groups of patients are at increased risk (21 June, p 1621). In addition to the mechanisms he discussed, the suppression of free water clearance due to inhibition of prostaglandin synthesis may be clinically important, particularly in the elderly. Prostaglandins regulate medullary blood flow,² inhibit active chloride transport by the medullary thick ascending limb of the loop of Henle,³ and antagonise the action of antidiuretic hormone,⁴ all mechanisms which contribute to urine dilution. Thus administration of non-steroidal anti-inflammatory drugs may lead to renal water retention in excess of sodium retention with the consequent development of hyponatraemia.

One case of hyponatraemia (serum sodium 118 mmol (mEq)/l) associated with ibuprofen ingestion has been reported in a man with a creatinine clearance of 12 ml/min.⁵ We have recently observed a similar degree of hyponatraemia (serum sodium 118 mmol/l) on two occasions in an 84 year old woman taking diclofenac 150 mg/day. Her creatinine clearance was 60 ml/min. The second time she was rechallenged with the drug, having regained normal serum sodium concentrations after fluid restriction. Within four days of starting the challenge her serum sodium concentration again fell to 115 mmol/l.

We are unaware of any other reports of hyponatraemia associated with non-steroidal anti-inflammatory drugs, either in published reports or recorded by the Committee on the Safety of Medicines (personal communication). However, as electrolyte disturbances tend to present with non-specific symptoms, this phenomenon might not be detected routinely. Since hyponatraemia has appreciable mortality,⁶ we feel that it is important to consider this adverse effect in the

elderly as well as in other patients with impaired renal function.

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- 1 Clive DM, Stoff JS. Renal syndromes associated with non-steroidal anti-inflammatory drugs. *N Engl J Med* 1984;310:563-72.
- 2 Lifschitz MD. Prostaglandins and renal blood flow: in vivo studies. *Kidney Int* 1981;19:781-5.
- 3 Stokes JB. Effect of prostaglandin E₂ on chloride transport across the thick ascending limb of Henle: selective inhibition of the medullary portion. *J Clin Invest* 1979;64:495-502.
- 4 Anderson RJ, Berl T, McDonald KM, Schrier RW. Evidence for an in vivo antagonism between vasopressin and prostaglandin in the mammalian kidney. *J Clin Invest* 1975;56:420-6.
- 5 Blum M, Aviram A. Ibuprofen induced hyponatraemia. *Rheumatol Rehabil* 1980;19:258-9.
- 6 Sunderam SG, Manthikar GD. Hyponatraemia in the elderly. *Ageing* 1983;12:77-80.

SIR,—The recognition of renal disease associated with the use of non-steroidal anti-inflammatory drugs has been slow.¹ Surprisingly, the association between the chronic use of the second line agents sodium aurothiomalate (gold) and penicillamine, used in the treatment of rheumatoid disease, and impaired renal function has not been established. Patients with rheumatoid disease are long term users of non-steroidal anti-inflammatory drugs, and some will also be long term users of gold and penicillamine. Treatment with both these second line agents is known to cause renal damage,^{2,3} but usually within 18 months^{4,5} with resolution when the drug is withdrawn.⁶ Glomerulonephritis has been reported on histological examination.⁷

We have recently studied 51 patients taking either gold or penicillamine for rheumatoid disease. Twenty seven had been receiving these agents for over 18 months and nine of them had grossly decreased glomerular filtration rate, as measured by 24 hour urine collection for creatinine clearance. Proteinuria was not significant in any of these patients. We are now carrying out further evaluation of their renal function as it is important to ascertain whether chronic immune complex deposition is causing the renal failure or whether long term use of non-steroidal anti-inflammatory drugs is the cause, as seems more likely.

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- 1 Orme ML'E. Non-steroidal anti-inflammatory drugs and the kidney. *Br Med J* 1986;292:1621-2.
- 2 Fernandes L, Berry H, Hamilton EBD. Historical perspectives on penicillamine. *JR Coll Phys* 1980;14:130-5.
- 3 Research Subcommittee of the Empire Rheumatism Council. Gold therapy in rheumatoid arthritis: report of a multi-centre controlled trial. *Ann Rheum Dis* 1960;19:95-119.
- 4 Walshe JM. Toxic reactions to penicillamine in patients with Wilson's disease. *Postgrad Med J* 1968;44(suppl):6-8.
- 5 Day AT, Golding JR. Hazards of penicillamine therapy in the treatment of rheumatoid arthritis. *Postgrad Med J* 1974;50(suppl 2):71-3.
- 6 Bacon PA, Tribe CR, Mackenzie JC, Jones JV, Cumming RH, Amer B. Penicillamine nephropathy in rheumatoid arthritis. *QJ Med* 1976;45:661-84.
- 7 Dische FE, Swinson DR, Hamilton EBD, Parsons V. Immunopathology of penicillamine-induced glomerular disease. *J Rheumatol* 1976;3:145-54.

The law tries to decide whether whooping cough vaccine causes brain damage: Professor Gordon Stewart gives evidence

SIR,—Your un-named legal correspondent summarises a hearing in the High Court on the case of Kinnear v the DHSS and others (10 May, p 1264). The hearing had been organised to include also the

general issue of whether or not pertussis vaccine could cause brain damage. Your article summarises six weeks of the hearing in six columns, five of which are concerned only with evidence given by me as the first of many expert and other witnesses to be called.

My evidence comprised four reports: one prepared at the request of the DHSS in 1983 (133 pages); one on the general issue written in less than six weeks in 1985 for the hearing (186 pages); one on the case Kinnear (18 pages); and one summarising bulky documentation on various other cases. I answered questions arising out of these reports and many other matters raised by three leading counsel and their advisers, and by the judge, in examination and cross examination lasting about 80 hours over 18 days.

Matters dealt with in close detail in my evidence included the history of pertussis vaccine since 1933 and its preparation, composition, and properties; the symptoms of suspected adverse reactions with special regard to convulsions, shock, and encephalopathy; the possibility in this context of coincidence or alternative reasons for such events; sudden and unexplained deaths after injections; the influence of concurrent factors such as infection, birth injury, and neurological contraindications; methods of detection, reporting, and investigation of suspected adverse reactions; all epidemiological surveys from 1945-85; and, by no means least, intensive investigation, including evidence from other witnesses, of cases identified by initials only in hospital and other records available to the court. I drew attention also to the lack of any system anywhere for obtaining reliable data about the frequency of adverse reactions and for correlating those which are recorded in routine use of a vaccine with crude toxicity tests in laboratory animals used for "safety," and hence to the need for parents and others to be alerted to the occurrence and nature of adverse reactions.

In summarising all this "evidence" in five out of the six columns allocated by you for the entire hearing your legal correspondent either wholly ignored or skimmed over most of it but did select for detailed verbatim attention a few errors in references and in calculations on three pages of my report on the general issue. Your correspondent drew attention also, and rightly, to some errors or misinterpretations of the methods of the National Childhood Encephalopathy Study, and to an error which I made in trying to recall three references in a verbal deposition given in a case, now settled out of court, in the United States of America.

These errors and some others were revealed in cross examination by Mr Anthony Machin, QC, leading counsel for the Wellcome Foundation, which had no responsibility in this case but was represented at its own request and had had, with my prior agreement and cooperation, open access to all my files and raw data (1974-85) on this subject, in my home and in the computer service of the University of Glasgow since March 1985, under the terms of court orders (1984 and 1985) with costs awarded in favour of myself.

I do not deny or excuse such errors on my part. Indeed, I am grateful to Mr Machin and to the considerable panel of experts, named and unnamed, convened by the Wellcome Foundation who have thereby corrected my evidence for the record. But each of these errors is on a point of detail, of minimal significance to the general issue, and with no bearing whatsoever on the case in question.

In England, general issues in law are decided from cases and precedents. It is therefore incorrect in a legal summary, and inexcusable in any objective report, for your legal correspondent to ignore all evidence given about the main case Kinnear and the other cases brought to the attention of the court

by myself and other witnesses. The omission of cross examination by leading counsel for the North West Thames Health Authority and Dr Joshua Stein, named as defendants, is incomprehensible. In this part of the cross examination, as in my report on the case, I pointed to gaps and inconsistencies in the evidence submitted to the court and stated explicitly that Dr Joshua Stein, named as fourth defendant, was not in my view negligent; nor did I see evidence of negligence by any other individual. Since negligence and not damage is the only basis for a legal award in England, this case and any other like it is unlikely to succeed in court. Not surprisingly, for this and other reasons, the case collapsed. Unlike some others submitted with identifying initials to the court, it was not in my view a convincing case, despite an award under the terms of the Vaccine Damage Act 1979 by a tribunal.

This was known beforehand and it is a matter for concern that the general issue was based on a hearing of such a case. This was and is why, in evidence submitted and due to be submitted had the hearing continued, I drew attention to a much wider range of cases, to the need for competent witnesses of recent and contemporary events, and to a pressing need for discovery of data held but not disclosed by the DHSS, the Committee on the Safety of Medicines, the Vaccine Damage Payments Unit and tribunals, three or more manufacturers, national and international regulating agencies, and various health authorities. I referred also to relevant hearings in court and in a sub-committee of the Senate in the USA, and to substantial data held by the Bureau of Biologies and by manufacturers about vaccine related accidents in various states.

Your legal correspondent mentioned none of this, either in the one column of general comment or in the five columns dealing with my "evidence." Such omissions make your article highly incomplete, inaccurate, and biased. It is unfair not just to me personally but to an important, unresolved question which is a matter of immediate and continuing concern to all parents, to all general practitioners and paediatricians, to many other doctors, and to those in authority who recommend and implement mass vaccination nationally and internationally. You have often criticised non-medical media for irresponsible journalism and broadcasting. I am writing now to direct this criticism to you yourself, and to ask you to give me right of reply by publishing this letter, with a suitable heading in your list of contents, and with an apology to me for incomplete and unfair reporting of the evidence which in fact I did give to the court.

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** Our original report on the Kinnear trial concentrated on Professor Stewart's evidence for two reasons. Firstly, by the time the report was prepared (necessarily some time before it was published) no other expert witnesses had completed their evidence. Secondly, Professor Stewart is widely recognised to be the foremost proponent of the argument that the risk of brain damage from whooping cough vaccine is higher than government figures show. We obviously could not cover every point in our article, and as it was the article was much longer than the average medicolegal article in the journal. We therefore decided to concentrate on what we judged to be the most important aspects of the cross examination.

We did intend to carry a further report on the trial, probably at its conclusion, but the case ended prematurely a few days after Professor Stewart