

and you have also observed clinical features, that's nice. But they're usually noisy data, as clinical data tend to be imprecise." But if that allele is put in some experimental system where one can have control over all the parameters, then, says Altman, you will be able to see the physiological response or behaviour for that particular allele.

That triad should give a pretty good picture of what is going on. "However, this is something that physicians are not being trained to think about or to act upon, and this is the challenge for medical education."

According to Altman, there will have to be some 'backward compatibility'. Some retraining will be necessary, but the onus will be on information-systems people to make this easy. No matter what is done with technology, primary-care physicians are still going to have

just 12 minutes per patient, explains Altman. So information systems will have to take less than one minute to help the physician figure out the major decision points, tests that need to be ordered, and the best treatment decisions. Medical informatics has been stressing physician support, which has been regarded as optional until now because good physicians did not need it — they could manage with their brains. "We are looking at a time when even the best physician, unless extremely specialized, is going to need information systems to help manage all the options. Primary-care physicians will need this because their responsibility is simply too broad," concludes Altman.

Brendan Horton

Brendan Horton is a golfer and freelance science writer.

e-mail: b.horton@naturedc.com

Improving the plight of the physician–scientist in the US

For a host of reasons, interest by physicians in careers in clinical research has been waning over the past two decades. Of particular concern is the area of patient-oriented research, which Nobel laureates Michael Brown and Joseph Goldstein of the University of Texas Southwestern Medical School in Dallas define as that which passes the "handshake test" — when the investigator meets the patient during the study.

Although some would argue about the extent of the problem, most would agree that, even though MDs and PhDs have maintained fairly similar success rates when competing for grants from the US National Insti-



Brown: 'funding at the root of the problem'.

tutes of Health (NIH), the number of applications from MDs has fallen far behind those from PhDs, making them an ever-decreasing fraction of those seeking funding. The NIH Director's Panel on Clinical Research reported a 30 per cent drop in first-time grant applications to the NIH from MDs between 1994 and 1996. Applications from PhDs fell just six per cent.

"There have been spotty attempts here and there to patch the problem," says Brown, "but no systematic attempt to fix it. The underlying problem has got much worse, and that is because of the way clinical departments are funded in this country." The growth of managed care, coupled with reduced levels of reimbursement from government health-insurance programmes, has eroded the financial security of academic health centres, placing greater pressures on clinical departments and physicians to boost revenue by providing clinical services to more patients. It is easy to see why academic pursuits often play second fiddle to clinical practice.

In some medical schools, a career in research is not actively promoted or held in such high regard as it once was. This, together with a paucity of clinical training and career-development programmes, a lack of mentors, and a feeling that clinical research grant applications were not getting a fair deal from NIH study sections (although a restructuring of the study sections is under way), have all contributed to physicians' declining interest in clinical research. The prospect of low pay (compared to clinical practice) over the lengthy training period, at a time when most physicians are saddled with debts of \$60,000–80,000, is also a factor.

Why should we care?

This is not to suggest that the biomedical research enterprise is grinding to a halt because physicians have been turning away from clinical research careers. Basic science is flourishing, and many MDs who opt for a career in research choose basic science over clinical studies, in part because the funding situation appears healthier. Increasingly, basic scientists are turning their attention to clinical problems, says Brown. It has become fashionable for basic biologists to affiliate to



After graduating from medical school, **Brenda Nicholson** (above) was intent on a career in clinical practice. But a three-year fellowship in haematology–oncology at Vanderbilt University Medical Center, Nashville, Tennessee, changed all that. **Now an assistant professor of medicine at the university, Nicholson recently received a five-year clinical associate physician, or CAP, award from NIH to further her patient-oriented research in breast cancer.** The CAP award, part of NIH's effort to

Clinical research in practice

attract young physicians into clinical research, provides 75 per cent of an NIH-capped salary. Nicholson, in return, will be expected to devote 75 per cent of her time to the projects outlined in the award.

Nicholson attended medical school at Wright State University in Dayton, Ohio, and followed this with an internship and residency in internal medicine at the Bowman Gray School of Medicine in Winston-Salem, North Carolina. Both colleges run clinically directed programmes with almost no exposure to research, says Nicholson, "and that's why when I came out of training and went into fellowship I had in mind that [ultimately] I was going to go into private practice.

Exposure really was the thing that stimulated me to want to stay [in academic medicine]." During her fellowship at Vanderbilt, Nicholson says she was given considerable responsibilities and opportunities, as well as a lot of positive reinforcement. **She credits her mentor, David H. Johnson**, deputy director of the Vanderbilt–Ingram Cancer Center and director of medical oncology, with helping to launch her career in academic medicine, and the new chairman of medicine **for actively encouraging young physicians to go after NIH funds.**

Vanderbilt is unusual, she says, in being strong both in basic science and clinically. She has managed to develop

collaborative projects with basic scientists, including a study to test the combination of tamoxifen and the monoclonal antibody Herceptin in patients with oestrogen-responsive tumours and metastatic breast cancer, a *BRCA1* gene therapy trial, and a study to test whether taxol can sensitize cancer cells to radiation therapy.

Now with a CAP award under her belt, which affords physicians the kind of mentoring and protected time needed to develop the skills to become independent investigators, Nicholson is very much on an academic medicine career track. She says: **"It's a career that's exciting, and allows you a balance between patient care and the creativity of doing studies."** **D. G.**

companies or to start their own, to try to develop new therapies. "The danger would be if medical schools drift so far away from science... that the students more and more see the research as irrelevant to medicine as they wish to practise it," he says.

Leon Rosenberg of the department of molecular biology at Princeton University, who was a member of the NIH director's panel, says: "We're not raising this issue because the system is falling apart today... we are concerned about the future." When former NIH director James Wyngaarden first drew attention to the problem 20 years ago in his article "The clinical investigator as an endangered species", Rosenberg says the message largely fell on deaf ears.

There are those, adds Rosenberg, who say that, if MDs do not stay in the world of clinical research, their place will be taken by well-trained PhD scientists. "I think that's a myopic view of the role that these different professionals can bring to a research system. MDs are conditioned by their experience with sick people, and the questions they ask are often formed from their experiences."

Initiatives launched

Both the US Institute of Medicine and the NIH director's panel have published reports and made recommendations for tackling the problem. Interestingly, the Federation of American Societies for Experimental Biology, an organization not usually noted as representing the interests of physicians, held a meeting in June on career opportunities for physician-scientists, and is due to present its report to its directors in December.

Both the published reports cited deficiencies in clinical research training, career development and mentoring. Institutions were found to be struggling to engage and launch physicians in careers in clinical research, with the quality of programmes varying widely. It's hard to train people who are good both in the clinic and at the bench, since the knowledge requirement is so enormous, says David Nathan, professor of medicine and faculty dean

for academic programmes at the Dana-Farber Cancer Institute in Boston, who was also a member of the NIH panel.

The Mayo Clinic in Rochester, Minnesota, operates a training programme supporting 10–12 'residents' each year, providing them with two years'



Nathan: 'knowledge requirement is huge.'

experience in a clinical research lab. "Programmes like ours were born of a frustration at not being able to train and attract these people into clinical investigative careers," says Gregory Poland, professor of medicine

in the Mayo Vaccine Research Group and associate programme director for the Mayo Clinic's General Clinical Research Center. In September, the clinic received one of the new NIH-funded K30 clinical research curriculum awards, which it will use to develop a masters programme in clinical research. A total of 35 five-year K30 awards were made by NIH during the programme's first year, each funded to the tune of \$200,000 per year.

It is essential to engage students in science while they are still in medical school and thinking about careers. Judith Vaitukaitis, director of NIH's National Center for Research Resources, says the agency plans soon to put out a 'request for applications' for its new medical student training programme. This is modelled on a programme at the University of Pennsylvania, Johns Hopkins University and Washington University. Students will take a year off from medical school and work with a clinical investigator.

Two career development initiatives were also implemented by NIH this year for entry-level and mid-career clinical investigators in patient-oriented research. Like the K30 training awards, these awards stemmed largely from recommendations in the Institute of Medicine and NIH panel reports. For those embarking on a career in clinical research, the K23 award provides between three and five years of support for mentor-supervised research projects. Applicants must have a clinical degree, have completed specialized training and fellowships, and hold an academic appointment at an institution with a general clinical research centre.

The K24 mid-career investigator award provides partial salary support to more experienced physician-scientists. It affords them the protected time they need, away from having to provide patient care, to conduct research and mentor young investigators. It offers between three and five years of support, and individuals are expected to spend up to 50 per cent of their time on award-related work. Vaitukaitis says the NIH funded 85 of 192 K23 applications this year and 81 of 181 K24 applications.

The other part of the training equation is good mentoring. But, with the pressures faced by clinicians today, it is easy to see why mentoring doesn't happen. Poland says he takes mentoring seriously and works a 75–80-hour week to meet his administrative, research and mentoring responsibilities. "I do it because it was done for me," he says.

Unfinished business

Although these NIH initiatives are a step in the right direction, they are fairly small scale. Private foundations (see web table, page 214), as well as pharmaceutical companies, have been long-standing supporters of clinical research. The Howard Hughes Medical Institute, for example, provides support to help launch medical students

In some medical schools, a career in research is not actively promoted or held in such high regard.

and physicians on a research career path. Although the number of MDs and MD/PhDs applying for its postdoctoral research fellowships dropped 45 per cent between 1996 and 1998, it is not known to what extent the NIH initiatives may be having an effect on application rates.

Nathan says that the issue of medical-school debt has barely been touched upon. Physicians emerge from clinical training at 32 or 33 years of age with large debts, and cannot find affordable housing for their families on earnings of \$40,000–60,000 per year without going further into debt, he says. "If I were NIH director I would get a panel together to look at that question." And, given the lack of minority groups in clinical research, which often translates into a lack of minority patients in clinical trials, perhaps any effort should be directed there first, he says.

The \$60-million Clinical Research Enhancement Act, which was reintroduced in the House of Representatives last May, addresses the issue of debt, among other things. "My view is that this is only in part an NIH problem," says Nathan, who feels that changes must be made on many fronts. Nathan would like to see the pulling together of key individuals from the top 10–15 research-oriented medical schools to determine what the deans think about this issue.

Given the apparent disincentives, one might be forgiven for asking why anyone would consider a career in clinical research. Rosenberg has an answer: "I've had the best career I could possibly imagine having had. Sure, it's been hard, and I've lived in two different worlds on more than one occasion, but that's what's been fun about it." **Diane Gershon**

Diane Gershon is assistant editor, new technology, at Nature Medicine.

e-mail: techmed@earthlink.net

Further reading

- Wyngaarden, J. B. *N. Engl. J. Med.* **301**, 1254–1259 (1979).
- *Careers in Clinical Research: Obstacles and Opportunities* (Institute of Medicine, National Academy Press, Washington DC, 1994).
- Goldstein, J. L. & Brown, M. S. *J. Clin. Invest.* **99**, 2803–2812 (1997).
- Nathan, D. *J. Am. Med. Soc.* **280**, 1427–1431 (1998).
- Rosenberg, L. E. *Science* **283**, 331–332 (1999).