#### PERSONAL VIEW Frank Davidoff

## We need better ways to pick new hypotheses to test

udging from the mass of clinical trials being published, the testing of hypotheses is flourishing in biomedicine.<sup>1</sup> This isn't surprising, given the currently dominant hypothetico-deductive paradigm, which has spawned a huge and well funded clinical trial apparatus. It does, however, make the current disrespect for studies that "merely" generate hypotheses all the more puzzling. (One major clinical journal, for example, tells authors who submit such papers that, "We think you picked the wrong journal; [we] rarely if ever publish hypotheses.") But we need falsifiable hypotheses; without them, what would we do randomised trials on?<sup>2</sup> Besides, having many candidate hypotheses increases the chances of discovering the small number of ideas that most effectively explain anomalous observations.3

Medicine's history of stubborn adherence to inadequate hypotheses about disease aetiology and therapeutic mechanisms undoubtedly contributes to the current caution in embracing new ideas. To make matters worse, the process by which hypotheses are created is mysterious, seemingly far outside rational scientific thought.<sup>3</sup> The great philosopher of science Karl Popper threw up his hands on this question, asserting that "there is no such thing as a logical method of having new ideas, or a logical reconstruction of this process . . . every discovery contains an 'irrational element,' or a 'creative intuition.'"<sup>4</sup> Blindness to the potential value of new ideas may also be deeply rooted in fear of failure, a disabling state of mind fostered by the pressure to conform that is inherent in all professions. This blindness may also be encouraged by the current system for awarding biomedical research grants, which some see as a sort of jobs creation programme for researchers; one which therefore plays it safetesting endless variations of the hypothesis that "drug X affects outcomes in disease Y," for example-rather than taking us in potentially transformative but riskier directions.5

Despite these intellectual headwinds, biomedical hypotheses somehow continue to emerge, but it's impossible to test them all, and it would be extraordinarily wasteful to do so even if we could. It is a key challenge, therefore, to decide which nascent hypotheses are formulated well enough to be worth testing. The clinical and social sciences have some structured mechanisms for deciding which hypotheses to test—for example, the systematic screening and assessment method,<sup>6</sup> and others



## There may also be drawbacks in developing new ways of generating and identifying fruitful hypotheses

used by private foundations and US government agencies.<sup>7-9</sup> Arguably, however, the principal driving force behind these mechanisms is the need for guidance in distributing limited research funds, rather than a judgment by the scientific community that estimating the potential scientific value of hypotheses is in itself an important professional responsibility.

Contrast this with the US grand jury system, the structured process, independent of the justice system, that determines whether "probable cause" exists in ambiguous criminal cases, a requirement for bringing those cases to trial.<sup>10</sup> Grand juries emerged centuries ago because the wider community recognised that justice would not be well served if such cases were either abandoned (because of failure to gather enough evidence) or were all brought to trial (which would swamp the courts with unjustified litigation). Clinical research is of course not criminal justice, but the grand jury system makes it clear that a profession can deal with its weak links if it has the will.

So what is to be done? Firstly, the clinical research community must affirm the vital role played by hypothesis generation and work to improve our understanding of the process. Secondly, as a matter of editorial policy, clinical journals must encourage publication of well founded studies that generate hypotheses. Thirdly, training in biomedical research must sharpen its focus on the creation of hypotheses, by using disruptive cognitive techniques such as lateral thinking, for example.<sup>5</sup> Fourthly, we must explore new and better ways to identify hypotheses worth testing—for example, by using open innovation communities<sup>11</sup>—and evaluating their effectiveness.

Cross disciplinary efforts to define criteria for well founded hypotheses are steps in the right direction—criteria such as clarity of constructs, measurability, explanatory power, description of causal mechanisms, parsimony, generalisability, and testability.<sup>12</sup> Finally, as Roberta Ness suggests, we should consider funding creative work separately from implementation studies; providing funding to laboratories or programmes as well as individual investigators; and exploring alternatives to the business model that underpins many health science centres—a model that focuses mainly on short term financial gain.<sup>5</sup>

There may also be drawbacks in developing new ways of generating and identifying fruitful hypotheses. Many pragmatic priorities—fiscal, political, and social—bear heavily on the conduct of science <sup>6-8</sup> and these must not be allowed to stifle support for promising ideas. For example, high visibility groups must not be allowed to push aside strong ideas from less well known sources that are seen as competitors. Establishing unequivocally which researchers proposed new ideas, particularly when they do so as part of a team, will go a long way towards protecting legitimate claims for academic promotion, and avoiding counterproductive disputes over patent rights.<sup>5</sup>

Current mechanisms for identifying promising hypotheses and selecting them for testing are haphazard, inefficient, and far from rational. Reshaping how we manage hypotheses will demand patience, because payoffs from this reshaping will take time. It will also demand greater tolerance for risk of failure, particularly among researchers and funders, because disruptive hypotheses often disappoint. But a reshaping of the paradigm is needed if we are to create a body of scientific knowledge that not only tells us what we know but also what we need to know.

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### BETWEEN THE LINES Theodore Dalrymple

## The Hippocrates prize

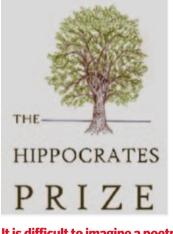
The Hippocrates prize is an annual prize for poetry, awarded since 2010 and open to anyone who has worked in the NHS. There is also a category for poetry about a medical subject, open to anyone in the world writing in English. Altogether there are thousands of entries, and the winning poems, the two runners up, and all the commended poems are published in a slim but elegant volume.

It is difficult to imagine a poetry prize open to people who have worked in accountancy, for example, attracting quite so many entries as this one.

The pleasures of the poems are various, as you would expect. Valerie Laws, for example, raises a purely intellectual problem in her witty poem *A Question for Neuroscientists*:

Where does a memory sit, when it's at leisure? Where does it cool its heels, await our pleasure?

Several poems are about anatomy, suggesting that the former discipline (or was it a ritual?) of dissection of a corpse in the education of medical students was of deep cultural and emotional significance. In *Anatomy*, for



It is difficult to imagine a poetry prize open to people who have worked in accountancy, for example, attracting quite so many entries as this one example, Jane Kirwan describes, perhaps laments, the decline of dissection:

Professor Cave bustles up to the raised dais,

skullcap, snuff, spotted bow-tie, twiddles his cuffs.

Nothing to be thrown away. "The rules" he tells us

"are plain. No skipping with intestines,

no jokes." Just formalin . . .

Sometimes the poems' images are striking, as in *Rorschach* by Andrew Thomas Martin, about doctors' interpretation of MRI scans:

They observe the emergence and dissolving of all the bats, angels and butterflies that fill your body

And in *Intensive Care, Friday Afternoon*, Kev O'Donnell describes each of the 16 beds in two lines:

#### Bed 15

a foreign student who hung herself, found with a stopped heart, now doing her best to die again. Bed 4

empty, cleaned by a nurse aid low winter sun through blinds. Bed 2 dying, curtains pulled

cold air falls.

The power of poetry to compress emotion is illustrated in a poem by Frances-Anne King about the wig of a child treated for leukaemia with chemotherapy. The wig is discarded as the child lies dying:

Her scalp shone smooth then, translucent as the linings of an oyster shell,

her freckles, pale tracings on a fading sea of face.

Theodore Dalrymple is a writer and retired doctor

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## MEDICAL CLASSICS

#### On the Edge of the Primeval Forest

A book by Albert Schweitzer

First published as Zwischen Wasser und Urwald in 1921

When read with contemporary eyes, Albert Schweitzer's book, subtitled "Experiences and Observations of a Doctor in Equatorial Africa," is a disconcerting mix of startling racism and yet still pertinent commentary on African suffering. Schweitzer, a Christian missionary, physician, philosopher, and musician who qualified in medicine at the age of 38, funded his first trip to the Ogowe (or Ogooué) River with organ recitals and a book on Bach. The description of trying to land a piano ("built for the tropics") and 70 cases



Schweitzer's book is a disconcerting mix of racism and pertinent commentary

by dugout canoe is surreal but understated. His wife was a nurse and their approach to medicine was cutting edge scientific (they were intrigued by sleeping sickness trypanosomes in the blood), hygienic (Mrs Schweitzer washes a lot of bandages), and weird (devoted to pith helmets, to avoid the deadly evil of the African sun).

I read this as a child and am alarmed that I then barely noticed the racism. I remembered the romance and the drama of night time encounters with hippos and of the awesome primeval forest: "a mighty network of roots, clothed with bright flowering creepers." And I remember the religion, which I shrugged off. As Schweitzer does, at times: "[the] humanitarian work to be done in the world should... call upon us as men, not as members of any particular nation or religious body." But who could read "blacks shall be in whites' quarters as little as possible" (for "fear of infection") without a shudder of disgust and horror? "It is impossible to rely upon the blacks," he also wrote.

But the book undoubtedly changed attitudes at the time, and reflected real commitment—my 1955 edition was prepared when Schweitzer, then 78, had been working in Africa for 40 years. So can it be forgiven for racist assumptions that now seem reminiscent of apartheid at its worst? Schweitzer genuinely struggled to understand how European ethics might not, and did not, fit local culture—culture that he learnt to respect, if not admire. He worked in his hospital on the Ogowe River throughout the first world war, which both horrified him and noticeably dented his conviction in European superiority.

The descriptions of his work, with a therapeutic armoury both pitifully limited and eerily familiar, put the lie to any suspicion that he saw those he treated as any less human than himself. He recognised and empathised with their pain, and he treated everyone with the same drugs and the same compassion (although even statistics are racial: in 1903, he notes, the mortality of whites in Libreville was 14%).

Schweitzer saw that most local suffering was imported: "who can describe the injustices and the cruelties that . . . they have suffered at the hands of Europeans?" And at the end he calls for responsibility among the better off: "Physical misery is great everywhere out here. Are we justified in shutting our eyes and ignoring it?" He didn't think so. In this he was well ahead of his time. And not wrong. Kate Robertson, specialty doctor, child and adolescent psychiatry, Shropshire Child and Adolescent Mental Health Service, Shrewsbury kate.robertson@doctors.org.uk Cite this as: *BM*/ 2012;345:e7930

#### FROM THE FRONTLINE Des Spence

## Warning: parental advisory

Confidently, my brother threw the huge new bowie knife at the door. The handle hit the wood, and it bounced wildly backwards, narrowing missing my ear. We laughed. "The best present ever," my brother said.

Few children get knives as presents these days. We were a generation whose parents were distant. We were largely ignored, rarely affirmed, yet paradoxically free, independent, and self contained. Those were harsher days.

Today's children seem not only materially indulged but also emotionally indulged and immature. I feel uncomfortable when parents suggest that their children are their "best friends" or sport fixed smiles as they say how wonderful their children are. We have our own "little emperor" phenomenon. What has become of parents and childhood?

Parenting is now big business. Coiffured PhDs sit on daytime television's sofas, flogging pseudoscientific parenting books and programmes. But parenting is confounded by so many things, such as circumstance, the kids'

STARTING OUT Kinesh Patel

Today's children seem not only materially indulged but also emotionally indulged and immature

and parents' personalities, and the age and number of children. So I spurn cookbook parenting, believing that parenting is not about simplistic lessons but only constant practice. The one certainty of parenting is its contradictions.

But parenting classes for all is now official government policy and is supported by the National Institute for Health and Clinical Excellence.<sup>1</sup> The rationale is obvious: give parents basic parenting advice and we prevent (and save money on) conduct disorders. This is simply a good idea based on simple reasoning. But a recent systematic review questions this certainty for a widely implemented initiative called Triple P.<sup>2</sup> The research, relying on unregistered trials, is open to selective reporting, is limited in long term outcomes, and is confounded by the quicksand that is self reported outcomes. The review casts doubt on effectiveness in the all important hard to reach groups.<sup>2</sup> Results from other large trials are emerging that challenge the effectiveness of universal parenting programmes.<sup>34</sup>

Could parenting courses do harm? These courses and books are undermining and put the notion of good parenting in constant flux. Parenting classes suggest that there are right and wrong parenting styles, rather than normal old "just getting by and doing our best." And what of the opportunity cost? Would these large resources be better spent on targeting the most needy or tackling the chronic underinvestment in health visitors? What parents really need is continuity and personalised advice.

But the corporate parenting business is eroding traditional local sources of advice on parenting such as health visitors, nursery staff, doctors, and grandparents. And the focus on parenting classes distracts us from the root causes of conduct disorders: poverty, family break-up, unemployment.<sup>5</sup> Aren't universal parenting programmes just tokenistic middle class social evangelism?

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# But Twitter uny ● Follow Des Spence on ds' Twitter @des\_spence1

## Revalidation: a missed opportunity

What do a washing machine and a tyre have in common? No: this is not a bad joke, although I may have been responsible for a few of those in my time. It is the quality labelling. When you buy a washing machine, it has a label that gives information independent of the manufacturer that tells you how good it is at washing and how much energy it uses. From this month, car tyres are subject to the same European regulations, so that you'll know before you buy how good the tyre is at gripping the road. These labels are useful. Rather than relying on brand names or seductive advertising, you have some objective information about what you are about to buy.

How does this relate to medicine? This month the General Medical Council introduces our own long awaited system of accreditation.<sup>1</sup> We will all have to provide a ream of evidence that we are participating in continuing professional development and quality improvement and that patients and colleagues think we're nice people. And at the end of this we'll get a stamp saying we're good enough to keep on working in the NHS.

This is a bit of a waste of time and a wasted opportunity. What is the likelihood of it picking up surgeons who are performing oxymoronic "cleavage sparing" mastectomies?<sup>2</sup> The feedback from accused surgeon Ian Paterson's patients was no doubt fabulous. The last thing we need is another box ticking exercise.

Now just imagine that the process provided each doctor with a grade that had to be displayed, comparing us against our peers. We are competitive beings in medicine, by our very nature. No one would want to be, or to employ, an E rated doctor: just think of the



What is the likelihood of it picking up surgeons who are performing oxymoronic "cleavage sparing" mastectomies? embarrassment. The competition to get a good score would drive standards up.

A look at John Lewis's website shows the results of transparent labelling over several years. The worst washing machine has an energy rating of A and the best a rating of A+++. New ratings have been added to the top of the scale as manufacturers make more and more energy efficient machines. Such a system could be introduced for doctors, without spending resources bribing us to remember, for example, to check the weight of patients with diabetes.

But perhaps the real benefit would be to acknowledge those doctors who are doing a truly good job. After all, most of us do perform well; wouldn't it be lovely to have that validated?

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