

LETTERS

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ANTIMICROBIAL RESISTANCE

Paradigm shift is needed



The focus on antimicrobial resistance highlights the challenges of providing healthcare when antibiotic effectiveness has changed.¹ Improved antibiotic stewardship is important, but new agents are also needed, especially to treat inherently resistant organisms (*Acinetobacter baumannii*) and those acquiring new resistance mechanisms (*Escherichia coli* and *Klebsiella* spp), yet the pipeline of new antimicrobials is running dry.

Economics explains why few antimicrobials are in development. Porter's model of competitive market dynamics provides useful insights.² The antimicrobial marketplace (and incentives for new product development) is influenced by the balance between the bargaining power of customers (patients, healthcare organisations, governments) and suppliers (drug companies), the threat of substitutes (alternative products including generics), and new entrants (generics companies). Currently, the balance is tipped towards antimicrobials being available at low cost. The high costs of developing new antibiotics and their potential short life span (due to resistance) make the antimicrobial business unattractive.³

Antimicrobials are cheap relative to their therapeutic and social benefit. In the UK, ceftriaxone for treating meningococcal meningitis costs £142 (€179; \$230) and can give many years of productive life after recovery. But treatments where life expectancy is limited, such as trastuzumab for metastatic breast cancer, cost substantially more. Pricing antimicrobials on the basis of their social and therapeutic benefits could incentivise the development of new agents and tackle this paradox.³

Unless we alter the mechanisms that have led to the current market failure, little progress

will be made. Livermore noted the urgency of the problem in 2003, yet there are still few new drugs or classes of antimicrobials.⁴ A paradigm shift in approach is required.

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Full response at www.bmj.com/content/346/bmj.f1601/rr/636987

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Shopping around makes it worse

I agree with Smith and Coast that the true cost of antimicrobial resistance cannot be overestimated.¹ In my general practice in west London, many patients from abroad, especially those from the US and some EU countries, are surprised and dismayed when I refuse to prescribe antibiotics for self limiting infections. Furthermore, many returning travellers see me as a follow-up after having been prescribed antibiotics while abroad for what sounds like a viral infection. They may even have bought antibiotics themselves from a pharmacist and self prescribed.

Patients can “shop around” in today's NHS and if unhappy with one doctor's treatment (or perceived lack of it) can find one who will give them what they think they need. Warning patients individually about the dangers of antibiotic resistance and the ticking time bomb is ineffective, so more public health campaigns and media coverage are essential to ensure that antibiotics are used more prudently, at least on a national basis.

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- 1 Smith R, Coast J. The true cost of antimicrobial resistance. *BMJ* 2013;346:f1493. (11 March).

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Don't underestimate the threat

Health economic evaluation has increasingly converged on an agreed set of principles and procedures based around probabilistic modelling, clinical trials, and meta-analysis. Smith and Coast's article on antimicrobial resistance shows us clearly and elegantly why these methods will probably fail us the moment we step outside the carefully controlled world of trials into the world of uncertain policy problems without clear answers.¹

The loss of antimicrobials or antimicrobial effectiveness does not, in this context, represent a choice between interventions, but a possible future state. Unlike other probabilistic states that might be represented in standard approaches to economic modelling, uncertainty replaces an identifiable probability, and the models will not deliver for us.

The underestimation of antimicrobial costs resembles the underestimation of downside risk in the models for derivatives that caused the banking crisis.² Both are geared around quantifiable probabilities and tend to assume normal distributions, but both fail to accommodate uncertainty and the potentially catastrophic costs of downside events (which may be much less unlikely than we think).³

Smith and Coast also remind us that we need to engage urgently with the history of the immediate pre-antimicrobial era—the 1930s to 1940s. A few retired clinicians may still be alive whose detailed knowledge of practice and procedures of that time should be documented and preserved.

The threat posed by antimicrobial resistance confronts our vision of a future that always improves. Without decrying the possible role for future technologies in helping us avoid this approaching cliff edge, it is surely sensible for us to reach back into the past as part of the “insurance” Smith and Coast rightly say we need to take out.

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TREATING TORTURE VICTIMS

Suspension verdict is unfair

As doctors who regularly work with survivors of torture we are well aware of the devastating short term and long term effects that torture has on those subjected to it. We also recognise the obligations on doctors stated in the World Medical Association's Tokyo Declaration and the United Nations Istanbul Protocol to avoid being in anyway complicit in torture.

We are, however, worried by the case of Dr Mohammed Al-Byati.¹ Although we realise that we are not privy to all the facts disclosed to the tribunal, the reported judgment appears contrary to natural justice.

The *BMJ* news report states that the tribunal accepted that Dr Al-Byati "had effectively no choice but to carry out orders." The tribunal's chairman is reported as saying that Dr Al-Byati "was a junior doctor whose behaviour was being controlled by a dictatorial, totalitarian regime . . . Dissent from orders was not tolerated." The chairman also stated that, even though the doctor's involvement was "outside his control," the tribunal imposed the maximum period of suspension because "such conduct is unacceptable."

In what sense is conduct over which someone has no control "unacceptable" and culpable?

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PLAIN PACKAGING

Switch to large pictorial health warnings on cigarette packs

The New Zealand government's announcement that it will bring in legislation for plain cigarette packs is a welcome public health development. However, the fine print says that the government will wait to see what happens with Australia's legal cases, so enactment of this legislation might be delayed.¹

The legal and arbitration processes surrounding Australia's plain packs legislation may take years to be finalised. In one process (with Philip Morris), the first arbitration hearing has been moved to February 2014.² There are



also cases in which Ukraine, Honduras, and the Dominican Republic are using World Trade Organization dispute panel procedures, and which have only started the procedural stages.³

In the meantime, New Zealand has a pictorial health warning on the front of 30% of packs, compared with 75% for Australia, Canada, and Brunei and 80% for Uruguay and Sri Lanka.⁴ Thailand will have 85%.⁷

Governments that, unlike Australia, are timid about the litigation risks of plain packs could still adopt large front of pack warnings now. For New Zealand, this could be done by a change of regulations that would not require new legislation. If the six countries above can have large warnings (and Uruguay can refuse to bow to Philip Morris litigation about their warnings) why can't others?

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TREATING ACL INJURIES

Authors' response to editorial on treating ACL injuries

Levy and colleagues misinterpreted our report on the five year outcome of treatment for rupture of the anterior cruciate ligament (ACL).^{1,2}

We assessed whether structured rehabilitation plus early ACL reconstructive surgery was superior to structured rehabilitation with optional delayed reconstruction.³ We found no significant

differences in primary or secondary outcomes between the two treatment strategies at five years. Knee stability was better in patients with surgical reconstruction but this did not translate into functional success. The median preinjury activity level of 9/10 indicated participation in competitive sports. Some 40% were active at their preinjury level at two years after injury,³ decreasing to 20% at five years,² with no difference between groups. Our results are consistent with a meta-analysis showing that 22-61% return to competitive sports.⁴

Levy and colleagues incorrectly stated that "significantly more meniscal procedures were performed in the optional delayed group." We reported that at two years: "Subjects assigned to rehabilitation plus early ACL reconstruction had a higher frequency of meniscal surgery at study initiation and a lower frequency of delayed meniscal surgery than did subjects assigned to rehabilitation plus optional delayed ACL reconstruction. Overall, the number of meniscal operations in the two groups totalled 40 and 50, respectively (P=0.20)."³ After five years, we again found no significant differences in meniscus surgery when analysed by intention to treat or as treated.² At five years after ACL rupture, we found no significant differences in radiographic osteoarthritis between the treatment groups.²

The practice of evidence based orthopaedics means integrating individual clinical expertise with the best available external clinical evidence from systematic research.⁵ The KANON trial currently represents the highest level clinical evidence.

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