Dear David

It's a broad generalisation to say there have been no new classes of antibiotics. There have been some but unfortunately not against many of the most deadly bacteria.

Bacteria are generally divided into 3 classes, the mycobacteria (TB etc), and Gram-positives (MRSA etc) and Gram-negatives (E coli etc). There have been a few new classes of antibiotic in recent decades against 2 of the 3, though not against Gram-negatives such as E coli, K. pneumoniae, A baumannii and P aeruginosa. Gram-negatives have an extra cell coat (2 instead of just one that Gram-positives have) which makes it much more difficult for antibiotics to gain entry. And these bacteria have also developed capability to pump out our antibiotics or degrade them rapidly. Those four Gram-negatives in particular are a major cause for concern, as we have had no effective new chemical classes invented against them since the 1970s. They are increasingly gaining resistance to our best antibiotics. There have been some new antibiotics against them launched onto the market but these are minor variations on the same old chemical templates. These are easier to discover but also easier for the bacteria to resist. We desperately need new chemical templates. All efforts have failed for nearly 4 decades.

Apart from the scientific problems, there are commercial problems too. The pharmaceutical industry cannot make money from antibiotics for several reasons.

First, they are very difficult to invent. I heard a talk by Sir Andrew Witty, CEO of GlaxoSmithKline in which he said it has proved to be the hardest area of drug discovery. Scientists from both GSK and AstraZeneca separately published major review articles summarising over a decade of research in each company trying to find new antibiotics, with no success in either company.

Second, the commercial model is broken. Antibiotics cost a lot to invent yet get used for only a few days when needed, compared with drugs for chronic indications such as cancer, high blood pressure and diabetes which are easier to invent and get used every day. So companies make little money from antibiotics.

Third, if a drug company does in future invent a stunningly good antibiotic, there will be intense pressure to reserve it for use as a last resort when other antibiotics fail, to save it from resistance for use in the most seriously ill patients. Again, this indicates low sales volume. It would need very high prices or a very different commercial model to overcome this problem. The review that David Cameron established under Jim O'Neill a few years ago proposed a new commercial model, and also John Rex at Astra Zeneca has been a thought leader on new models. I have attended several meetings with them both including meetings with politicians in parliament but progress seems to have stalled now we have a new government with other priorities.

Re amoxycillin, my view is that it should never be used alone. It has been an excellent antibiotic for over 3 decades, one of the best, but inevitably bacteria are becoming resistant to it. There is a version in which it is used alongside a resistance breaker called clavulanic acid, (co-amoxyclav is the commercial name, and here is the Wikipedia entry https://en.wikipedia.org/wiki/Amoxicillin/clavulanic_acid). This combination is still effective for many infections. I carry it myself when I travel in the Himalayas, as I will be doing in coming weeks.

Finally, I thought I would add some advice for subscribers if they get a serious infection. The first assessment should be to determine if it is a virus or bacterium. Incredibly we still do not have a rapid cheap way to find out. If it is a virus then there are no effective drugs so attention to the health of our immune system is the best approach. If it is a bacterium then one needs to press the physician to do the following a) take a swab for skin infections or a blood sample for systemic infections b) get the bacterium cultured in a lab to identify which bacterium it is c) get a susceptibility test done in the same lab to advise which antibiotics might work. There are so many bacteria and not all antibiotics work against them so this last step is essential for serious infections. The barriers are that GPs and hospitals can be reluctant to do this because of the extra cost and the results will take several days to come back. Again, our technology needs improving! Meanwhile the doctor has no choice but to take a guess and prescribe an antibiotic with no evidence it will work. If it does not, then the tests listed above should guide the second antibiotic prescribed.

Sorry if this is all a bit frightening. Several years ago we started the charity Antibiotic Research UK to inform the public on what needs doing and also to research ways to break resistance and save our most essential antibiotics. I hope we will be successful and save lives in coming years. My own father died of MRSA last year and it was horrible to observe the current state of treatment based on little or no real evidence of what might save him. At Antibiotic Research UK we are trying to change that so other families do not suffer in the same way.

With best wishes

David Brown (writing as Chief Scientist of Antibiotic Research UK).

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