took valdecoxib had an increased risk of stroke and heart attack, although re-examination of its clinical database of 8,000 patients with rheumatoid arthritis and osteoarthritis showed no increased cardiovascular risk in those taking valdecoxib for up to a year. Pfizer also said that it will be conducting a large study to see whether celecoxib increases the risk of heart attacks in osteoarthritis patients.

Merck said that its COX2 inhibitor in development, etoricoxib (Arcoxia), showed no significant difference in the number of serious side effects in osteoarthritis patients than those treated with diclofenac.

The European Medicines Agency is reviewing safety data on all COX2 inhibitors, and the FDA will hold an Advisory Committee in early 2005 to discuss the risk. One of the biggest issues they will face is putting the cardiovascular risk into context: does the risk of taking rofecoxib, and potentially other COX2 inhibitors, outweigh the risk of complications from gastrointestinal bleeding from taking NSAIDs and aspirin?

"You can't compare apples and oranges," says James Fries, Professor of Medicine at the Stanford University School of Medicine. "For most people the heart attack risk is pretty scary and the frequencies are similar in magnitude. More importantly, there are many alternatives, old and new, that are essentially as GI safe and do not increase cardiovascular risk."

"Selective inhibitors of COX2 remain a rational choice for patients at low cardiovascular risk who are at high risk of serious gastrointestinal complications, especially while taking traditional NSAIDs," says FitzGerald. "It would also seem prudent to avoid COX2 inhibitors in patients who have or are at risk of cardiovascular disease."

Patrono agrees, adding that "caution should apply to all inhibitors of COX2 because they would have the same impact on prostacyclin biosynthesis in the face of suppressed thromboxane biosynthesis."

doable but rarely considered up front by most biotechs embarking on drug discovery programmes."

"The major issues hampering the development of novel molecules have been in the identification, synthesis and optimization of active natural product 'hits' identified from various biological extracts," says Peter Tambros, CEO of VivoQuest, a natural-products-based company in Valley Cottage, New York.

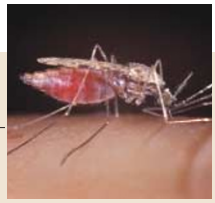
Many antibiotics have been made by semisynthetic modifications. Any modification has to not only improve the pharmacokinetics and pharmacodynamics of a drug, but, in the case of antibiotics, it must also try to overcome the problem of antibiotic resistance. As natural products are generally more structurally complex than small-molecule drugs, extensive modifications are tricky and complete synthesis of natural-product-like compounds is challenging.

However, minor modifications of novel natural compounds by semisynthetic methods shouldn't present too much of a problem, says Christopher Walsh, Professor at the Department of Biological Chemistry and Molecular Pharmacology at Harvard Medical School. Usually, chemists pick one or two sites for modification, says Walsh. "From this point of view, many — probably most — of the natural products that are therapeutic candidates will offer one or a few sites for selective modification."

So, there is the science to turn this crisis around, says Solomon Nwaka, Scientific Officer at the Medicines for Malaria Venture. "With appropriate resources, a clear structural strategy and support from all sectors, this impending gap in availability of antibiotics can be prevented."

Pooling these talents can only be beneficial, says Nathan. "What we have now is a great deal of expertise in antibiotic development — including first-hand knowledge, earned at great cost, of what does not work — that is being scattered as teams are broken up," he says. "We need a venue where teams can come back together with a charge to develop antibiotics, and the tools and compounds suited to the task."

NEWS IN BRIEF



Good news for malaria vaccine...

The Phase IIb success of a malaria vaccine developed by GlaxoSmithKline and the Malaria Vaccine Initiative (MVI) has provided the first real hope for protection against the disease. RTS,S/AS02A acts against the most deadly strain of the malaria parasite, *Plasmodium falciparum*, at the 'pre-erythrocytic stage'; that is, before the red blood cells become infected. During the first six months of the trial in Mozambique on 2,000 healthy children aged 1–4 years, 58% fewer children developed severe malaria with the vaccine, which is a fusion of immunogenic components from the surface of *P. falciparum* sporozoites with hepatitis B surface antigen, plus a proprietary adjuvant.

Alonso, P. *et al.* Lancet **364**, 1411–1420 (2004).

...but bad news for flu vaccine

Chiron has announced that it will not supply its influenza vaccine Fluvirin for the 2004–2005 influenza season, due to bacterial contamination of some of the doses. The United States felt the brunt of this vaccine shortage, as Chiron was expected to supply nearly half of the 100 million doses expected. Aventis-Pasteur, the other supplier of flu vaccines in the US, said it had made some extra doses of its flu vaccine to help address the problem.

Parkinson's trial halted

One of the most promising treatments in development for Parkinson's disease has faced a setback. Initial analysis of the preliminary Phase II data showed no clinical improvement in patients given Amgen's glial-derived neurotrophic factor (GDNF) compared with placebo after six months of treatment. But 4 out of the 34 subjects produced antibodies to the GDNF protein, raising fears that this could trigger a dangerous immune reaction with prolonged treatment. Researchers are trying to understand the discrepancy between these results and an earlier trial on 5 patients with GDNF who showed a dramatic recovery in their movements.

Nobel Prizes announced

The Nobel Prize in Chemistry for 2004 was jointly awarded to Aaron Ciechanover, Avram Hershko and Irwin Rose for the discovery of ubiquitin-mediated protein degradation. Their work showed how a molecule called ubiquitin acts as a 'kiss of death' by fastening onto a protein to be destroyed, and accompanying it to the proteasome, where it is degraded. The Prize in Physiology or Medicine went to Richard Axel and Linda Buck for their discoveries of odour receptors and the organization of the olfactory system.

Dogs sniff out cancer

Man's best friend could now be even more precious, as their super-sensitive noses might be able to detect cancer. Carolyn Willis at Amersham Hospital, UK, and her team trained six dogs of varying breeds to identify the urine of patients with bladder cancer, as it is thought that tumours release molecules into the urine that have a characteristic smell. The trained dogs were asked to choose between laboratory dishes of seven types of urine and to lie down in front of the one from a cancer patient. The dogs were correct more than 40% of the time, much greater than the 14% figure that would be expected if they chose by chance.

Willis C. M. *et al. BMJ* **329**, 712–714 (2004).