Dubinett. Also, while the researchers do not know how long the effect of THC lasts in the body, they believe that it probably has a cumulative effect and, like cigarette smoking, might decline when people stop smoking marijuana. 'THC interacts with specific receptors on immune cells and causes a specific immune effect. Therefore, the chances are that if people stop smoking marijuana, they will probably reduce their risk of cancer,' speculates Dubinett.

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Sharon Dorrell

Antibiotics: a possible treatment for regressive-onset autism

A new study has added further weight to speculation that autism might be linked to abnormalities of the bowel, at least in a subset of affected children. The study, conducted at the Rush-Presbyterian-St Luke's Medical Center in Chicago (IL, USA), reports significant short-term improvements with vancomycin treatment in a group of autistic children whose symptoms appeared after they developed chronic diarrhoea from treatment with broad-spectrum antibiotics[1].

Autism: the disease

Autism is a devastating, pervasive developmental disorder that usually manifests itself in early infancy. Autistic children lack social and language skills, exhibit repetitive behaviours and are unable to form normal relationships. The cause is unknown, but a US National Institutes of Health working group in 1995 cited a probable genetic susceptibility involving multiple, unidentified genes[2]. However, various studies have suggested a possible link with bowel abnormalities such as abnormal permeability and ileal-lymphoid nodular hyperplasia[3,4].

About one-third of cases are classified as regressive-onset, with the child appearing to develop normally for the first 1–2 years and then losing previously acquired skills. This happened to the son of Ellen Bolte, a co-author of the Rush-Presbyterian-St Luke's study. At 17 months, he developed chronic diarrhoea after three 10-day courses of various broad-spectrum antibiotics given for a middle ear infection. At 19 months, his behaviour and development deteriorated profoundly and he developed severe autistic features. Extensive testing revealed no discernible cause for his condition. Bolte developed the hypothesis that broad-spectrum antibiotics might disrupt the normal intestinal flora, enabling the growth of neurotoxin-producing bacteria[5]. These neurotoxins, she speculated, could cause the symptoms of autism.

She took the theory to Richard Sandler, director of paediatric gastroenterology at Rush Children's Hospital. Although sceptical, he agreed to treat the boy with vancomycin. After 2–3 weeks, he showed a rapid and dramatic improvement in his behavioural, social and language skills, and a reduction in repetitive and self-stimulatory behaviour. Unfortunately he deteriorated shortly after treatment ended.

Trial results

To see if the effect could be replicated, Sandler and colleagues set up an open-label trial with 11 children aged 43–84 months[1]. All had a definable, rapid onset of autistic symptoms after 12 months of age, two months or less after a course of antibiotics, and a persistent history of diarrhoea that had started before autism became apparent. They were given a baseline evaluation using a recognized developmental profile and the Child Autism Rating Scale; six were classified as having severe autism, two moderate and three mild. They were also videotaped at baseline and during therapy, and their taped activity was scored by a clinical child psychologist using criteria relating to behaviour, communication and social skills. Behaviour and communication were also rated by the study doctor at baseline, during therapy and at follow-up. They were given vancomycin at 500 mg day^{-1} for 8 weeks.

Eight showed an improvement in their videotape scores during treatment, and there was a statistically significant improvement in communication and behaviour scores for the group as a whole. In some cases, the improvements were impressive. However, all

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but one deteriorated during the 2–8 month follow-up period, usually within two weeks.

Their stools were analyzed before and after treatment, those from four patients undergoing 27 different types of culture for comparison with previously published data from adult controls. This analysis is not yet finished, but the team has already discovered a potentially interesting absence of anaerobic cocci.

Future studies

'Seeing most of these children apparently improve significantly was very exciting', says Sandler, but he cautioned that the work needs to be repeated by others. The mechanism behind the benefit from vancomycin is not known, but it might be related to the temporary elimination of a neurotoxin-producing bacterial pathogen. Clostridial species are thought to be the most likely bacterial agents[1,5]. 'The next step is to go back to the lab and try and find out why these effects may have been observed,' says Sandler. According to Bolte, 'careful analysis of the stool specimens would provide valuable information, but this is very time consuming, and research progress has been severely hampered by a lack of financial support'.

The authors emphasize that vancomycin, chosen because it is poorly absorbed in the gut, should not be used lightly because of the public health implications of any increase in resistance to it. However, says Bolte, 'We are, cautiously, very optimistic that the gut flora approach of antimicrobial treatment and probiotic therapy will eventually provide meaningful treatment for a subset of children with autism.'

According to Dr Bernard Rimland, Director of the Autism Research Institute (San Diego, CA, USA), the study merits attention 'as it casts light on both the cause and treatment of a large subset of autism.' However, he too is concerned about the use of vancomycin. 'A preferable approach would be to use substances known to enhance the immune system, such as certain vitamins, minerals and essential fatty acids. This would, hopefully, control the autism-causing pathogens without contributing to antibiotic resistance.'

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Jo Whelan

A new role for old weed killer

A range of compounds currently used as herbicides (the s-triazines) have been found to be possible future treatments for malaria, say scientists at Biomes (Pelham, MA, USA). This research examining the possibility of using chloroplast-specific poisons as antimalarial drugs was prompted by findings that a cellular organelle in the malaria parasite – the apicoplast – was genetically very similar to the chloroplast[1]. The function of the apicoplast is unknown but, explains Miles Hacker (President, Biomes), 'We reasoned that if the parasite has maintained this organelle all this time then it must provide some benefit. We further reasoned that it could be the Achilles heel of the parasite and a parasite-specific target.' They finally focused their attention on a group of chloroplast-specific herbicides that have been in use for over 30 years, the s-triazines.

Why the s-triazines?

Hacker explains that the s-triazines were selected for a number of reasons, 'They are safe and have LD_{50} values on a par with table salt, they have been in use for decades, and there is plenty of animal toxicology and pharmacokinetic data available, so clinical development time should be significantly decreased. Furthermore, excellent synthetic pathways for large scale production have already been developed and they are amazingly inexpensive.'

The s-triazines are cyclic structures in which the ring contains alternating carbon and nitrogen atoms. They kill plants by blocking photolysis-induced electron transport in chloroplasts[2]. The addition of a chlorine group increases both antimalarial efficacy and potency. Of the chloro-s-triazines studied by Hacker's team, atrazine (Fig. 1), propazine and simazine all exhibit antimalarial activity and, he says, 'They are as effective and potent *in vitro* as chloroquine, the gold standard for antimalarial drugs.'

The researchers found that atrazine, Biomes' lead compound, was also effective against multi-drug-resistant strains of the malaria parasite, *Plasmodium falciparum*, and the parasite has so far shown no signs of developing cross-resistance. 'We feel that there is no reason to think that the parasite will not become resistant to atrazine. New antimalarial drugs have a finite period of efficacy. Nevertheless, our hope is that the new drugs will provide benefit until a safe and effective vaccine is finally developed. Better use

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