OX26-transferrin-targeted PEGylated immunoliposomes carrying expression plasmids for the gene for tyrosine hydoxylase are an effective treatment for a rat ablation model of Parkinsonism [3]. Gene delivery for multiple brain diseases using targeting methods might, therefore, hold great potential. Bickel also highlighted the fact that gene chip and proteomics work is beginning to elucidate the physiology of known and unknown receptors on the blood–brain barrier endothelia; he suggested that transferrin and insulin receptors might be the trail-blazers for CNS delivery targets in the future.

Conclusions

Several key points emerged from the highlighted talks at the 2003 CRS meeting. There is a real patient need for more-effective modified release of newer drugs, using established delivery platforms, such as transdermal patches. Enhanced delivery systems will improve therapy and reduce side effects as a result of more appropriate plasma profiles. Oral delivery of vaccines remains elusive and is compounded by a poor understanding of the relationship between Peyer's patch uptake and mucosal immunity. Overall, however, developments within drug delivery and controlled release are encouraging; the scope for future advancements is immense and ranges from the therapeutic targeting of solid tumours, to accessing the CNS and elements of the immune system.

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Multiple Drug Resistant Bacteria

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The steady rise in the global burden of antibiotic resistance has received a lot of attention recently and belief is growing that we are losing the battle against bacterial infections, particularly in our hospitals. The introduction of a new antibiotic, a rare event in itself, is invariably followed, sooner or later, by the emergence of bacterial resistance to the agent. Accumulation of resistance genes in bacterial pathogens has been accelerated by the over-prescribing of antibacterial agents, by the transfer of resistance genes amongst bacteria and by the epidemic spread of resistant strains among patients. The emergence of multi-drug resistant Gram-positive pathogens, such as methicillin-resistant staphylococci (MRSA) and vancomycin-resistant enterococci (VRE), as a fundamental cause of hospital-acquired infections is a major concern; the isolation of the first vancomycin-resistant MRSA strain last year, from a catheter exit site, broadens the spectrum of infections that are untreatable with currently available antibiotics. Over the past ten years, many books have been published on the subject of antibiotic resistance and this volume now joins the list, with the aim of focusing on the problems caused by multi-resistance. The contributors review multi-resistance in a broad context, considering the biological, social and economic forces that have influenced the emergence of the multi-resistant genotype.

The book consists of seven chapters, charting the rise of antibiotic resistance, describing the processes by which Gram-negative and Gram-positive bacteria accumulate resistance genes on single genetic elements and in single bacterial cells, reviewing recent research on the roles of regulation of the stress response and efflux mechanisms in Gram-negative bacteria and taking a detailed look at VRE and MRSA infections. The final chapter examines the evolution of horizontal gene transfer in relation to the selection of antibiotic resistance. Most of the contributions are from internationally recognised experts in the field and are, therefore, authoritative tracts; much of what is covered has, however, been recently reviewed by others and hence, the informed reader, at which the book is aimed, will be familiar with the material. The usual argument, that rapid evolution of antibiotic resistance is not only making our current antibiotic solutions useless but is compromising our future efforts to control infections through chemotherapeutic intervention, is discussed in a refreshingly broad context: the role of non-antibiotic agents that are known to select or induce resistance phenotypes is covered in depth, and the contribution of the public, physicians, hospital personnel, veterinarians and the pharmaceutical industry are given appropriate

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consideration. A chapter on the development of the multi-resistant genotype in Gram-negative bacteria covers the key areas of the origin of resistance genes, translocation of resistance determinants from chromosome to plasmid and the mobilisation of resistance plasmids. However, the arguments are sometimes difficult to follow. Much better is the description of these processes in Gram-positive bacteria; the assembly of an arsenal of resistance mechanisms from an extended pool of determinants is competently explained.

Multidrug resistance can arise as a consequence of activation of the stress response, often by non-antibiotic agents, and the role of proteins of the *marRAB* and *soxRS* regulons are dealt with in detail, here. Expression of the multi-resistant phenotype is due to decreased permeability of the outer membrane of Gram-negative cells and the expression of efflux pumps, both of which are discussed in relation to selection and maintenance by both antibiotic and non-antibiotic agents. The role of efflux pumps is also addressed in the chapter on the resistance of biofilms (these heterogeneous bacterial communities are prevalent in several intractable infections) and there is an excellent review of the physical and physiological factors involved in the determination of the resistant biofilm phenotype. Although well written, the lengthy chapter covering VRE and MRSA covers an area that has received much attention in recent years and the emergence of VRSA is mentioned only briefly, creating the impression that reference to this development was added to the contribution at a late stage in the editorial process. The best is reserved until last – the short contribution on horizontal gene transfer is illuminating. The evolution of horizontal gene transfer is examined by gene ecologists in relation to the development of a new generation of anti-infective agents and the authors invoke competition models as a basis to examine the fate of genes.

It is difficult to ascertain the audience for this book; it is intended to serve microbiologists, health professionals, biotechnologists and pharmaceutical company personnel with an interest in bacterial antibiotic resistance but most of the issues covered also feature prominently in other, more comprehensive texts on antimicrobial drug resistance. Although a relatively short read, it is not the type of book suitable for 'dipping one's toe in the water'; there are several timely reviews that better serve this purpose.

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