Book reviews

Introduction to the Blood–Brain Barrier. Methodology, Biology and Pathology, Edited by W. M. Pardridge. Cambridge: Cambridge University Press. 1998. Hardback, pp. 486. £85. ISBN 0 521 58124 9

The concept of a blood–brain barrier (BBB) was first put forward by Ehrlich in 1902 and 7 years later, Goldman suggested that cerebral capillaries were responsible for blocking the movement of chemicals into or out of the brain. In 1967, confirmation of this idea came through the electron microscopy studies of Reese & Karnovsky. The BBB is formed mainly by cerebral capillary endothelial cells, a unique feature of which is the high-resistance ($8 \, k\Omega/cm^2$) tight junctions they form with their neighbours. The BBB maintains an ultrastable internal environment for neurones, and being relatively, rather than absolutely impermeable to chemicals, it allows the passage of nutrients (e.g. D-glucose) and metabolic waste products (e.g. urea), but also numerous xenobiotics, from psychotherapeutic drugs to environmental toxins.

Introduction to the Blood–Brain Barrier is a comprehensive text for which Professor Pardridge has assembled a team of eighty-eight international experts. Following his introductory chapter, there are forty-nine more, grouped into five sections: Methodology, Transport biology, General aspects of CNS transport, Signal transduction/ biochemical mechanisms and Pathology in disease states, together with an accurate and comprehensive sixteen-page index. Each chapter contains a useful bibliography of research papers and reviews current to 1997, and most include a helpful introduction and conclusion–summary.

Pardridge argues that an understanding of the biology of the BBB is important to a number of disciplines beyond neuroscience, and expresses disappointment that only a small number of laboratories are engaged in research. The aim of this book, which goes far beyond what the title 'Introduction' suggests, is to provide the reader with an in depth and wide ranging review of current research into the biochemistry, physiology, pharmacology and pathology of this structure.

Of most interest to this journal's readership would be the chapters on nutrient transport. Six true isoforms of the Na^+-independent glucose transporter (GLUT) have been identified, with GLUT1 accounting for some 90 % of the total brain glucose uptake. The gene coding for this 492 amino acid tetrameric protein is located on chromosome 1p and there are rare instances where its defective expression results in reduced glucose transport and seizures. The primary structure is highly conserved with human GLUT1 sharing a 96–97 % homology with rodent proteins. GLUT1 is stereospecific for D-glucose but does have a similar affinity for 2-deoxyglucose, the analogue used extensively in the study of brain energy production.

The essential large L-amino acids rapidly enter the brain via two main Na^+-independent carriers, system L1 for neutral amino acids and system y^+ for basic (cationic) amino acids. The gene CAT-1 for the latter is located on chromosome 13q and codes for a 629 amino acid protein. Also, high affinity receptors for LDL (K_d 16 nM), insulin (K_d 12 nM) and leptin (K_d 5·1 nM) have been found on the cerebral endothelium. The hormonal receptors are thought to be involved in both the response to the circulating peptides and receptor mediated transcytosis, and the LDL receptors, for example, in cholesterol uptake.

This well written multi-authored volume will certainly generate interest in what the editor regards as a neglected area of biomedical science. For an 'Introduction', I should have expected to see more basic cellular and gross neuroanatomy rather than just a single statement (p. 1): 'The blood–brain barrier (BBB) is formed by the brain capillary endothelial cells'. Furthermore, it is only on reaching chapter 40 that there is any historical overview of the subject. Unusually, the introductory chapter only makes reference to the contents of two of the succeeding chapters while the cross-referencing of material between chapters could have been better. Although you always expect some degree of overlap between contributors, it seems excessive between the chapters on the glucose transporter and rather annoyingly, different designations are used, GLUT1 and Glut 1, by different authors. This is also true for isotopes, e.g. [11C] in chapter 14 and Ga-68 (chapter 15).

The last section of the book makes you realise why there needs to be more investment in this area of research. The list of conditions where the BBB is damaged include Alzheimer's disease, multiple sclerosis, stroke, hypertension, and infection by HIV, *Neisseria meningitidis* and *Plasmodium falciparum*. Only by knowing more about the normal operation of the BBB will we begin to understand what happens when things go wrong and therefore be able to devise strategies for repairing and preventing the damage.

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Feeding Systems and Feed Evaluation Models. M. K. Theodorou and J. France. Wallingford: CAB International. 2000. £75. ISBN 0 85199 346 X.

This book addresses three main areas: feed evaluation, feeding systems and modelling responses to nutrients in animal production. Each chapter consists of a review by different researchers, most of whom are considered to be leading experts in their field. The international make up of the contributors' list means that systems from different

countries have been compared. The book also attempts to cover most farm animal species and companion animals.

Tremendous advances have been made in feed evaluation, so we can now describe feed materials very accurately in terms of their chemical composition, physical properties and digestibility. However, as stated in the preface, such numbers are useless without suitable systems for describing animal requirements and responses. In feed formulation, you are usually asking either: 'what combination of ingredients do I need to produce optimum economic or biological performance from my animals?' or: 'what level of production can I expect from my animals if I offer the following diet?'. The first question needs a requirement-based system and the second needs a response-based system. Both approaches are reviewed in this book.

Each chapter of the systems section combines a thorough review of existing systems with discussion of shortcomings and suggestions for the future. Most requirement-based systems have been around for at least 30 years and are based on similar nutritional concepts for different species. Animals require a certain quantity of energy and protein to maintain themselves and produce products. Losses of consumed energy and protein are divided into faecal, urinary and gaseous components, together with the heat increment. The remainder is metabolizable energy or protein that is used by animals (net energy and protein) with varying efficiency. Variations on this theme are found where requirements for specific nutrients, e.g. amino acids, can be readily determined. One gets the impression from reading this book that current systems have major limitations and inaccuracies. Much research effort over the past 30 years has been directed at improving estimates of variables in systems that may be inherently flawed. For example, diets supplying the same theoretical quantity of energy may be predicted to yield the same quantity of product but, in practice, may support different levels of production because of differences in their nutrient composition. Even those systems that are based on broader nutritional concepts can be unreliable, due to factors such as extrapolation between species, assuming constant values for conversion factors that are really variable, using mean values rather than a range of responses. Added to these conceptual limitations are the major inaccuracies involved in the basic measurement of hypothetical entities like 'metabolizable energy' in feedstuffs, animals and products.

If the systems section describes historical developments, the modelling section should describe the future. It does to a certain extent, since most chapters suggest that models are the way forward. However, most chapters also suggest that current models are not yet good enough to reliably predict animal responses. The descriptions of the models themselves, and the discussions on modelling principles, make very interesting reading and should provide useful guidance for researchers in this area. It appears that response models suffer from the same drawbacks as the systems described previously. Empirical models are easier to generate, understand and use, but are not accurate; mechanistic models are complex, and are potentially accurate, but lack sufficient experimental information to realise their potential. This is analogous to feeding systems, e.g. energy, where it is easy to measure gross energy in the laboratory, but this tells you nothing about the requirements of an animal. One hopeful observation is that new research findings can be incorporated into mechanistic models to improve accuracy. Some models may even identify areas where further research is required to fill gaps in the current knowledge.

Looking at the book overall, the balance between species is slightly biased in favour of ruminants; this reflects the greater complexity of the ruminant digestive system as well as the research interests of the editors. There is a wide variation in writing style for different chapters, with some chapters giving a general overview and others describing specific topics in detail. This is good, since variety adds to the interest of the book, but in some instances the coverage is somewhat sparse. For example, minerals and vitamins feature quite prominently in both of the chapters on feeding systems for pigs and poultry, yet do not feature at all in the four chapters on feeding systems for ruminants and horses. The chapter on companion animals is somewhat disappointing. It appears to have been added as an afterthought and the authors acknowledge that the diversity of species means that none can be dealt with in depth.

The main messages from this book are that feed evaluation is accurate, but we may be evaluating the wrong things since feeding systems are outdated and modelling is in its infancy. The main question that arises is whether we should carry on improving the accuracy of conceptually flawed feeding systems or should we develop robust prediction models? The answer is not clear, which will be good news for research workers on both sides. It may not be such good news for farmers, but extreme accuracy is unnecessary when you have a whole herd, flock or shoal to feed.

This book should prove useful for people who need an overview of feeding systems and feed evaluation models, such as university lecturers and students of animal nutrition. Some of the technical discussions on nutritional concepts and modelling approaches will be valuable for researchers, but the lack of depth and firm recommendations means that further reading would be required by most professional nutritionists.

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