

# PostScript

## LETTER

### Funisitis and raised interleukin 6 concentrations in gastric aspirates at birth

From the second trimester to near term, fetuses in utero can swallow up to 500–1000 ml amniotic fluid a day, which assists in normal development of the gastrointestinal system.<sup>1,2</sup> The aims of this study were to determine whether the concentration

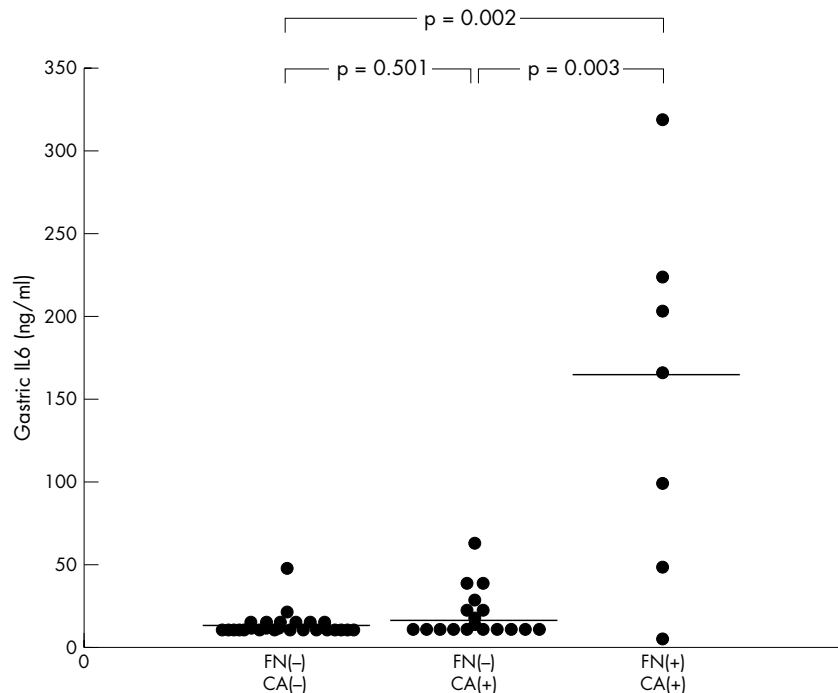
of gastric interleukin 6 (IL6) immediately after birth was associated with funisitis, the histological hallmark of fetal inflammatory response syndrome,<sup>3</sup> and whether measuring the gastric IL6 concentration would be an effective method for identifying funisitis.

In a prospective pilot study conducted at the Ulsan University Hospital in South Korea between November 2002 and August 2003, 59 newborns at <35 weeks gestation and their mothers were investigated for gastric IL6 concentrations at birth and the presence of funisitis and chorioamnionitis. Fetal gastric fluids were aspirated at the time of

delivery with a 5F orogastric feeding tube and clarified by centrifugation at 20 000 *g* for 10 minutes at room temperature. Gastric IL6 concentrations were measured by immunoassay (Becton Dickinson Pharmingen, San Diego, California, USA), and the presence of funisitis and chorioamnionitis were diagnosed based on histological examination according to the criteria given by Salafia *et al.*<sup>4</sup>

Seven umbilical cords (12%) were identified as having funisitis. All patients with funisitis had chorioamnionitis. Twenty two placentas (37%) showed chorioamnionitis only (without funisitis). Thirty patients (51%) had no evidence of neutrophilic infiltration in membranes and umbilical cords. Babies associated with funisitis were less mature, weighed less, and had a lower five minute Apgar score at birth than those not associated with funisitis (table 1). Of seven infants whose umbilical cords showed funisitis, six had raised (defined as  $\geq 30$  ng/ml) gastric aspirate IL6 concentration. In contrast, only two of 52 infants without funisitis had raised gastric IL6 ( $p < 0.001$ ). The median gastric IL6 concentrations were 167.9 ng/ml (range 0.1–326.8) in the funisitis group and 1.5 ng/ml (range 0.1–54.4) in the non-funisitis group (2.3 ng/ml (range 0–54.4) in the chorioamnionitis only group and 1.5 ng/ml (range 0.1–38.8) in the control group) (fig 1).

Although these are preliminary data, our results suggest that the measurement of IL6 concentration in gastric aspirate in premature infants immediately after birth may be a safe and effective method for identifying intra-uterine infection of fetuses, such as cordocentesis.<sup>5</sup> Further research in a larger number of study subjects should be considered to clarify the association of gastric cytokine with funisitis.



**Figure 1** Gastric interleukin 6 (IL6) concentrations at birth according to the presence or absence of funisitis and chorioamnionitis. Study subjects were allocated into one of three groups: funisitis group (FN(+))CA(+), chorioamnionitis only group (FN(-))CA(+), and control group (FN(-))CA(-). FN, Funisitis; CA, chorioamnionitis.

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**Table 1** Basic details of study subjects according to the presence or absence of funisitis

	Funisitis (n = 7)	No funisitis (n = 52)	p Value
<b>Mother</b>			
Maternal age (years)	30.7 (4.6)	32 (4.8)	0.35
Caesarean section	5/7 (71%)	45/52 (87%)	0.20
PROM	3/7 (43%)	16/52 (31%)	0.43
Preterm labour	2/7 (29%)	17/52 (33%)	0.57
Antenatal steroids	4/7 (57%)	19/52 (37%)	0.30
<b>Neonate</b>			
Gestational age (weeks)	28.9 (3.9)	32.3 (2.4)	0.02
Birth weight (g)	1230 (460)	1720 (610)	0.02
Male	5/7 (71%)	31/52 (60%)	0.49
5 min Apgar score <7	4/7 (57%)	9/52 (17%)	0.04

Data shown as mean (SD) or number (%). PROM, Premature rupture of membrane.

- 3 Gomez R, Romero R, Ghezzi F, et al. The fetal inflammatory response syndrome. *Am J Obstet Gynecol* 1998;**179**:194–202.
- 4 Salafia CM, Weigl C, Silberman L. The prevalence and distribution of acute placental inflammation in uncomplicated term pregnancies. *Obstet Gynecol* 1989;**73**:383–9.
- 5 Naccasha N, Hinson R, Montag A, et al. Association between funisitis and elevated interleukin-6 in cord blood. *Obstet Gynecol* 2001;**97**:220–4.

## BOOK REVIEWS

### Evaluating the processes of neonatal intensive care: thinking upstream to improve downstream outcomes

Edited by Joseph Schulman. London: BMJ Books, 2004, £20.00, pp 145. ISBN 0 7279 1833 8



This book tackles the issue of quality of care from a rather different angle, challenging the reader to examine and optimise the processes involved in neonatal intensive care rather than focusing solely on individual outcomes. It seeks to unravel the complex interplay between

the many different components that contribute, directly or indirectly, to patient care. The book centres on the view that changes will only come about if we acknowledge that the neonatal unit and the people and activities within it function not in isolation, but within the context of a much larger system. Likewise, within the confines of the unit itself, a multitude of smaller systems operate together to produce what we have come to recognise as good patient care. It is the interrelationships between these systems that determine the effectiveness and quality of the care given. Likening the “system” of the neonatal unit to a production system, the author uses the methods successfully adopted by Japanese car manufacturers to illustrate ways in which this can be approached to improve quality and “customer service”. At first sight, this may seem an inappropriate comparison, but the author convincingly outlines a number of parallels between the two.

A number of the methods suggested for improving the process of care seem obvious and appeal to a common-sense approach. However, there can be few who would not welcome simple and effective ways of avoiding unnecessary activities and achieving motivation of staff! The author stresses the importance of understanding the processes of care before we can successfully evaluate them. He then aims to equip the reader with the necessary tools to collect, analyse, summarise, and present data. Some methods covered, such as the use of sensitivity, specificity, and receiver operating characteristic curves in evaluation of diagnostic testing will be familiar

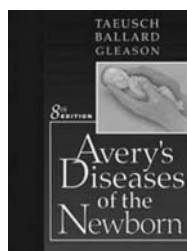
to many readers. Others, for example process mapping to break down a care process into bite-size components, Pareto diagrams to illustrate relative importance of problems encountered, and control charts may be techniques that have not been encountered previously. The specific techniques are explained clearly, using examples that are, for the most part, easy to follow. One could imagine being able to use them as adjuncts to the more familiar analytical and statistical methods. Recognising that change for the better cannot be achieved by analysis alone, but relies heavily on the personnel involved in implementation, the author helpfully devotes some time to this towards the end of the book. Lastly, a checklist summarising some of the book’s important points is a useful addition as an appendix.

The book is short and easy to read, with a layout that is logical and accessible. Its style is friendly and chatty, if bordering on the patronising at times. The recurrent use of Japanese terminology can become rather tedious, but does not detract from the book’s content, which is interesting and useful. It will be of particular interest to those whose work involves the organisation of data collection and analysis for clinical audit, governance, benchmarking, and research. However, any clinician who wishes to develop a deeper interest in the evaluation of care will find this book stimulating and informative.

E M Boyle

### Avery’s diseases of the newborn, 8th edition

Edited by H William Taeusch, Roberta A Ballard, Christine A Gleason. Published by Elsevier, 2004, £89.00, hardback, pp 1598. ISBN 0721693474



*Avery’s diseases of the newborn* has reached its eighth edition with a substantial update of all chapters. In reviewing it like any large textbook, it is necessary to formulate basic questions about its purpose. It is hard to imagine that

anyone would read every single word, yet almost all of us have at least one great tome sitting on our shelves, and, in many cases, they are simply gathering dust. Books like this are meant to be used in clinics, on the wards, or at home by our telephone, so that we can refer to them when a chance remark triggers a memory of something last heard of when we revised for the Membership examination! They make a good starting point for presentations when the alternative would be time spent in the library or on the computer (if you can ever get your children off yours!). Books like this will, no doubt, continue to be written and will, no doubt, also continue to be read.

My second thoughts on reviewing this book were “Where does this book sit within UK based neonatal practice?” It is a

collaborative work written by over 100 specialists, only one of whom currently works in the UK. The epidemiology, ethics, and whole ethos of this book are, not surprisingly, drawn from largely North American data and experience, and, it could be argued that the book is less relevant than Rennie & Robertson. Nonetheless the book is easily read and well referenced—for example, the chapter “Bacterial sepsis and meningitis” has over 90 references—thus making the book a good starting point for reading for any trainee project.

The delays between the writing of and the publication of large textbooks will always mean that they are almost out of date as soon as they are published, and this textbook is no exception. Newer synthetic surfactants containing proteins or polypeptides were first reported in medical literature as long ago as 1996, with several of these recently reaching the clinical trial stage, yet these developments are condensed to a single paragraph. Likewise discussion of surfactant use in conditions other than respiratory distress syndrome is also brief, with little mention of its use other than in meconium aspiration syndrome and pneumonia. Books such as this are meant to provide the necessary background information to allow the reader to do their own search of a topic, and in this respect *Avery’s diseases of the newborn* works well.

There are some idiosyncrasies when it comes to the order of the chapters—for example, newborn resuscitation follows chapters on initial evaluation and routine care, and the chapter on surfactant treatment precedes those on respiratory failure in preterm and term infants.

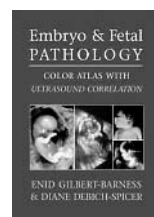
So faced with a choice between this book and Rennie & Robertson, which would I choose? Well if you can ignore the obvious North American bias, this is an excellent and very readable resource, and it is also considerably cheaper. If you do not mind the occasional trip to the library to look at Rennie & Robertson for a UK perspective of epidemiology and ethics, you could buy two copies of this book (one for your office and one for home) and still have change left for another textbook.

This book will certainly find a place on my shelf. I cannot see it gathering as much dust as some “great tomes” despite the fairly minor shortcomings mentioned above. I would recommend it to anyone looking to add a neonatal textbook to either their own personal or unit libraries.

S B Ainsworth

### Embryo & fetal pathology: color atlas with ultrasound correlation

Enid Gilbert-Barnes, Diane Debich-Spicer. Published by Cambridge University Press, 2004, £195.00 (hardback), pp 675. ISBN 0521825296.



Paediatric pathology has always been a shortage specialty, but recent criticism of pathologists in the United Kingdom has led to further recruitment difficulties within the field such that

many centres no longer have a dedicated specialist. Perinatal autopsy consent rates are in relentless decline throughout the world, and exposure of clinicians and pathologists to detailed examination of congenital abnormalities and disease states has become very limited. As a result there is concern that the perceived value of the perinatal autopsy among clinicians and the public is suffering.

This atlas of perinatal pathology contains over 2000 photos and illustrations, which are a vast resource for anyone working in perinatal medicine. It coordinates information from anatomy, embryology, radiology, ultrasound, and genetics to assist in the assessment of the fetus. With over two thirds of fertilised ova resulting in non-survival and 60% of stillbirths being unexplained, the challenge for those working in obstetrics is to identify such pregnancies and pre-empt fetal loss and morbidity. To this aim, the ultrasound correlation with pathology is insubstantial, and the emphasis of this book is very much on gross pathology. Exceptions to this include a very informative section on ultrasonography describing the limitations of antenatal screening (only one third of all fetal anomalies are detected by routine screening) and the ultrasound of genitourinary abnormalities.

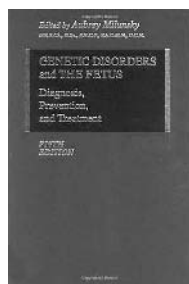
From a clinician's perspective, each chapter includes comprehensive genetics and pathogenesis of each disorder. The clear, well structured embryology section is enlightening after tedious undergraduate lectures, which have long since been bound and filed in the darker recesses of my hippocampus alongside the reproductive capabilities of the fruit fly. Although this book is lightly peppered with ultrasound images, those working in antenatal ultrasonography might appreciate the images of more common pathologies such as congenital diaphragmatic hernia and central nervous system abnormalities, as well as more recent three dimensional images. Detailed lists of investigations for particular features look helpful, but an inconsistent approach to chapter structure and headings is irritating and confusing, as are numerous errors in spelling, content, and cross references. The intended readership includes all perinatal clinicians as well as pathologists, but the autopsy chapter is confusing in its order and lacks any reference to histology.

Of particular interest is the developmental pathology describing extremely early gestations supported by ultrasonography and the detailed cardiology specimens, which demonstrate a wide range of complex abnormalities. The value of this atlas has to be the wealth of fascinating, meticulously dissected pathology specimens and the authors' brave endeavour to explain the pathogenesis of so many complicated conditions. In its appeal to such a broad range of specialties, this book often falls short of detail, but the message is clear: autopsy remains an important and valuable tool in both elucidating diagnoses and delineating congenital abnormality, and the continuing need for thorough and dedicated paediatric pathology services is undisputed.

J-C Becher

**Genetic disorders and the fetus: diagnosis, prevention, and treatment, 5th edition**

Edited by Aubrey Milunsky. The John Hopkins University Press, 2004, £160.50 (hardback), pp 1177. ISBN 0 8018 7928 0



The prospect of a genetic disorder in a pregnancy can often instil abundant confusion and trepidation in the doctors caring for the family, let alone the affected family themselves. Genetic disorders, although often rare as individual conditions, collectively affect a

significant number of pregnancies. With our increasing knowledge of the genetic basis of many conditions, the revelation of the human genome, and increasing technological advances available, the options available for diagnosis and management of these conditions are constantly expanding. Against the backdrop of the medical management of these situations the complex ethical issues which arise must be considered with equal importance.

The 32 chapters of this publication have contributions from international experts in their individual field. Each subject is covered in a comprehensive and easily digested manner and the reference list following each chapter is a valuable resource for those wishing to probe more deeply in to the area in question. The scene is set with an introductory chapter discussing the principles and practices of genetic counselling with particular reference to the areas of pre-conceptual, perinatal, and postnatal counselling. In other chapters, both the benefits and limitations of prenatal testing techniques, such as chorionic villus sampling and amniocentesis, are explored. The difficult area of prenatal diagnosis of sex chromosome abnormalities and the resulting decision making dilemma faced by parents is also addressed. In addition to genetic diagnostic techniques such as chromosome analysis and DNA testing, other modalities are discussed, including ultrasound and maternal serum screening. Two whole chapters are dedicated to maternal serum screening with particular discussion of multi-analyte second trimester maternal serum screening for chromosomal and neural tube defects, and also the increasing adoption of first trimester serum screening together with fetal ultrasound markers. The ultrasound detection of fetal abnormality is well illustrated, and a chapter on fetal magnetic resonance imaging brings this book right up to date with the advances in prenatal imaging technology. While still very much in the research arena, the analysis of fetal cells and fetal DNA and RNA from the maternal circulation holds possibilities for future prenatal diagnosis, and these areas are explored. Chapters on preimplantation genetic diagnosis and fetal therapy discuss the applications of these recent but expanding developments.

Chapters reviewing the prenatal diagnosis of specific conditions such as fragile X syndrome, cystic fibrosis, various metabolic

conditions, and blood disorders allow easy reference to these particular conditions individually. There is also discussion of the prenatal diagnosis of adult onset disorders such as malignancies and neurodegenerative conditions, and the ethical dilemmas that these situations pose are highlighted. The difficult area of termination of pregnancy is well covered along with guidelines, techniques, limitations, and complications.

As we increasingly turn to electronic sources for information, it is still extremely useful to have an up to date, authoritative, and comprehensive text at hand. This approachable and very readable book will be of great help to geneticists, obstetricians, and paediatricians alike, and would also be of interest to primary care physicians, midwives, and medical students.

E Sweeney

**Textbook of neonatal resuscitation, 4th edn (multimedia CD-ROM)**

Edited by Dana A V Braner. Published by American Heart Association and American Academy of Pediatrics, 2004, £21.00, pp 224. ISBN 1581100566



This A4 sized book together with its CD contains the seven lessons that constitute the Neonatal Resuscitation Program (NRP), a course teaching resuscitation at birth, devised jointly by the American Academy

of Pediatrics and the American Heart Association. Lesson one provides an overview and presents the principles of resuscitation, and lesson two describes the initial steps. The remaining five lessons deal with the use of a bag and mask, how to do chest compressions, a description of endotracheal intubation, a lesson on medications, and the final lesson deals with special considerations such as congenital malformations, pneumothorax, post-resuscitation care, and dealing with situations outside hospitals. The text is liberally scattered with line drawings illustrating techniques and equipment.

Each chapter deals with its subject in smaller sections, and after each is a series of questions relating to that section to be answered by the candidate before proceeding to the next. The entire series of questions are asked again at the end of the chapter. In the centre of the book are two pages of colour photographs of a number of different babies, full term, preterm, growth retarded or not, blue, pink, meconium stained, floppy or vigorous. There is also a group of four photographs of the view of the oropharynx and larynx during laryngoscopy. At the end of the book are two structured scenarios used for testing those undertaking the NRP course. Finally the text includes a reprint of the International Guidelines for Neonatal Resuscitation as published in *Pediatrics* in September 2000.

The CD takes one through the text, questions and all, and intersperses this with diagrams, short animated sequences, and occasionally video sequences of action with

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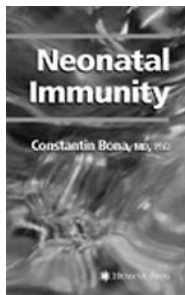
real babies or training dummies. Some of these are helpful, but others are perhaps confusing. For example, there are some excellent video clips of the view down a laryngoscope during intubation, but only the last of the four colour photographs of laryngoscopy in the text is helpful. In one animated sequence, a dummy is shown breathing at exactly the same rate and in the exactly the same manner during both normal breathing and the gasping phase after primary apnoea. A later attempt to illustrate gasping by a similar animated drawing is equally ineffective.

Overall my feelings about this text are mixed. Used as designed, as part of a training programme and with supervision from an experienced colleague trained in the niceties of this programme I am sure it works well. As a stand alone text for learning about resuscitation at birth, I feel it is less successful. The physiology of asphyxia is inadequately explained, thus reducing the value of the overview and encouraging rote learning rather than understanding. Compared with the complexities of resuscitation at other times of life, the resuscitation of the newborn is simplicity itself. This text makes it seem complicated and full of traps for the unwary. International guidelines on all aspects of resuscitation are currently being drawn up and will be published at the end of 2005. The facility on the CD which allows one to update the programme from the AHA website will then be able to prove its worth.

S Richmond

### Neonatal immunity

Constantin Bona. New Jersey: Published by The Humana Press, 2004, \$135.00 (hardback), pp 400. ISBN 158829319X



Having thoroughly searched our modest special care unit library, I decided that there is most definitely a space on the shelf for this text on neonatal immunity. Whether or not it actually deserves such a resting place is a matter for debate. In the introduction the author states that the book aims "to present classical and current information and discuss cutting edge discoveries that will hopefully lead to new horizons in biological research and result in scientific progress in vaccination of infants, stem cells, gene therapy, and transplantation." He does not mention whether or not it will help the busy physician. Undoubtedly the book is aimed at an audience with a more established immunological knowledge than I have, but I believe there is much to commend this text to the general paediatric and neonatal reader with an interest in the mechanisms of newborn sepsis. The *Textbook of neonatology* (Rennie and Robertson) contains approximately 16 pages on neonatal immunity, which provide a good summary of the key points. This book has 302 pages with over 1200 references. My first recommendation would be to spend a few more pence and buy a luminous green pen to help highlight the relevant text and key areas of data that you may wish to retain from some chapters which at times focus heavily on experimental evidence and are liberally dosed with confusing acronyms.

Each chapter deals with a specific area of immunity except for the first, which provides a relatively concise account of the structure and function of the immune system in

vertebrates in general. Sample headings are: the phenotypic characteristics of neonatal B cells, the effect of maternal antibodies on the B cell response, the neonatal cytokine network, fetal and neonatal tolerance. Throughout the text the author reaffirms classical proven knowledge on how the fetus and newborn fight infections through innate, humoral, and cell mediated mechanisms with informative sections on the transfer of maternal antibodies, expression of MHC molecules, T cell development, and tolerance. However, he challenges accepted wisdoms and offers new hypotheses to help explain why neonates exhibit increased susceptibility to antigenic challenge, while demonstrating that their T and B lymphocytes will produce effector and memory cells in certain conditions when correctly presented with antigen in a favourable cytokine environment. The protective and immunomodulatory capacities of maternal antibodies are discussed in detail, with experimental support for their potentially adverse effects on active immunisation of the neonate and infant. An excellent account of important autoimmune conditions including myasthenia gravis, lupus, allo-immune thrombocytopenia, and thyroid disease is given, which I am sure will provide succour to the clinical reader when struggling with some of the detailed research data on mice, monkeys, and zebra fish.

Fetal and neonatal immunity is a fascinating but complicated topic, which this book addresses both thoroughly and expertly, but its experimental detail may appeal more to the specialist immunology community. It is difficult to know whether this text will prove successful in competing for that space on the NICU shelf; at £75 it represents a significant outlay for most paediatric budgets, but if you do take the plunge don't forget your highlighter pen.

G Millman