PostScript

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Isolated bone marrow mycosis in a patient presenting with consumptive symptoms

The incidence of systemic mycoses is increasing as a result of the escalating number of patients who are immunocompromised because of diabetes mellitus, haemodialysis, organ and bone marrow transplants, chemotherapy for cancer, and infections with human immunodeficiency virus (HIV), in addition to the broad use of antibiotics.[1] If such predisposing factors for fungaemia are absent, fungal infections are rarely considered in the differential diagnosis when clinical status non-specifically worsens. The diagnosis of fungal infections is based on histology, cultural evidence, or serological tests.[2] Histological proof of mycosis is regarded as very reliable, because the pathogenic agent can be unequivocally detected within the affected structures.[3] Bone marrow examination might be a useful tool for the examination of cryptic infections, especially in HIV positive patients, with an overall diagnostic yield of 32% and 6% for fungal diseases, respectively.[4] However, so far, isolated bone marrow mycoses in non-neutropenic, immunocompetent patients, without evidence of fungaemia or septicaemia, have not been reported.

We report the case of a 76 year old female patient who had experienced a 13% weight loss over six months. She complained of increasing tiredness and night sweats but denied having dyspnoea or pains. Her body temperature was 37.3℃. Laboratory examination revealed a raised platelet count (582×10^9/litre), C reactive protein (154 mg/litre), and sedimentation rate (21 mm/hour), but normal parameters for electrolytes, glucose, haemoglobin $A1_c$, serum proteins, and liver enzymes; in addition, she was negative for hepatitis (hepatitis B virus (HBV) and HCV) and HIV serology, and had a normal differential blood count. Transferrin was slightly reduced and ferritin was raised. Thus, an underlying malignant disease was suspected. Both computerised imaging of the chest and abdomen and coloscopy were normal. A gastric biopsy revealed minimal reactive mucosal changes without *Helicobacter pylori* infection. An *x* ray of the skull showed right maxillary sinusitis. Histological examination of the nasal mucosa revealed mucocele without evidence of fungal structures. Blood culture analyses, including specific subcultures for fungi, were negative on three different occasions. Finally, a trephine bone marrow biopsy was performed to exclude lymphoma or leukaemia. Myelopoiesis was left shifted, but the remaining haemopoiesis was otherwise unremarkable. Notably, scattered within the bone marrow interstitium and around vascular structures, elongated budding yeast and pseudohyphae with branching and constriction at the septa and production of oval blastospores near the septa were histologically detected (fig 1). The microorganisms stained positively in the periodic acid Schiff reaction, but remained to a great extent negative in the Grocott stain and, therefore, were considered consistent with candida species. A minimal interstitial bone marrow necrosis close to the pseudohyphae[3] was observed (fig 1, lower left). Because the biopsy was formalin fixed, it was not submitted for culture. The angiocentricity of the mycotic elements and the discrete interstitial necrosis close to the pseudohyphae were notable for their pathogenicity. Nevertheless, the possibility of contamination was considered. However, the patient's skin was clinically unremarkable and thoroughly disinfected before performing the biopsy, and the bone marrow trephine had been fixed immediately. Thus, an isolated bone marrow mycosis highly suspicious for candida species was diagnosed. Aimed serological examination revealed raised anti-*Candida albicans* IgG and IgM antibodies (enzyme linked immunosorbent assay; IBL, Hamburg, Germany). The patient was given amphotericin B (0.3 mg/kg) and flucytosine (150 mg/kg) intravenously for 50 days and her clinical condition gradually improved. No fungal structures could be detected in two control

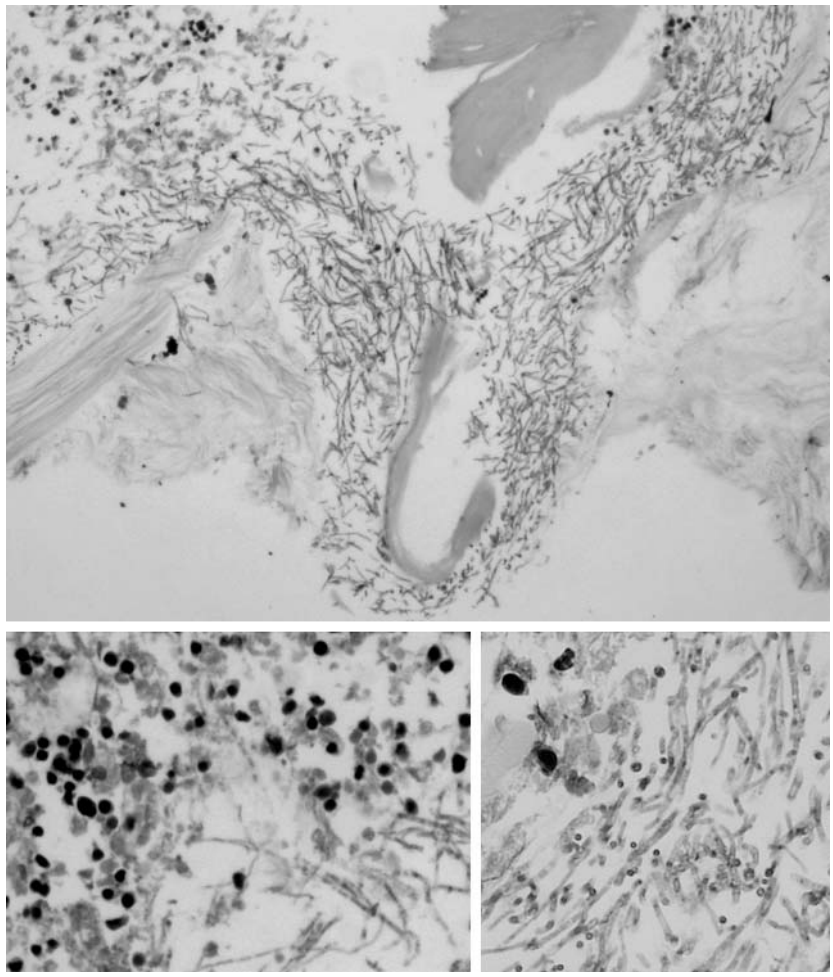

Figure 1 Isolated bone marrow mycosis, overview (upper). Discrete interstitial bone marrow necrosis close to the mycotic elements (lower left). Budding yeast and pseudohyphae with production of oval blastospores (lower right).

bone marrow biopsies two and three months after initial diagnosis. No obvious portal of entry for this fungal infection could be elucidated. Except for the advanced age of the patient, all other risk factors for fungaemia, such as an infection with HIV, HBV, or HCV, diabetes, or immunosuppression were excluded.[1]

A trephine bone marrow biopsy can play a key role in the diagnostic investigation of patients with obscure consumptive symptoms. Isolated bone marrow mycosis can occur in immunocompetent patients even without an obvious portal of entry.

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The exploding bullet

The article entitled ''Health and safety at necropsy'' by Julian Burton provides a detailed and well written narrative regarding both the risks and hazards faced by professionals during postmortem examinations.[1] Despite the presence of a relatively large publication base regarding this topic, important aspects are highlighted, including transmissible spongiform encephalopathies and the more modern, but potentially dangerous, advances in medical technologies. However, we would wish to clarify the issues that the author raises regarding exploding bullets. The difference between a true exploding bullet and a projectile designed to fragment on impact is one of great importance, and one that may cause confusion, as would appear to be the case within this article.

Bullets are composed of a casing containing an explosive powder charge, which, on striking, forces the end projectile element out at speeds of up to 1500 metres/second, depending upon the ammunition and the type of gun used. The projectile causes soft tissue damage through crushing, creating a temporary cavity that contains hot gases. The tissue is compressed radially from the centre of the cavity and, depending on its elastic properties, results in tears to structures (as seen with injuries to solid abdominal viscera). The recoil of the tissues, together with the dissipation of the gases, causes the soft tissue to collapse inwards on itself, the resultant defect being the permanent cavity.

Expansion, or hollow point, bullets are specialised bullets designed to deform upon impact because of a collapsible space within the projectile tip. The result is that a single projectile will inflict greater overall damage to a target, allowing an increased transfer of kinetic energy compared with a standard bullet. The ''benefits'' include a decreased risk of ricochet because the overall penetration distance is reduced; however, some of the older ammunition failed to expand on impact as a result of pieces of clothing obstructing the cavity.

Prefragmented, or frangible, bullets are composed of a prescored outer jacket with a plastic round nose containing compressed lead shot within. The result is a controlled explosion on impact producing increased damage and less clothing related problems. The tips, however, possess no explosive charge.

Burton describes the Winchester Black Talon SXT bullet, but erroneously includes this within the heading of exploding bullets.[1] It is, in fact, a type of expansion bullet. The tip is coated with a black lubricant and has a hollow point possessing six prescored serrations designed rapidly to open outwards upon impact. The jacket of the bullet is thickest at its tip, unlike most hollow point bullets, to provide support for the claw-like petals as the bullet passes through the body. The result, in theory, is a wider permanent cavity created by a single projectile, thus increasing the likelihood of damage to a vital structure. The bullet was voluntarily removed from the market in 1994 and remarketed as the Ranger SXT, and later as the Ranger Talon, both available only to law enforcement officers. Despite media assertions, these projectiles are not ''armour piercing'', the title relating purely to a widely reported manufacturing error in one brand of body armour, which resulted in a recall of this product. Although such expansion bullets do indeed pose a health and safety hazard, because of the sharp edges of the deformed projectile, there is no risk of explosion at necropsy.

True exploding bullets were first described over a century ago and, although not actually in use at that time, were prohibited under the St Petersburg Declaration of 1868, which states that explosive or inflammable projectiles, with a weight of less than 400 g, should never be used in the time of war. Examples include the Russian 7.62 mm ×54R machine gun ammunition with an internal charge of tetryl and phosphorus, and later handgun cartridges containing Pyrodex charges, with or without mercury additives.[2] It should also be noted that individuals can easily obtain instructions for the creation of their own bullets. The most infamous use of such bullets was the attempted assassination of President Reagan in 1981 by John Hinckley, who used ''Devastator'' bullets (Bingham Limited, USA) composed of a lacquer sealed aluminium tip with a lead azide centre designed to explode on impact. Although frequently referred to in works of fiction, they are rarely encountered in forensic practice, because sales have been restricted following the incident in 1981. Projectiles that have failed to detonate are also not as sensitive to movement and heat as mentioned in the article; the author refers to an article on this topic, but fails to acknowledge a follow up letter correcting Knight's original mistakes.[2 3] Burton has, unfortunately, reproduced these errors in his text. In addition, unexploded bullets are safe on exposure to *x* rays and ultrasound.[4] The quantity of explosive is small and, if it fails to detonate on high velocity impact, is unlikely to explode during postmortem examination. We would indeed agree with the assertion that safety glasses should be used during necropsy examination of ballistic victims; however, as Burton himself details within his own book, such eye protection should be routine practice, regardless of the cause of death.[5]

A footnote on the topic should include the mention of armour piercing incendiary round ammunition used during recent conflicts that possesses explosive points, such as the Raufoss Multipurpose Projectiles (Nammo, Norway; http://www.nammo.com), which are fired from anti-vehicle guns of varying calibre. These are not designed or produced for use against personnel. In fact, the rounds will pass through the body unexploded and are thus unlikely to be present in bodies from military conflicts. As such, it is also argued that they do not contravene the St Petersburg Declaration. If present with a body, they are safe to handle, transport, and store. They also comply with NATO standards ensuring complete handling safety, even following vertical drops of up to 15 metres.

Finally, it is interesting to note that the Devastator bullet was developed in the 1970s for use by sky marshals, to minimise the risk of penetration of the plane fuselage when incapacitating a hijacker; a concept that appears to be returning in light of recent world events.

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The role of mast cells in bone marrow diseases

We read the article by Horny *et al* describing bone marrow mast cell (MC) specific protease expression patterns in cases of systemic mastocytosis and myelodysplastic syndromes (MDS) with great interest.[1] An increase in bone marrow MCs is a known feature of various haematological diseases, including myeloproliferative disorders and acquired severe aplastic anaemia (SAA). Although the MC increase is clonal in mastocytosis and benign in acquired SAA, its nature is not fully understood in myeloproliferative and myelodysplastic disorders.

Acquired SAA and hypoplastic MDS share several clinical and bone marrow features, and are often difficult to distinguish. Both conditions respond to immunosuppressive

treatments. Is the increase in numbers of MCs in these conditions simply an innocent consequence of haemopoietic cell injury sparing MCs or, alternatively, does it contribute to the development of severe bone marrow hypoplasia/aplasia in return? MCs have long life spans and they probably are not directly affected by the attack against the stem cell compartment, resulting in relative MC increases in the bone marrow. Low to normal stem cell factor (SCF) values have been shown in SAA, unlike the increased concentrations of other haemopoietic growth factors.[2] This may be explained by greater dependency of MC survival and growth on SCF than other growth factors and by a negative feedback control mechanism in a population that is already supplied by an autocrine pathway. In support of this explanation, a reaction mimicking systemic mastocytosis was observed in a patient with aplastic anaemia who was treated with SCF, which was accompanied by a partial and transient haemopoietic recovery.[3]

MCs with various enzyme expression patterns may mediate different functions in certain tissues in which they exist. These patterns may also be related to the maturational stage of MCs. Nevertheless, the predominant MC type in certain tissues may be determined by the environmental needs. We think that the coexistence of chymase expressing MCs (MC_C) and chymase and tryptase expressing MCs in physiological conditions reflects a naturally occurring balance that contributes to tissue homeostasis. It is known that MCs can act as antigen presenters, in addition to being effector elements of the human immune system. Mast cells can kill target cells through the secretion of cytokines, such as tumour necrosis factor α and serine proteases, and potentially through direct cell to cell interactions. Granzyme H, one of the MC serine proteases, has chymase activity,[4] and chymase is known to induce apoptosis in target cells.[5] It has also been shown that the mast cell derived cell line P815 contains granzyme B RNA. In contrast, tryptase, another MC protease, is a well known mitogen that could induce growth of certain cells, such as airway smooth muscle cells, fibroblasts, and neuronal cells.[6] Tryptase expressing MC (MC_T) are often found in tissue repair sites characterised by fibrosis.

The predominance of MC_T in systemic mastocytosis and patients with MDS was consistent with the typical presence of hypercellular marrow in these conditions.[1] Although the authors did not provide the number of cases with hypoplastic MDS in their series, the frequency is 5–10% in the adult literature, suggesting that most, if not all, of their cases had normocellular or hyperplastic MDS. The autocrine production of SCF with increased tryptase activity might have contributed to the extremely hypercellular bone marrow in those cases. The authors also described hypocellular bone marrow associated with a focal increase in MC with strong chymase expression in a case of indolent systemic mastocytosis, which suggests a possible MC_C contribution to hypocellularity. We recently showed an association between MC persistence and poor outcome in childhood SAA following immune suppression.[7] In another study, we demonstrated longterm liquid culture grown human bone marrow MC cytotoxicity against human leukaemia cells.[8] It is possible that those MCs had strong chymase expression. Regardless of the mechanisms involved, an increase in MCs, preferentially MC_C, may contribute to the hypocellularity seen in acquired SAA and hypoplastic MDS. This explanation is also consistent with the lack of fibrosis in acquired SAA and hypoplastic MDS, which could be secondary to specific MC_C increase.

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Malignant transformation of a recurrent vestibular schwannoma

Malignant nerve sheath tumours are uncommon tumours, particularly those that affect cranial nerves. They are most frequently seen within the context of neurofibromatosis type II. Malignant transformation of benign cranial nerve sheath tumours has been reported on very few occasions.[1–4] We report a case of malignant nerve sheath tumour arising as a recurrent tumour at the site of a previous benign schwannoma.

Tissue was received from the resection of a mass surrounding and involving the right acoustic nerve of a 53 year old man who had previously undergone resection of a tumour involving the same site. Histology from the previous resection, seven years earlier, had shown the tumour to be a benign vestibular schwannoma. Several years before the final resection, our patient had undergone a short course of radiotherapy in an attempt to reduce tumour size. He had no stigmata of neurofibromatosis type II and reported no family history of the condition.

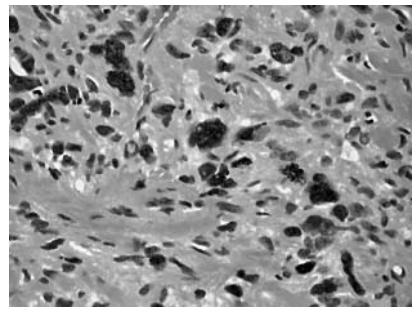

Figure 1 Malignant area within tumour; original magnification, ×20.

The specimen was received as fragments of haemorrhagic tissue measuring 5 ml in aggregate. The specimen was processed routinely for histological examination, including immunohistochemistry.

Microscopic examination of the tissue showed adjacent foci characteristic of both benign and malignant nerve sheath tumours. There were areas composed of irregularly arranged spindle cells with elongated wavy contours characteristic of Antoni A type cells. These areas showed mild nuclear pleomorphism; no mitoses or necrosis were seen. The features were typical of a benign schwannoma. Other areas of tissue were very hypercellular, showing highly pleomorphic spindle cells with bizarre, hyperchromatic nuclei. Scattered giant cell forms were seen, as were zones of necrosis. There was a high mitotic count of, on average, 12 mitoses/10 high power fields in the malignant areas. The appearances were those of a malignant nerve sheath tumour. Both the benign and malignant tissue showed positive staining for S100 and vimentin. The malignant tissue showed positive staining for Ki67, with a staining index of 20%. The benign tissue showed a Ki67 index of less than 1%.

Sections from the original tumour were reviewed. All of the sections showed typical features of a benign schwannoma with cellular and poorly cellular areas (Antoni A and B). Sections were stained for Ki67 and all were negative. The histological features were similar to the benign areas of the later tumour.

Malignant transformation of benign nerve sheath tumours is extremely unusual and reported cases are few.[1–4] We believe that our case represents such an example.

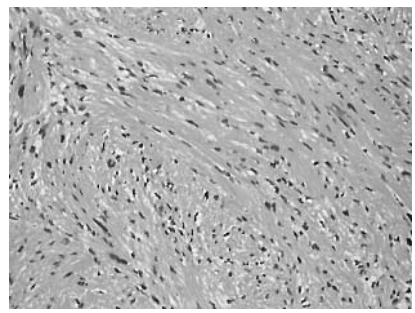

Figure 2 Benign area within tumour; original magnification, ×10.

A previous resection from the same site showed a schwannoma with no evidence of malignancy, and similar benign areas are present in the current biopsy. This supports our assumption that this malignant tumour has arisen by transformation from the previous lesion. An issue with this case is the history of previous radiation. It has been reported that irradiation may induce neurofibrosarcoma.[5] These cases report malignancy arising within previously normal nerves and do not describe the induction of malignancy within a previously benign tumour. Regardless of this possible aetiology, we believe that this case represents malignant transformation within a previously benign vestibular schwannoma, and therefore presents a rare case.

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Best practice guideline on microbiological investigation of infertility requires further review

The best practice guideline on the investigation of infertility briefly comments on appropriate microbiological investigations.[1] However, there are several issues that we feel merit further consideration.

The need to check the rubella immunity status of the female partner is highlighted. This point is also stressed by the Royal College of Obstetricians and Gynaecologists (RCOG).[2] Testing for blood borne viruses (antibodies to hepatitis B surface antigen, human immunodeficiency virus, and hepatitis C) is also commented upon in the best practice guideline as a general investigation and has been similarly suggested in a recent clinical review.[3] However, no such guideline has been issued by either the RCOG or the British Fertility Society. Nevertheless, the Human Fertilisation and Embryology Authority has set a deadline of the end of 2004 for the screening of all women/couples participating in licensed infertility treatments (in vitro fertilisation, intracytoplasmic sperm injection, donor gamete therapy) for blood borne viruses.

The wisdom of this approach is questionable for two reasons. First, if testing of subfertile couples is part of the continuum of their care from preconception to birth, then why repeat the process when pregnant women will routinely be offered blood borne virus (and syphilis) screening during their antenatal care? Second, because the prevalence of blood borne virus infection in patients seeking infertility advice will probably be low (possibly $< 1\%$), where is the evidence that universal blood borne virus screening is cost effective?

We believe that scarce financial resources would be better spent on a screening programme for asymptomatic chlamydia infection in the infertile population. This should be based on a chlamydia molecular amplification test, using urine, lower vaginal swabs, or endocervical swabs, and not chlamydia serology, as has been suggested previously.[3] Screening for chlamydia is not mentioned in the best practice guideline but is recommended by the RCOG. This is particularly important in women who will be undergoing uterine insemination as part of their fertility investigation or treatment. In general, this will mean routinely testing women less than 25 years of age.[4] One in 10 sexually active women in England is currently thought to be infected with chlamydia.[5] Those identified as chlamydia positive could then be offered blood borne virus screening linked to a genitourinary counselling service.

Finally, the best practice guideline makes no comment on screening for cytomegalovirus immunity. Although not routinely recommended, cytomegalovirus IgG testing should be considered both for women who receive donor gametes (sperm or oocytes) and the donors of such gametes.

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BOOK REVIEWS

Pathology of the Pancreas, Gallbladder, Extrahepatic Biliary Tract and Ampullary Region

Lack E. (£145.00.) Oxford University Press, 2003. ISBN 0 19 513392 7.

Superb! The author has succeeded in producing an excellent textbook covering an extensive range of pathology, including both common and exotic entities.

As the title suggests, this book is divided into three parts: ''I. Pancreas'', ''II. Gallbladder'', and ''III. Extrahepatic biliary tract and ampullary region''. The first chapter, entitled ''Embryology, anatomy, and function of the exocrine and endocrine pancreas'', includes original artwork and makes for very interesting and informative reading.

The approach is extremely methodical and the text is comprehensive. The text is written under appropriate headings/subheadings, which makes it easy to read. Where relevant, there is additional information on frozen section and fine needle aspiration. I found that the book covered most common entities in detail and I do not see how this area of pathology could have been covered any more extensively. Special mention must be made about the excellent illustrations used in this book. The text is supported by over 1000 high quality, colour illustrations. These include well chosen colour images of gross and microscopic pathology, in addition to numerous colour artwork illustrations that enhance the text. Pertinent ultrastructural images are also included.

This is not meant as a major criticism, but if there is any downside, it has to be the small size of the print, which was smaller than that of most other pathology textbooks.

This book is an absolute must for histopathologists reporting on specimens of the pancreas, gallbladder, extrahepatic biliary tract, and ampullary region. I also strongly recommend this book to pathology trainees and other clinicians. I predict that this book will become one of the standard pathology textbooks on pancreatic, gallbladder, and extrahepatic biliary diseases.

D Govender

Worms and Human Disease – Second Edition

Muller R. (£35.00.) Cabi Publishing, 2002. ISBN 0 85199 516 0.

This book is the second edition of *Worms and disease: a manual of medical helminthology* first published in 1975.

It covers this branch of parasitology in sufficient detail, especially because significant advances have been made since 1975 in immunology, molecular biology, diagnosis, and treatment aspects of this complex branch of medicine.

The text is balanced by core information and additional descriptions without resorting to elaborate and bulky text, which would have increased costs and added little to its use as a ready reference.

It succeeds as ''a practical guide in human helminthology for physicians and medical technologists'', and will find favour among postgraduate students in tropical diseases, undergraduate medical, zoological, and tropical engineering students, and technologists.

However, it does not cover detailed pathology and aspects of differential diagnosis, perhaps reserved for more specialised textbooks, which may not appeal to the intended wider reader base.

The reader is given adequate references, most of which are derived from the 1980 to 2000 period.

The life cycles and illustrations (including maps and drawings) are useful, with commendable appendices at the end of the book (notably Appendix 2 dealing with the glossary of helminth terms and Appendix 3, which covers the location of helminths in the human body).

The overall impression is that the book is a worthy addition to any medical library, and it is highly recommended for students in both clinical and laboratory medicine, workers in

these disciplines, and allied sciences where helminthology has a bearing.

A Essa

Cancer Cytogenetics: Methods and Protocols

Swansbury J, ed. ($89.50.) Humana Press, 2003. ISBN 1588290808.

The discovery of the Philadelphia chromosome by Nowell and Hungerford in 1960 greatly stimulated interest in cancer cytogenetics. Once banding techniques were refined in the 1970s, the field of cancer cytogenetics blossomed and benefited tremendously from the wealth of information that was quickly amassed. Today, the field is still growing rapidly with the advent of molecular cytogenetic techniques, such as fluorescent in situ hybridisation (FISH), multicolour FISH, spectral karyotyping, and comparative genomic hybridisation. However, there are fewer cancer cytogenetics laboratories than clinical cytogenetics laboratories because of the lower demand for this service. This is changing rapidly, as new prognostic associations are constantly being discovered. Therefore, Dr John Swansbury aimed to help those wishing to start a cancer cytogenetics service by putting together *Cancer cytogenetics: methods and protocols*.

Dr Swansbury wrote most of the book himself, but excellent contributions were made by some very prominent cancer cytogeneticists. The book is designed such that a chapter of background material on a certain topic is followed immediately by a technical chapter on the same topic. Chapters included most of the main areas of interest in cancer cytogenetics, such as myeloid disorders, acute lymphoblastic leukaemia, other lymphoid disorders, solid tumours, and FISH. There is also a chapter on the interpretation of cytogenetic findings, which is extremely important in malignancies. The background chapters are generally well written in a simplistic way for the novice. Cancer cytogenetics can be a very intimidating field for those not familiar with it, and Dr Swansbury does a good job of introducing it. The technical chapters are quite comprehensive and also very well written, with step by step and easy to follow protocols. There are plenty of explanations and trouble shooting suggestions for the many things that can go wrong in a cancer cytogenetics service laboratory.

One of the drawbacks of the book is that it does not put enough emphasis on the importance of prognostic FISH markers in haematological disorders and solid tumours. This is a rapidly growing field, and FISH plays an important role not only in the diagnosis of a malignancy, but also in the prognosis and response to treatment. FISH plays such a large part in the cancer cytogenetics laboratory today that it would have been useful to spend more time on its clinical applications. The book could have benefited also from a chapter on quality control and quality assurance. The service laboratory is very different from a research laboratory, and one must be sure of the results that are reported. It would be best to implement quality control and quality assurance measures right from the start, rather than to change things after a mistake has been made. Quality measures are crucial in all aspects of the cancer cytogenetics service, from culture set up and harvesting, to metaphase analysis, FISH probe validation, right through to reporting.

This book is aimed at the novice and does a very good job in getting one started with a cancer cytogenetics service. However, nothing can replace experience, and it is highly recommended that anyone starting out in the field should visit an established laboratory to see first hand how things are set up. I have no hesitation in recommending this book to any cytogeneticist interested in expanding their service to include malignancies, or to anyone interested in starting up a cancer cytogenetics laboratory.

K Chun

Manual of Clinical Microbiology, 8th Edition

Murray P R, Baron E J, Jorgensen J H, *et al*, eds. ($189.95.) ASM Press, 2003. 1 55581 255 4.

The manual of clinical microbiology, published by ASM Press, is a favourite of mine because of its immense detail and vast coverage of the field. The first edition was published in 1970, with subsequent editions following at four to six yearly intervals, and culminating in this 8th edition, which has been expanded into a two volume set with 141 chapters and 2113 pages, written by 230 authors and an international editorial board composed mainly of microbiologists from the USA.

The manual of clinical microbiology is a colossal resource, which is very well presented and beautifully illustrated. Volume I includes sections on ''General issues in clinical microbiology'', ''The clinical microbiology laboratory in infection detection, prevention and control'', ''Diagnostic technologies in clinical microbiology'', ''Bacteriology'', and ''Antibacterial agents and susceptibility test methods''. Volume II includes sections on ''Virology'', ''Antiviral agents and susceptibility test methods'', ''Mycology'', ''Antifungal agents and susceptibility test methods'', ''Parasitology'', and ''Antiparasitic agents and susceptibility test methods''.

The chapter on ''Mycobacterium: phenotypic and genotypic identification'' is 24 pages long, contains 170 references, and begins with an extensive description of phenotypic identification tests for mycobacteria, with tabulated data for the various cultural and biochemical tests, along with 16 large colour photographs of macroscopic and microscopic colonial morphology. Then there is a short discussion of mycobacterial genomes, including reference to the propensity within the genome for the production of enzymes involved in fatty acid metabolism (as compared with *Escherichia coli*, for example), and the fact that the genus has an extremely clonal population structure, with genomic variation largely caused by insertion sequence movement rather than by point mutations. This leads into a section on ''Genotypic identification of mycobacterial strains'', which begins with an introduction describing the development of the polymerase chain reaction (PCR) and restriction endonuclease analysis for detection of mycobacteria and the seminal work of Amalio Telenti. This is followed by a discussion of aspects and uses of commercially available identification probes (AccuProbe and INNO-Lipa), genome sequencing, markers for species identification within the *Mycobacterium tuberculosis* complex, and direct amplification tests, including the amplified *M tuberculosis* direct test and Amplicor PCR test. Following this are sections on ''Strain typing'', ''Immunodiagnostic tests'', ''Quality assurance'', and ''Interpretation and reporting of results''.

My only criticism is that occasional chapters are a little light. For example, the chapter on ''Antifungal agents'' is only 10 pages long and would have benefited from additional consideration of the relative merits of the recently expanded range of available antifungal agents.

In conclusion, I will continue to use this excellent and detailed resource in its updated form primarily as a reference text because of its comprehensive content, good organisation and therefore ease of access to relevant sections, beautiful presentation, and particularly its academic depth relating to the practice of clinical microbiology.

J Kerr

Cytokines and Chemokines in Infectious Diseases Handbook

Kotb M, Calandra T. ($145.00.) Humana Press, 2003. ISBN 0 89603 908 0.

Cytokines are soluble protein molecules that facilitate communication between cells of the immune system, and as such, orchestrate immune responses required to eliminate or localise invading infectious agents. Therefore, these molecules have obvious relevance to the study of infectious disease.

This book is divided into sections on cytokines in infectious disease, Gram negative infection, Gram positive infection, mycobacterial infection, other bacterial infection, fungal infection, parasitic infection, viral infection, cytokines as therapeutic agents in infectious disease, and anticytokine based therapy in treatment of infectious disease.

Certain chapters contain comprehensive information that is well presented, such as that on cytokine patterns in severe invasive group A streptococcal infections. However, others are superficial and inadequate, such as that on cytokine gene polymorphisms and host susceptibility to infection. This chapter contains sections on tumour necrosis factor α, interleukin 1 (IL-1), IL-1ra and other cytokines. However, the possibilities for a chapter on this topic are extensive and should also include sections on at least interferon γ (IFNγ) and IL-10.

The section on cytokines in viral infections is superficial, with chapters only on viroceptors, human immunodeficiency virus (HIV) infection, and viral hepatitis. Chapters one might expect in this section would be those on Epstein-Barr virus induced cytokines and the relevance of this to diseases such as cancer and rheumatoid arthritis; Kaposi's sarcoma associated herpesvirus and the relevance of its IL-6 homologue to lymphoma, etc, etc. It seems odd to have a section on cytokines in viral infection and then to consider only three examples.

The section on cytokines as therapeutic agents in infectious disease contains chapters on IFNγ, IL-2 for HIV, and the use of granulocyte colony stimulating factor/granulocyte–macrophage stimulating factor. The section on anticytokines as treatment considers only septic shock, streptococcal toxic shock, and necrotising fasciitis.

Although the book could be very useful in some contexts, such as sepsis and HIV, it lacks overall depth and clarity of structure and remit.

J Kerr

Differential Diagnosis by Laboratory Medicine

Mesko D. ed. (£35.00): Springer-Verlag, 2003. ISBN 3 540 43057 1.

What do you do when you get phoned in your laboratory office by a clinical colleague asking you what are the 10 causes of a raised urine δ aminolevulic acid? Well, you could disconnect the phone and hope they don't call back, you could start gabbling and say you have never heard of it, or alternatively you could consult this book! This 1000 plus page text is, indeed, a treasure trove of useful laboratory facts.

The book covers thoroughly many laboratory parameters in various biological materials. Other useful features were a detailed description of medications and how these may interfere with laboratory tests, and a section listing laboratory findings in a variety of clinical conditions. I also found the tables of what sampling tubes were necessary for particular laboratory tests extremely helpful. To add to this there are tables of reference ranges for numerous laboratory tests and also conversion factors for changing conventional units to SI units.

This vademecum is written by a group of experienced laboratory workers and covers clearly many aspects of clinical biochemistry, haematology, microbiology, and immunology and is a worthy addition to any clinical laboratory's bookshelf. I heartily recommend it.

M Crook

CALENDAR OF EVENTS

Surgical Pathology for the Practising Pathologist

16–19 January 2004, Doubletree La Posada Resort, Scottsdale, Arizona, USA

Further details: Department of Continuing Education, Harvard Medical School, PO Box 825, Boston, MA 02117-0825, USA. (Tel: +1 617 384 8600; Fax: +1 617 384 8686; Email: hms-cme@hms.harvard.edu)

Surgical Pathology for the Practising Pathologist: Selected Topics

26–29 March 2004, Sanibel Harbour Resort and Spa, Fort Myers, Florida, USA

Further details: Department of Continuing Education, Harvard Medical School, PO Box 825, Boston, MA 02117-0825, USA. (Tel: +1 617 384 8600; Fax: +1 617 384 8686; Email: hms-cme@hms.harvard.edu)

Medicare India

6–8 April 2004, Pragati Maidan, New Delhi, India

Further details: Rob Grant, Kinex Log, 5 New Quebec Street, London W1H 7DD, UK (Tel: +44 (0) 207 723 8020; Fax: +44 (0) 207 723 8060; Email: rob.grant@kinexlog.com; Website: www.medicare-expo.com or www.kinexlog.com)

Diagnostic Histopathology of the Breast

10–14 May 2004, Hammersmith Hospital (Imperial College Faculty of Medicine), London, UK

Further details: Wolfson Conference Centre, Hammersmith Hospital, Du Cane Road, London W12 0NN, UK. (Tel: +44 (0) 20 8383 3117/3227/3245; Fax: +44 (0) 20 8383 2428; Email: wcc@ic.ac.uk)

Practical Pulmonary Pathology

27–30 July, 2004, Brompton Hospital, London, UK

Further details: Professor B Corrin, Brompton Hospital, London SW3 6NP, UK. (Tel: +44 (0)20 7351 8420; Fax: +44 (0)20 7351 8293; Email: b.corrin@ic.ac.uk)

ACP Management Course for Pathologists, 2004

8–10 September 2004, Hardwick Hall Hotel, Sedgefield, County Durham, UK

Further details: V Wood, ACP Central Office, 189 Dyke Road, Hove, East Sussex BN3 1TL, UK. (Tel: +44 (0) 1273 775700; Fax: +44 (0) 1273 773303; Email: valerie@pathologists.org.uk

CORRECTION

The Scotland and Newcastle epidemiological study of Hodgkin's disease: impact on histopathological review and EBV status on incidence estimates. Jarrett RF, Krajewski AS, Angus B, *et al. J Clin Pathol* 2003;**56**:811–6. In the key to fig 3A EBV− should have been shown as triangles and EBV+ as squares.