Correspondence

Killing *Yersinia enterocolitica*

In a recent article, Gibb *et al*[1] presented studies dealing with the role of *Yersinia enterocolitica* in transfusion transmitted disease. They proposed that the increased number of reported transfusion complications during recent years, caused by *Y enterocolitica* infected blood components, is related to the use of additive solutions for red cell storage, which brings about a decrease in complement activity. They showed that dilution of plasma with an additive solution to a concentration corresponding to that in red cell units decreases complement killing of *Y enterocolitica* strains at 20°C. These authors assume that the blood of subjectively healthy donors contains *Y enterocolitica* organisms which possess a virulence plasmid rendering them resistant to complement. The organisms are thought to be present free in the donor's plasma. When collected blood is cooled to 20°C, the plasmid is no longer expressed and the organisms become sensitive to complement. The authors suggest that the normal two to six hour delay before separation into components may not be enough for complement killing.

This hypothesis is very interesting and Gibb *et al* presented some evidence in support of it. They do not mention, however, that there is another possible explanation. We have suggested that *Y enterocolitica* organisms are transferred intracellularly in donor leucocytes, where they are obviously protected from the action of plasma complement.[2] After days or weeks of storage, any leucocytes present in red cell units will begin to disintegrate, releasing any organisms they contain. *Y enterocolitica* can grow rapidly at 4°C. Whether the storage medium is undiluted plasma or plasma diluted with an additive solution, no killing by complement will be expected at this temperature, particularly if the bacteria are released after more than a week of storage.

This alternative hypothesis is compatible with the observation that most of the severe complications have been seen with blood units stored for ≥21 days. That no *Y enterocolitica* complications were reported before 1975 may be explained by a combination of insufficient identification of species before the 1970s and that red cells were generally stored for less than 21 days at that time.

The mechanism by which *Y enterocolitica* causes these complications is not just of academic interest. As suggested by Gibb *et al*, the length of time collected blood is held at 20–25°C is important, whether bacteria are present free in donor plasma or whether blood has been contaminated during collection or component separation. Complement killing of *Y enterocolitica* was quick in Gibb *et al*'s study and in a previous study by my group.[3] Removal by phagocytosis is likely to be slower. However, if the major mechanism of transmission of *Y enterocolitica* is via leucocytes infected in vivo, the most logical way of overcoming this problem would be to remove the leucocytes from the red cell preparations, either by removing the buffy coat layer, as is done in many European countries, or by leucocyte filtration.

When discussing possible ways of improving the safety of transfusion, it should be remembered that severe transfusion complications as a result of *Y enterocolitica* infected blood products are extremely rare. The interested reader is referred to a recent review of the subject.[4]

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1 Gibb AP, Poling N, Murphy WG. Failure to kill Yersinia enterocolitica by plasma diluted to the concentration found in red cell units. *J Clin Pathol* 1996;**49**:434–6.
2 Högman CF, Gong J, Hambraeus A, Johansson CS, Eriksson L. The role of white cells in the transmission of Yersinia enterocolitica in blood components. *Transfusion* 1992;**32**:654–7.
3 Gong J, Rawal BD, Högman CF, Vyas GN, Nilsson B, Gustafsson I. Complement killing of Yersinia enterocolitica and retention of the bacteria by leucocyte removal filters. *Vox Sang* 1994;**66**:166–70.
4 Högman CF, Engstrand L. Factors affecting growth of Yersinia enterocolitica in cellular blood products. *Transfus Med Rev* 1996 (in press).

Dr Gibb comments:

Professor Högman's hypothesis was discussed in a previous study by myself and colleagues.[1]

Professor Högman and I agree that those *Y enterocolitica* cells which go on to multiply in donated blood probably survive for some time inside human cells. We disagree about the location of the bacterium at the time of blood collection. As this is such a rare event, we may never know the answer with any certainty, but evidence from animal models suggests that invading *Y enterocolitica* is an extracellular pathogen.[2 3] The plasmid borne, temperature regulated virulence factors of *Y enterocolitica* code for resistance to phagocytosis, as well as complement resistance, at 37°C.[4] These virulence factors are not expressed at low temperature so that complement mediated bacterial killing, or entry into cells, might occur some hours after blood has been collected. If complement mediated killing is impaired by plasma dilution, then this would presumably increase the probability that bacteria could reach a safe intracellular location.

The point in history at which *Y enterocolitica* became a problem is important because of its possible relation to changes in blood transfusion practice. There was an isolated case in 1975, but no further cases were reported until 1982, about the time when additive solutions were introduced into practice.[1] This suggests that growth of *Y enterocolitica* in blood was exceptionally rare before 1982, but that it could be detected if it did occur.

Readers will be aware of the major contribution of Professor Högman to the development of additive solutions for red cell storage.[5 6] It is clear that this work has had important benefits in improving the supply of red cells and plasma products. I have speculated that this process may also have contributed to the growth of *Y enterocolitica* in donated blood. I agree with Professor Högman that this speculation is not proven. Even if there was a proven link, it is likely that the benefit from improved red cell and plasma supply outweighs the possible harm from the rare occurrence of transfusion related *Y enterocolitica* infection.

The harm done by *Y enterocolitica* in blood transfusion is small when compared with other current problems. Nevertheless, we should attempt to understand what has happened and consider strategies to prevent it.

1 Gibb AP, Martin KM, Davidson GA, Walker B, Murphy WG. Modelling the growth of Yersinia enterocolitica in donated blood. *Transfusion* 1994;**34**:304–10.
2 Lian CJ, Hwan WS, Pai CH. Plasmid-mediated resistance to phagocytosis in Yersinia enterocolitica. *Infect Immun* 1989;**55**:1176–83.
3 Hanski C, Kutschka U, Schmoranzer HP, Naumann M, Stallmach A, Hahn H, *et al*. Immunohistochemical and electron microscopic study of interaction of Yersinia enterocolitica serotype 08 with intestinal mucosa during experimental enteritis. *Infect Immun* 1989;**57**:673–8.
4 Poerregard A. Interactions between Yersinia enterocolitica and the host with special reference to virulence plasmid encoded adhesion and humoral immunity. *Danish Med Bull* 1992; **39**:155–72.
5 Högman CF, Hedlund K, Zetterström H. Clinical usefulness of red cells preserved in protein-poor mediums. *N Engl J Med* 1978;**299**:1377–82.
6 Högman CF, Andreen M, Rosén I, Åkerblom O, Hellsing K. Haemotherapy with red-cell concentrates and a new red-cell storage medium. *Lancet* 1983;**i**:269–72.

Book reviews

Laboratory Techniques In Rabies. 4th edn. Meslin F-X, Kaplan MM, Koprowski H, eds. (Pp 476; SW Fr 115.00.) World Health Organisation Publications. 1996. ISBN 92 4 154479 1.

This is a fourth and decidedly fatter edition of a book which is already an indispensable tool for rabies scientists. The editors, Meslin, Kaplan and Koprowski, deserve to be congratulated for a skilful updating, and the WHO for making it available at a reasonable price (SW Fr 115.00 and SW Fr 85.00 in developing countries).

Some of the content is unchanged from the previous edition because there has been no need for change—for instance, the chapters on examination for Negri bodies and the electron microscopy of rabies viruses. Other chapters are right up to date, for instance Tordo's review of the molecular biology of rabies and his discussion with Sacramento and Bourhy of the use of PCR in diagnosis, typing and epidemiological study of rabies.

Different readers will use this book for different purposes. General readers who want to update themselves on rabies will find the first 50 pages very instructive. Specialists in rabies diagnosis, vaccine and standardisation will find their needs equally well served later in the book. At the heart of the book is a series of chapters by expert authors on practical rabies procedures, but in spite of the multi-authored approach, all of the chapters are easy to read. This does credit to the editors and means that the volume is the obvious current source to go to for an exposition of any laboratory technique associated with the study of rabies.

The book is also a salutary reminder to UK readers that throughout most of the world rabies is a serious threat to human and animal health, and that its control is a continuous struggle between what is most desirable and what is possible and affordable. Alongside the newer diagnostic and therapeutic procedures linger classic ones like mouse inoculation and the use of sheep brain vaccines and equine serum for post exposure

treatment. As the editors comment this is not ideal. To quote (p11) "in view of the short delay in obtaining the result, isolation of all rabies virus in cell culture should replace intracerebral mouse inoculation wherever possible" and (p223) "most of the rabies vaccines used for post-exposure treatment of humans are still produced from brain tissue. The Semple-type vaccine remains the most widely available rabies vaccine in the World... Post exposure treatment with brain tissue vaccines may induce severe neurological complications and vaccine failures are more frequent than with the new generation of cell culture vaccines and highly purified duck embryo vaccines. However, [they] are more difficult to produce... and... more expensive."

This book is an indispensable reference book and the best single rabies text available. It contains important current data on advances in rabies diagnosis—for example, in the use of the sensitive mouse neuroblastoma cell line in diagnosis and antibody determination, and the application of 'molecular' techniques. Buy it—or at least persuade your librarian to do so!

P P MORTIMER

Atlas of Endometrial Histopathology. Second revised and expanded edition. Dallenbach-Hellweg G, Poulsen H. (Pp 218; DM 268.00.) Sponger. 1996. ISBN 3 540 60908 3.

This is the second edition of an atlas first published in 1985. The current edition differs from the previous volume in having an additional chapter on gestational disease. Despite this, this edition is shorter than the previous one, a feat accomplished by separating the text from the figures illustrating the features described in the relevant condition. Whilst this eliminates the extensive areas of unused paper which were a feature of the previous edition, it is rather inconvenient and the book now has more in common with an extensively illustrated short text book than a conventional atlas.

In the initial section entitled "Technical Remarks" the authors describe fixation of endometrial samples with 4% neutral formaldehyde as ideal. This is at variance with the opinion of many British gynaecological pathologists who prefer to use Bouin's fixative which provides more uniform fixation of the endometrial stroma. The authors also recommend the routine use of at least two and up to four stains for interpreting endometrial specimens. I suspect that many British pathologists would find this an unwelcome intrusion into their working day. I was disappointed that there was no mention of the contribution that ancillary investigations such as hysteroscopy or transvaginal ultrasound make in diagnosis. In many centres these have become as much a part of the routine investigation of the endometrial cavity as tissue sampling. Furthermore, the challenges encountered in interpreting samples obtained by office techniques such as the Vabra aspirator and Pipelle sampler are not mentioned.

The text includes a range of differential diagnoses for each of the morphological appearances described—a feature which many pathologists, particularly the most junior trainees, will find useful. Some of the terminology seems to differ from that used routinely in the UK and I do not believe that the grading of adenomatous (complex) endometrial hyperplasia or of high grade serous papillary and clear cell carcinomas is practised routinely in this country.

This book would be a useful acquisition for the medical library of undergraduate and postgraduate medical schools which train junior doctors in pathology and gynaecology. Those who would feel more comfortable with a book which adheres to British terminology and which provides text rather than extensive colour illustration, might wish to compare it with the upcoming second edition of Buckley and Fox's *Biopsy Pathology of the Endometrium* before making a decision to purchase.

M K HEATLEY

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Notices

Cytopathology for Histopathologists

February 3–7 1997

This is an intensive course in basic cytopathology suitable for all candidates preparing for the MRCPath and Diploma in Cytopathology examinations, as well as established histopathologists requiring revision. It is organised by the Department of Cellular Pathology, Northwick Park Hospital (Dr Eamon Leen). The programme will consist of lectures, microscopy sessions and discussions. Topics will include cytopathology of the cervic, urine, respiratory tract, serous effusions, and fine needle aspiration of breast, lymph nodes, salivary glands, and other sites. In addition, keynote lectures will be given by Dr Amanda Herbert (Overview of cervical cytology screening) and Professor Sebastian Lucus/Dr Nick Francis (Cytology of infectious disease). The course is limited to 30 participants. Royal College of Pathologists' approval for 29 CME credits is envisaged (as per 1996). The course fee is £350.00, which includes lunch, refreshments and a course dinner.

For further information, please contact: Dr Eamon Leen, Department of Cellular Pathology, Northwick Park Hospital, Harrow HA1 3UJ. (Tel: 0181 869 3312; fax: 0181 864 1933.)

UMDS Dermatopathology Update

Friday February 21 1997

Venue: St Thomas's Hospital, London

Morning—Melanocytic Tumours Update Speakers: RW Sagebiel, R Barnhill, M Cook, BM Maguire.

Afternoon—Pre-circulated slide seminar

For further information, please contact: Dr PH McKee, Department of Histopathology, St Thomas's Hospital Medical School, Lambeth Palace Road, London SE1 7EH. (Tel: 0171 928 9292 exn 2295; fax: 0171 922 8322.)

Postgraduate Course

Current Concepts in Surgical Pathology

November 11–15 1996

The Department of Pathology, Massachusetts General Hospital, Harvard Medical School, will present a postgraduate course in Surgical Pathology under the direction of Drs NL Harris, RH Young and EJ Mark.

The course is designed for pathologists at resident and practitioner levels. It will provide in-depth review of diagnostic surgical pathology with emphasis on morphological features, newly recognised entities and new techniques, presented by the faculty of the Department of Pathology, Massachusetts General Hospital. Instruction will be primarily be lecture, but will also include discussion periods. Each participant will receive a comprehensive course syllabus.

The course has Category 1 accreditation for approximately 35 hours CME credit by the American Medical Association. The fee for the course is $845.00 (£545.00) (residents and fellows $650.00 (£419.00)).

For further information, please contact: Department of Continuing Medical Education, Harvard Medical School, 25 Schattuck Street, Boston, MA 02115, USA. (Tel: 617 432 1525.)

Forthcoming Royal College of Pathologists Symposia

Cytopathology update:
Developments and controversies
in cervical and breast cancer screening
Friday 6 December 1996

Practical problems for a coroners pathologist: Hope to cope
Thursday 30 January 1997

New aspects of micronutrients in disease
Wednesday 19 February 1997

Diet and cancer
Thursday 13 March 1997

The above meetings are open to members and non-members of the College. All meetings will be held at the Royal College of Pathologists, London.

Further details and application forms can be obtained from: Scientific Meetings Officer, RCPath, 2 Carlton House Terrace, London SW1Y 5AF. (Tel: 0171 930 5862 ext 24/25.)

Postgraduate Course in Gynecologic and Obstetric Pathology

March 24–28 1997

The Departments of Pathology, Massachusetts General Hospital and Brigham and Women's Hospital, Harvard Medical School, will present a postgraduate course in Gynecologic and Obstetric Pathology under the direction of Drs RE Scully, RH Young, CP Crum, to be held at the Four Seasons Hotel, Boston.

This five day course is designed primarily for pathologists and pathology residents, but will also be of interest to gynaecologists with an interest in pathology. It will provide an in depth review of gynaecological and obstetric pathology with emphasis on morphologic diagnostic features and clinicopathological correlation. Special attention will be paid to recent advances and newly recognised entities. Instruction will be primarily by lecture but will also include discussion periods. A new feature of the course this year will be the opportunity to review glass slides of selected unusual cases in the laboratories of the Massachusetts General Hospital during the evenings. Each participant will receive a comprehensive course syllabus. The course has Category 1 accreditation for approximately 36 hours CME credit by the American Medical Association. The fee for the course is $795.00 (£530) (residents and fellows $575.00 (£383)).

For further information, please contact: Department of Continuing Education, Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, USA. (Tel: 617 432 1525; fax: 617 432 1562.)