DOUGLASS HANLY MOIR PATHOLOGY

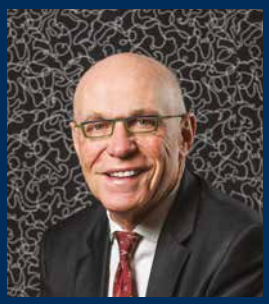
Quality is in our DNA

Doctors' Newsletter

ISSUE 3 | 2018

Focus on Microbiology

www.dhm.com.au



I'm delighted to provide these opening words for the third Doctors' Newsletter for 2018 and, as always, thank the individual authors for their contributions.

This issue has an infectious theme. Dr Miriam Paul's article relates to antibiotic stewardship, a concept which impacts on the professional life of any practitioner who prescribes antibiotics. Antibiotic overuse and misuse are important drivers of antibiotic resistance; stewardship is the process of education and persuasion of prescribers so that evidence-based principles inform their decisions to treat and their choice of antibiotic. Current susceptibility information forms an essential part of that evidence base.

Parvovirus B19 infection is the subject of an article by Dr Ian Chambers, who has also adapted an article on the investigation of gastrointestinal infection. Written by Dr Lyn Waring of Melbourne Pathology (a laboratory in the Sonic Healthcare group), we thank her for allowing us to republish her article in this newsletter.

We hope you enjoy this final Newsletter for 2018. As well as being directly relevant to the daily practice of many readers, we hope that the articles included are of general interest to most. Thank you for your continuing support and all the very best for 2019.

Dr Colin Goldschmidt
MBBCh, FRCPA, FAICD
CEO, Douglass Hanly Moir Pathology

Laboratory investigation of gastrointestinal infections

Most cases of acute gastroenteritis in adults have an infectious cause but clinical presentation rarely allows confident distinction between a bacterial, parasitic or viral aetiology. Clinical history and presentation often contain clues however definitive diagnosis requires laboratory testing. Most cases of infectious diarrhoea are self-limiting; specific treatment is not just unnecessary but contraindicated and therefore laboratory investigation is hard to justify. However, there are very important exceptions which demand both investigation and treatment. Clinical assessment is necessary to identify that subset of patients for whom laboratory investigation is essential and identification of a diarrhoeal pathogen is of more than academic interest.

Bacterial pathogens

Bacterial pathogens are detected by culture or by PCR. PCR provides more sensitive detection but it covers a more limited range of pathogens and cannot provide antibiotic susceptibilities. Overall, the improved sensitivity of detection and rapidity of results makes PCR a very important diagnostic tool in gastrointestinal disease.

Shigella species cause a potentially severe diarrhoeal illness that is frequently travel-associated and is both foodborne and sexually acquired. While it is often self-limiting, the severity of the illness and the high potential transmissibility of infection mean that treatment is recommended for all culture-positive cases. Shigella species are closely related to enteroinvasive strains of *E. coli* (EIEC), which may cross-react and cause false-positive results in the Shigella PCR. Therefore, the definitive diagnosis of shigellosis requires culture-confirmation of a positive Shigella PCR result. This is generally a self-limiting illness for which treatment is not indicated.

Other bacterial pathogens included in the multiplex PCR panel are Salmonella species, *Yersinia enterocolitica* and *Clostridioides difficile*.

Viral pathogens

Norovirus is a particularly important cause of infectious diarrhoea in hospitals and nursing homes because of its high transmissibility and potential for causing outbreaks. It is critical to establish the diagnosis promptly so that appropriate infection control precautions are implemented.

Rotavirus has a similar potential for causing outbreaks among unvaccinated children in institutions. Rapid diagnosis and communication of results are vital aspects of infection prevention and control.

There is no specific antiviral treatment available for viral gastroenteritis. Fluid and electrolyte replacement is the mainstay of treatment and isolation/contact precautions for prevention of cross-infection.

Parasites

Faecal parasites can be detected by microscopy or PCR, with the latter providing greater sensitivity. In Australia, the most common (and uncontroversial) parasites that cause diarrhoea are *Giardia lamblia, Cryptosporidium parvum* and *Entamoeba histolytica*. Most cases of amoebiasis are diagnosed in returning travellers but cases of locally acquired infection have been identified in gay men in Sydney.

Blastocystis hominis and *Dientamoeba fragilis* are rather more controversial parasites which are diagnosed with high frequency by microscopy and PCR. Interpretation of positive results requires caution because both can be identified in asymptomatic individuals.

Many other parasites can cause gastrointestinal infections but may or may not cause diarrhoea. Some, such as *Strongyloides stercoralis and Taenia solium* (pork tapeworm) are particularly important for their invasive capacity whereas *Enterobius vermicularis* (pinworm or threadworm), cause other symptoms, such as pruritis ani, and would require specific treatment.

Important information

Include clinical notes on referral

- Returned traveller, country of travel, symptoms, eosinophilia, if immunosuppressed/HIV; in these patients, request for Faecal PCR and OCP for full parasite testing.
- If febrile and returned from a tropical/sub-tropical area, consider blood cultures, CRP, FBE, LFT and FMC, for investigation of suspected typhoid/paratyphoid.

FAECES COLLECTION
1. **Brown-top jar:** Culture, OCP and PCR
2. **SAF preservative:** OCP (*Dientamoeba fragilis* in particular)

Antibiotic sensitivities of common pathogens

In a recent review, Douglass Hanly Moir Pathology has identified more than 65,000 *E. coli* isolates from urine samples collected from people in the community in NSW (not including nursing homes). Thirty thousand *Staph aureus* isolates were grown from non-urine specimens. We have analysed the antibiotic sensitivities of these and other common organisms, in order to provide a guide to appropriate empiric antibiotic treatment choice.

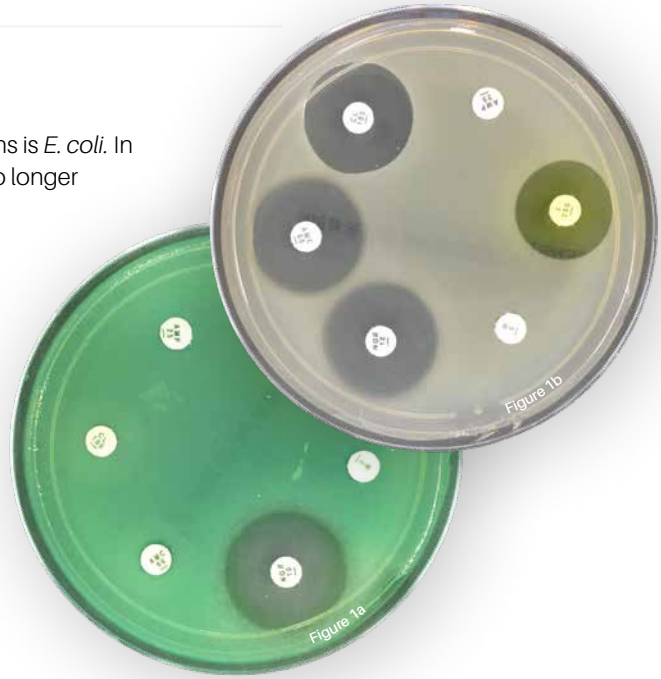
Dr Miriam Paul
MBBS, MM, FRACP, FRCPA
Clinical Microbiologist & Infectious Disease Physician

Urinary tract pathogens

The most common organism isolated from non-hospital urine specimens is *E. coli.* In our laboratory, only 56% are sensitive to amoxycillin, which is why it is no longer recommended for empiric treatment. Seventy-seven per cent of *E. coli* are sensitive to trimethoprim, and 93–94% are sensitive to cephalexin, nitrofurantoin (e.g. Macrodantin) and to amoxycillin plus clavulanate (e.g. Augmentin).

Other Gram-negative organisms, such as *Klebsiella, Serratia* and *Enterobacter,* are much less frequently isolated, and some species are intrinsically resistant to more antibiotics. Of note, *Pseudomonas* is intrinsically resistant to most oral antibiotics, except for norfloxacin and ciprofloxacin.

We increasingly isolate ESBL (extended spectrum beta-lactamase) producing strains, particularly in those who have travelled overseas and carry the organism asymptomatically in their bowel for some time. These strains are resistant to all penicillin-related antibiotics and cephalosporins. If multiresistant, an antibiotic called fosfomycin can be tested on request; however prescribing this antibiotic requires Special Access Scheme (SAS) approval.



Oral antibiotic sensitivity testing

Figure 1a. Pseudomonas only sensitive to norfloxacin (NOR)

Figure 1b. *E. coli* resistant to ampicillin (AMP) and to trimethoprim (W)

Ten to fifteen per cent of urine isolates are *Enterococcus spp.*, which are usually sensitive to amoxycillin, nitrofurantoin and intravenous vancomycin. *Enterococcus* is intrinsically resistant to cephalosporins and trimethoprim. Occasionally, vancomycin-resistant *Enterococcus* (VRE) is isolated, particularly from nursing home residents. This does not require treatment in asymptomatic colonised patients but indicates the need for infection control precautions in an institution, as it is highly transmissible.

URINARY TRACT PATHOGENS (% sensitive)						R = Always resistant
ORGANISM	Amoxycillin	Trimethoprim	Cephalexin	Amox/Clavulanate	Norfloxacin	Nitrofurantoin
E. coli	56	77	93	94	94	94
Klebsiella	R	89	95	96	97	28
Proteus	87	81	98	99	98	–
Enterococcus	98	R	R	98	R	99

Amoxycillin and ampicillin have equivalent antimicrobial susceptibilities. Amoxycillin is reported because it is available for both oral and parenteral use. Ampicillin is only available for parenteral administration.
Source: DHM data, 2017 Antibiogram

Respiratory tract pathogens

Streptococcus pneumoniae is the commonest bacterial pathogen. Decreased sensitivity to penicillin may occur however this is not usually clinically significant in respiratory infections.

Haemophilus influenzae only causes 5% of community-acquired pneumonia, more commonly in COPD patients. Twenty-eight per cent are resistant to amoxycillin, but most remain sensitive to Augmentin. Ninety-eight per cent are sensitive to doxycycline. This organism is resistant to erythromycin, and other macrolides, such as clarithromycin and azithromycin, may be associated with treatment failure so are not recommended.

Mycoplasma pneumoniae has become increasingly resistant to macrolides (this cannot be tested for individual patients), so erythromycin/roxithromycin/clarithromycin are no longer recommended for treatment of community-acquired pneumonia, except in children under 8 years of age and pregnant women. Doxycycline is recommended for all others.

RESPIRATORY TRACT PATHOGENS (% sensitive)				
ORGANISM		Amox/Clavulanate	Doxycycline	Eryth/Clarithromycin
S. pneumoniae	Penicillin 99	99	83	79
H. influenzae	Amoxil 72	91	98	–

Source: DHM data, 2017 Antibiogram

Soft tissue pathogens

Staphylococcus aureus is the commonest cause of wound infections. Only 5% are penicillin sensitive, while 89% remain sensitive to flucloxacillin/cephalexin. In our laboratory, 11% of *S. aureus* isolates from the community are MRSA (resistant to flucloxacillin/cephalexin). In comparison, 47% of *S. aureus* isolates recovered from nursing home residents are MRSA. MRSA is increasingly being recovered from patients who have never been hospitalised, as well as from those with past hospital contact. Approximately one third of these MRSA are resistant to clindamycin but most remain sensitive to cotrimoxazole (e.g. Bactrim or Septrin), which is available as a syrup for treatment of children. Most of these MRSA are also susceptible to doxycycline.

Group A (*Streptococcus pyogenes*) and Group B (*Streptococcus*), which also causes cellulitis, both remain sensitive to penicillin. Thirteen per cent are resistant to erythromycin, and 21% are resistant to doxycycline.

SOFT TISSUE PATHOGENS (% sensitive)				
ORGANISM	Penicillin	Erythromycin/clindamycin	Doxycycline	Cotrimoxazole
S. aureus	5	80	95	97
Strep A/B/C/G	100	87	79	–

Source: DHM data, 2017 Antibiogram

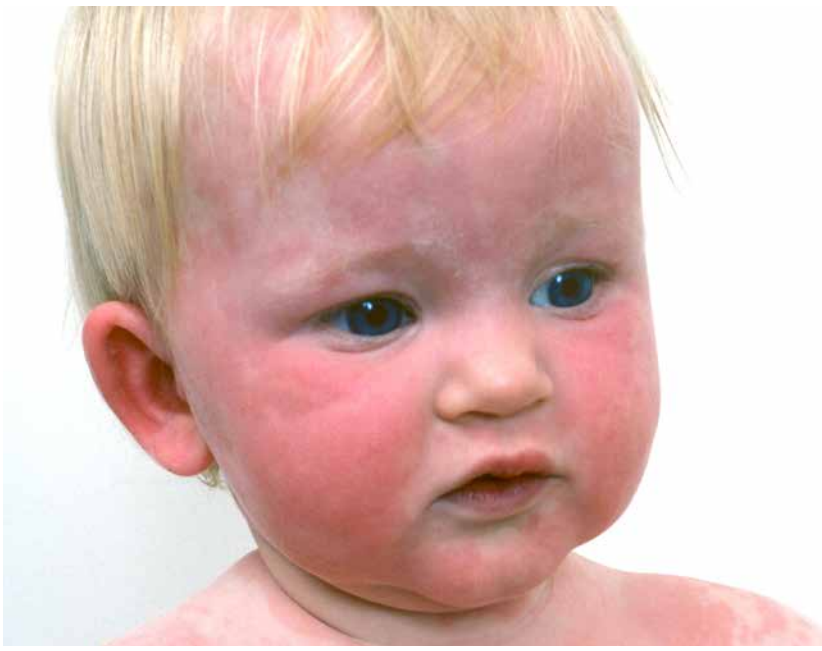
For further information, or to discuss a patient, please contact one of our Microbiologists on (02) 9855 5312.

Parvovirus B19 infection: Trivial except when it's not

Each year at around this time (late winter to spring), we see an increase in the number of serologically-confirmed infections with parvovirus B19. These infections are usually trivial in nature and benign in outcome, but there are important exceptions to this rule. This article will review the typical presentation and course of infection with parvovirus B19, discuss its potential adverse outcomes and in whom that potential is greatest.

Dr Ian Chambers
MB, ChB, FRCPA, MASM
Clinical Microbiologist

Parvovirus B19 was discovered and named in 1975 by virologists working at the University of Sydney. It is the predominant genotype (of three) which are pathogenic for humans. Infection is common, occurring sporadically and in clusters, it has a clear seasonality (late winter through to spring) and also has an epidemic cycle with a 4–5 year periodicity. While 50–80% of adults have parvovirus IgG and are regarded as immune, there remains a significant proportion of the adult population who are susceptible to infection.



Slapped-cheek appearance of a child with Fifth disease

Infection and its complications

Humans are the only known host for parvovirus B19 and erythroid progenitor cells are the most susceptible to infection. This susceptibility is mediated by the P antigen which is present on erythrocytes, megakaryocytes and myocardial cells, and which acts as a receptor for the virus. This is the cellular basis of infection and is the interaction which leads to its consequences. The anaemia and thrombocytopenia which are usually subclinical in a normal individual may, in those with increased red blood cell turnover (for example, sickle-cell disease, haemoglobinopathies), lead to significant falls in haemoglobin and, potentially, aplastic crisis. Because B19 is cytotoxic to fetal red blood cell precursors, fetal infection may cause severe anaemia, high cardiac output failure and non-immune hydrops. Unlike rubella, which has a similar presentation and with which it can cross-react in serological assays, B19 has no association with congenital malformations.

Clinical presentation

The clinical presentation of infection is highly variable; Fifth disease, slapped cheek disease and erythema infectiosum all refer to the same febrile exanthem, without significant sequelae, occurring in young children, while an adult frequently presents with fever and arthralgia/arthritis but with no rash at all. However, the same adult with sickle-cell disease may present in aplastic crisis and, in pregnancy, there is a risk of hydrops fetalis, myocarditis and fetal death. In general, the typical presentation of B19 infection in children and its benign outcome require laboratory confirmation relatively infrequent. By contrast, the more variable and dramatic clinical presentation in adults, the absence of any rash rather than the presence of a typical one and, in women, the threat of adverse pregnancy outcomes lead to a much greater reliance on laboratory diagnosis.

Laboratory diagnosis

Generally, diagnosis of parvovirus B19 infection is serological. IgM is usually detectable from just before the onset of symptoms and present in >90% of people by the time of onset of the rash. Detectable IgM is suggestive of infection but not conclusive, unless an IgG seroconversion is also demonstrated or (if IgG was also present at the time IgM was detected) there has been a significant rise when testing is repeated after two weeks. When infection has been diagnosed in a pregnant women, there is little reason to attempt definitive diagnosis in the fetus. Parvovirus PCR can provide that confirmation however it requires amniocentesis to obtain the required specimen.

Erythema infectiosum (Fifth disease, slapped cheek disease)

These terms all refer to the same presentation of parvovirus B19 infection in childhood. After an incubation period of 4–14 days, and a non-specific prodrome of fever, malaise and rhinorrhoea, a red, macular rash appears on the cheeks, fading to become more lacy and erythematous after a few days. There is no such typical presentation in an adult (see above), with rash being variable or absent. Joint pain and swelling, however, are almost as typical of adult infection as a slapped-cheek rash is in childhood.

Parvovirus B19 infection in pregnancy

Around 40% of women of child-bearing age are susceptible to parvovirus infection. The highest infection rates are seen in school teachers, day-care workers and women with school-aged children in the home. The obvious common factor is their greater likelihood of being exposed to children with erythema infectiosum and that exposure being sustained for longer. Transmission is thought to be through respiratory droplets, with infectivity lasting from one week prior to the rash until the time of onset of the rash. Between 25 and 50% of susceptible household contacts of a case will acquire infection, of whom up to 50% will do so asymptomatically. Therefore, unless women are aware of their potential exposure there is a significant risk of acquisition going undetected.

The incidence of parvovirus infection in pregnancy is approximately 1–2% and vertical transmission occurs in about 50%. The risk of hydrops is low (estimated incidence, 3–6%) but there is an overall excess fetal loss of 10% for infection acquired in the first 20 weeks of pregnancy. The fetus is particularly susceptible to hydrops in the second trimester when haematopoiesis is occurring in the liver. During this time, there is a 34-fold increase in red cell mass and a reduction in the life span of the red blood cells. In pregnant women with proven recent infection, the overall fetal death rate of hydrops or its treatment is 0.6% according to ASID guideline.

Management of proven parvovirus B19 infection in pregnancy

When maternal infection is proven or is highly likely, it is not necessary to prove that vertical transmission has occurred but the fetus should be monitored by frequent ultrasonography. This allows the early detection and assessment of both myocardial dysfunction and fetal hydrops, but more importantly, it makes possible the early detection of fetal anaemia, prior to the development of hydrops. The peak systolic velocity (PSV) of the waveform in the middle cerebral artery can detect moderate to severe fetal anaemia with a sensitivity of 100%, followed by intra-uterine transfusion.

References

- Palasanthiran P, Starr M, Jones C, Giles M [Eds.]. Management of Perinatal Infections [Internet]. Australasian Society for Infectious Diseases (ASID) Inc. 2014. <https://www.asid.net.au/resources/clinical-guidelines> (Accessed Oct 2018) (Keywords Management of perinatal infections)
- Cennimo D. Parvovirus B19 Infection [Internet]. Medscape. 2017. <https://emedicine.medscape.com/article/961063-overview> (Accessed Oct 2018)
- AABB. Human Parvovirus B19 [Internet]. January 2013: TRANSFUSION 2009; 49 (Suppl):107-109S. <www.aabb.org> (Accessed Oct 2018) (Keywords Human parvovirus B19)

DOUGLASS
HANLY MOIR
PATHOLOGY

Our Doctors' Newsletters contain articles written by our pathologists which focus on current issues and recent developments in pathology. Suggestions from you, which we invite wholeheartedly, are the best guarantee that our Doctors' Newsletter becomes a resource of maximum possible interest, information and relevance. If you have any topics you would like to suggest please feel free to contact Dr Ian Chambers (Medical Editor, DHM Publications) at med.ed@dhm.com.au.

Please note, this Newsletter can also be viewed on our website via the Clinician Publications link.

We look forward to hearing about your topics of interest and encourage your participation.

Dr Ian Chambers
MB, ChB, FRCPA, MASM
Medical Editor

DOUGLASS HANLY MOIR PATHOLOGY PTY LIMITED • ABN 80 003 332 858
A subsidiary of SONIC HEALTHCARE

14 GIFFNOCK AVENUE • MACQUARIE PARK • NSW 2113 • AUSTRALIA
P (02) 9855 5222 • **F** (02) 9878 5077
MAIL ADDRESS • LOCKED BAG 145 • NORTH RYDE • NSW 1670 • AUSTRALIA

www.dhm.com.au

DHM-DN-Issue3-2018-D00169