Meningococcal disease is the leading cause of death from infection among children and young people in the UK, and it is difficult to recognise and treat.

In this article...

- Details of the epidemiology and pathophysiology of meningococcal disease
- How to identify the signs and symptoms

Author Anne Dowson is senior sister and clinical educator in paediatric intensive care, St Mary’s Hospital, Imperial College Healthcare Trust.


Meningococcal disease is a leading cause of death in children and young people. It causes two major disease processes, meningococcal septicaemia and meningococcal meningitis, and often results in long-term health complications.

It remains a difficult disease to recognise and treat. This article, part one in a two-part series, discusses the epidemiology of meningococcal disease and explains its pathophysiology as well as signs and symptoms.

Part 2, to be published on 19 March, will review diagnosis, management and prevention.

Despite advances in the recognition and management of meningococcal disease (MD), it remains a leading cause of death in children and young people worldwide (Paul et al, 2011). In the UK, it is the leading cause of death from infectious disease in children aged under five years (National Institute for Health and Care Excellence, 2010).

The term “meningococcal disease” encompasses infection caused by Neisseria meningitidis, also known as meningococcus. It results in either meningococcal septicaemia (infection of the blood) or meningococcal meningitis (inflammation of the meninges), or a combination of both (Driver, 2013). The disease often develops suddenly and its progression can be rapid, requiring prompt recognition and early, effective treatment (Vyse et al, 2013). It can also be notoriously difficult to recognise, as initial symptoms can mimic less-serious viral infections; this presents a real challenge to health professionals (Thompson et al, 2006).

Epidemiology

*N. meningitidis* is a common bacterial commensal found in the nasopharynx of humans (Driver, 2013); carriage of the bacteria has been reported in 8% to as many as 25% of individuals, mainly in adolescents and young adults (Stephens et al, 2007).

Meningococcal disease is not as highly infectious as commonly believed – transmission is through droplet inhalation (Driver, 2013) so close contact is required, for example through household contact or by kissing (Wilcox, 2012). Transmission does not necessarily result in invasive disease and may just lead to colonisation (Stephens et al, 2007).

The factors that cause some individuals to develop symptoms of the disease are not yet wholly understood. However, environmental conditions such as overcrowding, smoking, concurrent viral infections and immune response are all believed to have an effect (Stephens et al, 2007).

*N. meningitidis* is a Gram-negative diplococcus (round bacterium, often seen in the form of two joined cells) with a polysaccharide capsule (Fig 1). Thirteen serogroups of meningococcus have been identified based on different polysaccharide capsules (Stephens et al, 2007); the majority of invasive
The development of specific antibodies is the most important immunoprotective mechanism to combat MD (Pathan et al., 2003). This can be explained by a pattern of incidence that is highest in the first year of life, after the reduction of transplacentally acquired maternal antibodies, and becomes less common throughout childhood and into adulthood as individuals develop their own antibodies (Stephens et al., 2007).

Incidence of MD in Europe and the US across all age groups is reported at 1-3 cases per 100,000 (Halperin et al., 2012; Harrison et al., 2009). However, in sub-Saharan Africa, where epidemics of group A MD are common, it can be as high as one case per 1,000 people (Vyse et al., 2013). The disease is mainly seen in children under four years of age, with a second peak incidence in adolescence (Nadel, 2012).

Young children are particularly susceptible due to their immature immune systems, while adolescents are at increased risk due to the high carriage rates in this age group and social/environmental factors that increase the risk of transmission (Nadel, 2012).

Seasonal patterns are also seen in MD, with incidence peaking in winter months (Health Protection Agency, 2011). This appears to follow increases in upper respiratory viral infection and influenza.

Pathophysiology

Meningococcal disease generally presents as meningitis, septicaemia or a combination of both (Driver, 2013). Other terms used are meningococcaemia (meningococcal septicaemia) and fulminant meningococcal septicaemia (rapidly progressive meningococcal septicaemia with severe shock) (Driver, 2013; Vaina et al., 2013). It has been reported that 15% of children with MD have meningitis alone, 25% have septicaemia alone and 60% have both meningitis and septicaemia (NICE, 2010). The disease can cause variable degrees of illness severity, ranging from a mild bacteremia to severe sepsis with multi-organ failure (Nadel and Kroll, 2007).

Meningococci can evade normal immunological defence mechanisms through the action of the polysaccharide capsule, which prevents the binding of antibodies to the bacteria (Atkinson et al., 2012). This leads to colonisation in some individuals. In other situations, which are not completely understood, the meningococcus is able to pass through the nasopharyngeal mucosa into the bloodstream and subsequently penetrate the blood–brain barrier and penetrate the cerebrospinal fluid (CSF) (Pathan et al., 2003). When meningococci invade, they initiate an immune response largely precipitated by the release of endotoxin (Pathan et al., 2003).

Considering a local inflammatory response makes it easier to understand the more complex inflammatory processes involved in MD (Fig 2). In health, the inflammatory response is beneficial and restricted to the local site of infection but, in a bloodstream infection such as MD, the...
vast quantities of endotoxin in the blood lead to an uncontrolled and exaggerated inflammatory response (Robson and Newell, 2005). The subsequent widespread release of inflammatory mediators causes systemic vasodilation and increased capillary permeability, which ultimately leads to haemodynamic instability (Porth, 2011).

**Septicaemia**

In MD, the shedding of the outer coat of the meningococcus releases endotoxin, which initiates a cascade of events resulting in endothelial (blood-vessel lining) damage (Pathan et al, 2003). Microvascular injury, which occurs systemically, explains the pathophysiological events of meningococcal septicaemia. Widespread increased capillary permeability leads to a hypovolaemic state, where there is loss of albumin, fluid and electrolytes from the intravascular space.

Blood flow through vessels is normally tightly regulated and controlled by endothelial cells, which secrete substances to maintain vessel patency and blood flow (Porth, 2011). In MD, the endothelial lining is disrupted through damage, therefore encouraging platelet adhesion and the initiation of the clotting cascade. In addition to activation of the procoagulant pathway, (which promotes clotting), there is concurrent impairment of the anticoagulant pathways (which prevents clotting); these opposing symptoms are best described by the term "disseminated intravascular coagulation" (Stephens et al, 2007). This is a complication of many disorders including meningococcal septicaemia; it involves uncontrolled clotting, which affects perfusion and causes tissue ischaemia as microvasculature becomes blocked.

Increased clotting means there is a decrease in the availability of clotting factors, leading to uncontrolled bleeding, for example from mucous membranes such as gums or more significant bleeding causing pulmonary haemorrhage; this can exacerbate hypovolaemia and causes the characteristic purpuric rash. Myocardial dysfunction can also occur due to hypovolaemia and resulting loss of cardiac output; it is thought that it is directly related to the negative effects of endotoxin and inflammatory mediators (Pathan et al, 2003).

This systemic inflammatory response leads to a state of organ hypoperfusion and cellular hypoxia. In the absence of oxygen and nutrients, cells use anaerobic respiration in order to produce adenosine triphosphate (ATP), an essential source of energy in the body. Anaerobic respiration is less efficient, producing less ATP and also producing lactic acid as a by-product. These reactions lead to intracellular dysfunc- tion, creating a vicious cycle whereby ongoing hypovolaemia leads to insuffi- cient delivery of oxygen and nutrients, causing cell death, which triggers a further inflammatory response that aggravates fluid loss (Porth, 2011).

In children with meningococcal septicaemia, the symptoms can be on a con- tinuum ranging from a simple uncomplicated infection to severe sepsis with multi-organ dysfunction (Robson and Daniels, 2008). The range of definitions and terminology can cause confusion among health professionals.

**Systemic inflammatory response syndrome (SIRS)** is characterised by the presence of at least two of the following four criteria (Goldstein et al, 2005):

- Core temperature of >38.5°C or <36°C;
- Tachycardia: mean heart rate of more than two standard deviations (SDs) above normal for age – for example, for a one-year-old child, this would represent a heart rate of >180 beats per minute;
- Mean respiratory rate of more than two SDs above normal for age – for example, for a one-year-old child, this would represent a respiratory rate of >34 breaths per minute;
- Leukocyte count elevated or depressed for age.

Sepsis is defined as SIRS with known or suspected infection. Severe sepsis is defined as sepsis with either cardiovascular organ dysfunction, acute respiratory distress syndrome or two or more other organ dysfunctions (Goldstein et al, 2005).

**Meningitis**

Patients with meningitis alone will have minimal signs of the systemic inflammatory response described above, as meningococci may not have proliferated in the blood but localised and proliferated in the CSF.

The inflammatory process occurring within the meninges causes oedema as a result of increased vascular permeability, which can lead to raised intracranial pressure and neuronal damage (Hoffman and Weber, 2009). Patients will have signs of meningeal inflammation and display meningism (neck stiffness, photophobia and headache) (Wilcox, 2012).

**Signs and symptoms**

The signs and symptoms of MD can be difficult to assess, largely because the initial symptoms are often non-specific and may be mistaken for a trivial viral infection (Watkins, 2012). However, a positive outcome from MD is strongly linked to early recognition and treatment of the disease, so the difficulty in recognising it is a cause for concern for many health professionals (Nadel and Kroll, 2007). Thompson et al (2006)

**FIG 3. NON-BLANCHING RASH ON DARK SKIN**
investigated the clinical recognition of MD and found the classic symptoms of non-blanching rash and signs of meningitis develop late in disease progression. They also found that the three most common early signs are:
- Leg pain;
- Cold extremities;
- Abnormal skin colour.

The signs and symptoms for both meningitis and meningococcal septicaemia have common themes but are also relatively non-specific. The non-blanching rash is widely described in the literature and media as a major sign of meningococcal disease; however, as many as 20% of cases present with no rash or a maculopapular rash (Thompson et al, 2006). It is vital that health professionals are alert to the significance of a non-blanching rash but as this is a relatively late sign of MD, they should also be alert to the other less-specific signs and symptoms. In addition, rashes are also found that the three most common early signs are:

- Leg pain;
- Cold extremities;
- Abnormal skin colour.

Children suspected of having MD should be fully examined and their vital signs measured during the initial assessment. The speed with which the illness progresses and the level of parental concern are additional factors to consider as part of the overall clinical judgement (NICE, 2010).

**Septicaemia**

Early signs for septicaemia include fever, vomiting, lethargy, reduced oral intake and leg pain, (NICE, 2010). Box 1 lists further signs and symptoms of meningococcal septicaemia.

**Meningitis**

Common early signs of meningitis include fever, nausea and vomiting, headache, irritability and lethargy (Hoffman and Weber, 2009). More specific signs are neck stiffness, photophobia and altered consciousness level (Watkins, 2012). Box 1 gives a full list of signs and symptoms.

The specific signs of raised intracranial pressure include reduced consciousness level, focal neurological signs, abnormal posture, abnormal pupillary response and papilloedema (NICE, 2010).

**Conclusion**

Nurses must be aware of the signs and symptoms of MD if they are to identify quickly the patients who have the condition to allow for prompt treatment to minimise risk of complication.

Part 2 of this series will discuss the treatment and prevention of MD.

**References**


**USEFUL RESOURCES**

- Meningitis Research Foundation
  www.meningitis.org
- The Meningitis Trust
  www.meningitis-learning.org
- National Meningitis Association (US)
  www.mnaus.org
- National Travel Health Network and Centre's Meningococcal Meningitis factsheet
  tinyurl.com/nathnac-meningitis
- World Health Organization
  Meningococcal Meningitis factsheet
  tinyurl.com/WHO-meningitis

“**We must see challenges as opportunities, not threats**”

Ann Casey  p24