Introduction

The following sections are not intended to be a summary of the individual chapters within this supplement. Rather they are the salient learning points about *Clostridium difficile* infection. It is hoped that these points may serve as a basis with which to understand the risk factors, disease process, management and control of this increasingly reported infection.

Pathogenesis

- Not all strains are equally virulent.
- The cellular mechanism of action of toxins A and B, the glucosylation of Rho family proteins, is identical.
- There is inter-strain heterogeneity of toxin A and B gene sequences.
- Strains producing only toxin B have been detected.
- Much of the pathology may be immunopathology resulting from the action of recruited neutrophils.
- Some individual adults may be naturally immune to the actions of toxin A.
- There is evidence that gut mucus glycopeptides are chemoattractants for *C. difficile*.
- Toxin B may cause diarrhoea in humans.

Diagnosis

- Stools for toxin assay should be tested fresh or stored at 4°C before testing.
- Optimum laboratory investigations include toxin assay and culture on diarrhoeic stools only.
- An alternative strategy involves storage of toxin-positive stools at 4°C or -20°C for later culture for outbreak investigation if necessary.
- Quality-controlled cultural methods must be in place before culture is attempted.
- Commercial kits that detect both toxins A and B have an advantage over those that detect toxin A alone.

Epidemiology and typing

- The population in the community may be exposed to *C. difficile* from a variety of environmental sources but the diseased human gut is the most important reservoir.
- Epidemiological investigations can be adequately performed by a number of typing methods although standardization will be achieved best by a molecular typing method, probably based on PCR ribotyping.
- Carriage of strains from the community into the hospital may result in sporadic cases of *C. difficile*-associated diarrhoea.
- Surveillance data from hospitals in England and Wales shows that one PCR ribotype of *C. difficile* is present in 33 of 58 hospitals and accounts for 57% of all isolates submitted for typing.
- Strains originating from the environment and patients in the community are more diverse than those commonly causing hospital infection.
- Identical types of *C. difficile* may be found in the UK, Belgium, USA and Australia.
- Toxin A-negative/toxin B-positive strains are responsible for 3% of the strains received for typing in England and Wales.
- Phenotypic typing methods dependent on cell surface properties correlate well with one another.
- Strains of the same serogroup can be differentiated into distinct genotypes.

Clinical impact and cost

- Toxin-producing *C. difficile* is the commonest identifiable cause of nosocomial diarrhoea.
- The elderly are the main susceptible patient group.
- Although carriage rates are high in neonates, disease incidence is extremely low.
- Other at-risk patients include the immunosuppressed and those undergoing gastro-intestinal surgery, with severe underlying disease or with a long hospital stay.
The annual cost of *C. difficile* infection to an average-sized district general hospital has been calculated to be approximately £400,000, which includes 2100 lost bed days.

**Antibiotics**

- Previous antibiotic therapy is the main risk factor.
- Cephalosporins and aminopenicillins are the most frequently cited causes of *C. difficile* infection.
- Aminoglycosides, fluoroquinolones and ureidopenicillins have a low propensity to induce *C. difficile* infection.
- The most successful single control measure to reduce symptomatic disease is antibiotic restriction.
- Antibiotic policies need to be policed and reviewed continually.

**Treatment**

- Approximately a quarter of initial symptomatic episodes will resolve spontaneously.
- Metronidazole and vancomycin are similarly effective and the former is the antibiotic of choice when specific treatment is required.
- The majority of symptomatic recurrences of *C. difficile* infection are due to reinfection (with new strains) rather than relapse.
- New treatments are required which address the continued heightened susceptibility of some patients to *C. difficile*.
- Biotherapeutic approaches to treatment are attractive concepts but are largely unsubstantiated.
- Brewer’s yeast and *Saccharomyces boulardii* preparations cannot be assumed to be equivalent.
- Immunological treatment and preventative approaches require further evaluation.

**Infection control**

- *C. difficile* spores may survive for months/years and are often widely distributed in the ward setting.
- Symptomatic patients should be isolated to reduce the dissemination of *C. difficile*.
- Approximately a quarter of patients who symptomatically respond to treatment still have *C. difficile* (culture or toxin)-positive faeces. There is no rationale for the continued isolation of asymptomatic individuals.
- There is a paucity of studies on both hand and environmental disinfection for the removal of *C. difficile*.
- The current recommendation is for handwashing with soap and water.
- Compliance with handwashing is often poor without repeated reinforcement.
- The most important factors governing the efficacy of environmental disinfection are probably the frequency and thoroughness of cleaning.
- Routine environmental decontamination is usually detergent-based, with hypochlorite preparations reserved for faecal spillages.