Helicobacter pylori is a small, spiral-shaped, highly motile gram-negative bacterium that is related to Campylobacter and colonizes non-acid secreting mucus of the stomach and upper intestinal tract [1]. It is urease, catalase, and oxidase positive. Originally called Campylobacter pyloridis and then corrected to Campylobacter pylori, the bacteria were renamed again due to taxonomic data as Helicobacter pylori in a new genus, Helicobacter.

Infection with H. pylori is very common, with approximately 50% of the world’s population infected [2]. Once present, infection will often become chronic and persistent and evidence shows strong correlation between its presence and gastrointestinal diseases like gastritis, peptic ulcer disease, gastric carcinoma and MALT lymphoma [3].

**History**

H. pylori was discovered by Marshall and Warren in 1982 [4] resulting in what was at the time, a divergence from the archetypal understanding of gastric disease. It was commonly thought that stress and diet were the only causes of peptic ulcers however the work of Marshall and Warren identified and isolated Campylobacter-like organisms (CLO) in ulcer biopsies. This discovery was met with much scepticism and resulted in an infamous example of tenacity and scientific endeavour. In 1985 Marshall performed self-inoculation by CLOs and exhibited symptomatic gastritis, which he subsequently treated successfully with metronidazole and bismuth salts, thereby proving their ability to cause gastritis [5]. Their work on H. pylori and the resulting paradigm-shift in the understanding of gastric disease led to them being awarded the Nobel Prize for Medicine in 2005.

**PATHOLOGY**

H. pylori is considered a type I carcinogen and is the most common cause of infection-related cancers, representing 5.5% of the global cancer burden [6].

While in most cases infection with the bacteria is asymptomatic, long-term carriage significantly increases the risk of developing diseases. Studies have reported approximately 10% develop peptic ulcer disease, 1 to 3% develop gastric adenocarcinoma, and 0.1% develop mucosa-associated lymphoid tissue (MALT) lymphoma [7]. The pathogenicity of H. pylori and subsequent risk of cancer is dependent on both the bacterial and host genotypes as well as environmental exposures [8].

Two loci play a part in determining the virulence of H. pylori; the cag pathogenicity island (cag PAI) and vacA. The cag PAI encodes the CagA protein, often used to broadly differentiate between strains, which is tyrosine phosphorylated inside the host cell resulting in increased cellular migration and has been linked to oncogenesis [9]. As well as encoding for CagA, cag PAI also delivers H. pylori protein, often used to lead to staining or culture of biopsy samples [16].

**Diagnosis**

A number of techniques have been developed to diagnose H. pylori infection and can be grouped broadly into invasive and non-invasive methods.

Invasive methods include culture and histology, and require accessing the stomach either by endoscopy or an alternative such as nasogastric tube or oro-gastric brush and obtaining a biopsy. The endoscopic features of H. pylori infection are not specific and difficult to detect using standard methods, however improvements in imaging and microscopy have led to better detection and subsequently better biopsy samples being obtained [14]. Several tests can be performed on the gastric mucosa biopsy: Rapid urease test (RUT), histology, smear (cytology), culture and polymerase chain reaction.

The RUT is similar in principle to the urea breath test described below, however it requires a sample of gastric mucosa or mucus which is brought into contact with urea and the hydrolysis artefacts are detected. The initial test used phenol red which changes from yellow to pink or red as the pH increases due to CO₂ production [15]. This method was evaluated in detail in 1989 by McNulty et al and found to be a cheap and rapid alternative to staining or culture of biopsy samples [16].

A number of staining methods are available for histological investigation of biopsy samples for H. pylori, most commonly a routine haematoxylin and eosin (H&E) stain. In the UK according to the latest guidelines from Public Health England, microscopy is carried out using carbol fuchsin or Sandiford’s stain. Staining and examination of the stained...
Cytology, and more specifically, imprint cytology has been evaluated as a cheap, rapid preparation using Gram or Giemsa stains need only be performed if the culture result is with regard to patient care and treatment options due to its poor performance characteristics. Invasive testing methods are unfeasible for routine testing in laboratories, and while of use in specific cases, non-invasive alternatives should be used. It is clear from looking at existing data that blood serology testing, while being a cheaper option, does not lead to long term savings, with regard to patient care and treatment options due to its poor performance characteristics. The urea breath test is expensive and does not offer much in the way of benefits with regard to sensitivity and specificity which in turn impacts the long term cost savings in patient care. Stool antigen testing seems to combine performance and cost effectiveness. However, the increase of antimicrobial resistance it is becoming more important to conduct further testing once H. pylori infection has been confirmed to provide diagnoses with the resistance/ susceptibility profiles required to make effective treatment decisions. References