Gastroenteritis and Diarrhoea: A syndromic approach to laboratory diagnosis of disease

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INTRODUCTION

Aimed at practising professionals in the field of microbiology Syndromic Algorithm S7 - Gastroenteritis and Diarrhoea is a diagnostic tool which aims to streamline the process of diagnosis by promoting rapid, accurate test selection.

Annually in the UK, there are an estimated 17 million sporadic cases of infectious intestinal disease (IID). UK data from the Infectious Intestinal Disease 2 study 2011 identified Norovirus as the most common cause of IID (followed by Rotavirus, Sapovirus and *Campylobacter* species), and overall emphasised the under diagnosis of enteric viruses in all age groups[1]. The burden of community and healthcare IID is considerable; correct identification and reporting of causative organisms is essential for the development of appropriate control strategies, for improving patient outcomes (by narrowing of antimicrobial treatment), and for reducing the adverse effects of broad-spectrum antibiotics thereby contributing to good antimicrobial stewardship.

The 'Syndromic Algorithm' approach was developed in 2009; the algorithms form part of the pre-analytical stage of the investigative process and recommend the correct pathway for the investigation of a sample, based upon the clinical setting.

S7 gives a comprehensive overview of microbiological tests appropriate for patients presenting with infective gastroenteritis and diarrhoea, identifying correct specimen type and differentiating between suitable primary and secondary testing dependent on patient history (clinical features and epidemiological information)[2]. The algorithm includes molecular, serological, microscopy and culture testing for a wide range of organisms represented in a schematic design for ease of use[2,3].

DEVELOPMENT

The development of the document began in 2009, and the final version was issued on the 23rd of December 2013.

Development of the document included:

- discussion at five UK SMI National Working Group meetings
- two rounds of wide consultation
- twenty two comments were received from:
  - National Health Service, Hospital and Public Health England (PHE) clinical laboratories in England, Scotland and Wales
  - PHE reference laboratories and departments
  - PHE gastrointestinal infections programme board
  - PHE Health Protection Services and Health Protection Units
  - Centre for Environment, Fisheries and Aquaculture Science
  - Overseas laboratories

The PHE (formerly Health Protection Agency) gastrointestinal programme board carried out an audit of enteric laboratory practice in England in 2012. The audit compared laboratory practice to the standards set out in the following UK SMI documents:

- B 10 - Processing of Faeces for *Clostridium difficile*
- B 30 - Investigation of Faecal Specimens for Enteric Pathogens
- B 31 - Investigation of Specimens other than Blood for Parasites

The audit concluded that the UK SMIs needed to be more prescriptive with regards to test selection criteria for faecal samples[4]. The full report can be found at: http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317134944297

S7 aims to collate this criteria information in one document, supported by the associated UK SMIs for detailed information on testing methodology.

DEVELOPMENT AND QUALITY ASSURANCE

UK SMIs are produced by the Standards Unit, and are developed, reviewed and updated through a wide consultation process with users and other stakeholders. To subscribe to consultations alert get to http://www.hpa.org.uk/smi

The process follows the AGREE tool and resulting documents reflect best evidence based practice. Where evidence is not available, the documents are based on national working group consensus decisions.

The Standards Unit has a well established, robust quality system where continual improvement is embedded within the work system.

- The National Institute for Health and Care Excellence (NICE) has accredited the process used to produce UK SMIs.
- The process for the development of SMIs is also certified to ISO 9001:2008.

NICE accredited www.nice.org.uk/accreditation

S7: GASTROENTERITIS AND DIARRHOEA – SYNDROMIC ALGORITHMS[1-4]

Figure 1. UK SMI S7 – Gastroenteritis and Diarrhoea ~Sporadic Cases

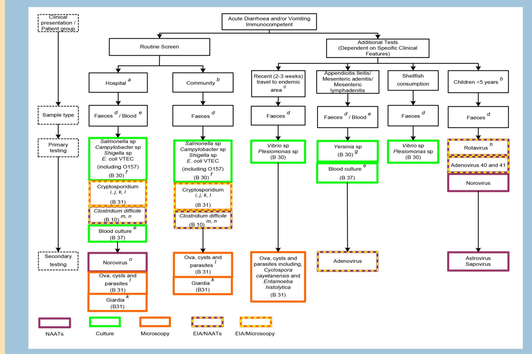


Figure 2. UK SMI – S7 Gastroenteritis and Diarrhoea ~ Outbreaks

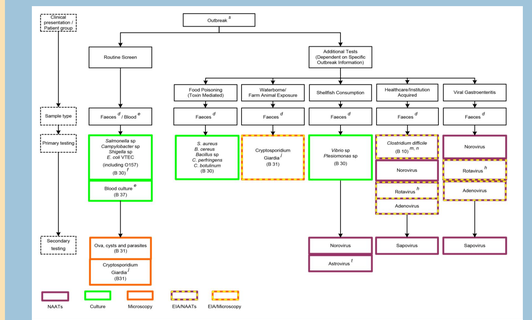
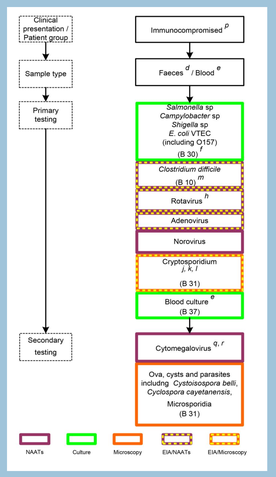


Figure 3. UK SMI – S7 Gastroenteritis and Diarrhoea ~ Immunocompromised



FOOTNOTES

a) For gastroenteritis and diarrhoea acquired in a hospital setting, clinicians and laboratories should consult local policy on the "three day rule" for the microbiological investigation of faecal samples in their department.
Laboratories considering applying the "three day rule" should undertake analysis of their submission and positivity data and undertake an informed risk assessment.
Clusters of diarrhoea cases must be investigated.
The "three day rule'' does not apply to *C. difficile*. Testing for *C. difficile* is required for inpatients as soon as infective diarrhoea is suspected.
The "three day rule'' suggests that faecal samples from patients should not undergo microbiological investigation except under the following circumstances:
- Those inpatients developing diarrhoea within three days of admission
- Adults with nosocomial diarrhoea only if one of the following is applicable:
  - Aged 65 or more with pre-existing disease causing permanently altered organ function.
  - Patients who are HIV positive.
  - Patients with neutropenia.
  - Suspected nosocomial outbreak (eg *Salmonella*).
- Those with suspected non-diarrhoeal manifestations of enteric infections.

b) The algorithm recognises that sporadic causes of viral infection managed in the community will only be diagnosed in those aged <5 years.

c) Endemic areas for the following organisms include:
- *Vibrio* species and *Plesiomonas shigelloides*: Asia, Africa and Latin America.
- *Cyclospora cayetanensis*: Tropics including Haiti, Guatemala, Peru and Nepal.
- *Entamoeba histolytica*: Central and South America, Africa, and India.

d) Methods with varying sensitivities and specificities for testing of faeces are available. Alternative diagnostic techniques may have potential advantages and disadvantages and should therefore be evaluated and validated prior to use. Molecular methods (eg multiplex PCR) and enzyme immunoassays (EIA) may perform better than plate based methods, and should therefore be considered for use where available following validation to ensure appropriate clinical interpretation.

FOOTNOTES CONTINUED

e) Blood cultures are only recommended if the patient presents as systemically unwell.

f) Testing for other organisms such as non O157 Verocytotoxic *E. coli* (non O157 VTEC), *Yersinia enterolitica*, *Yersinia pseudotuberculosis*, and *Aeromonas* species may be required depending on clinical details. Other organisms such as Enterotoxigenic *E. coli* (ETEC), Enteropathogenic *E. coli* (EPEC), Enteroinvasive *E. coli* (EIEC), *Clostridium septicum* and *Edwardsiella tarda* may be isolated through routine investigations.

g) Culture after discussion with medical microbiologist.

h) Testing criteria: Laboratories may opt to test only during the seasonal increase.

i) Testing criteria: All symptomatic patients (presenting with stools that take the shape of container) should be tested for *Cryptosporidium* infection.

j) The sensitivity of modified Ziehl Neelsen microscopy for detecting Cryptosporidia is significantly less than for other tests.

k) Giardia has been shown to have similar prevalence to Cryptosporidium; laboratories may wish to consider adding Giardia to the primary testing set based on local risk assessment and operational capabilities.

l) Ova, cysts and parasites (OCP) are not routinely included in the primary testing set as yields are extremely low. If more parasitology is required, other than Cryptosporidium and Giardia, a request for OCP should be submitted following consultation with a microbiologist.

m) A two stage testing approach is recommended by the Department of Health. Refer to current guidelines.

n) Testing criteria: Hospital inpatients ≥ 2yrs, Community ≥ 65yrs or < 65yrs where clinically indicated.

o) Consider testing for Norovirus on hospital inpatients of all age groups. If a Norovirus outbreak is suspected, consider submitting stool samples as early as possible during the acute phase of the illness.

p) Patients who are immunocompromised include those with inherited or acquired abnormalities of the immune system and patients who have had organ transplant, immunosuppressive therapy, or steroid treatment. Not all tests in this flowchart will be appropriate for all immunocompromised patients. Discussion with a clinician is required to establish the degree to which the patient is immunocompromised, and therefore the relevance of each test. Cross refer to outbreak algorithm for additional tests if an outbreak is suspected.

q) Nucleic Acid Amplification Tests (NAATs) testing on blood and/or faecal samples. Consider biopsy.

r) Varicella zoster virus and herpes simplex virus infections may also cause colitis in the immunocompromised. Epstein Barr virus related lymphoproliferative disease may present with gastrointestinal symptoms.

s) All outbreak samples should be discussed with the microbiologist and the outbreak response lead to agree appropriate tests based on the clinical and epidemiological information available. The outbreak investigation would usually be led by the infection control team (hospital outbreaks) or the public health team (community outbreaks).

t) Astrovirus may also be considered; seafood-related outbreaks have been documented.

DISCUSSION

The inclusion of clinical details is essential to the optimal processing of samples, and it is recognised that the algorithms perform best when sufficient, relevant, clinical details are provided at the time of sample submission. The following information, as well as patient identifiable information, should be recorded on the request form:

- acute/outbreak case
- immune status
- healthcare or community acquired. If patient is hospitalised, date of admission and date of symptom onset should be included
- recent foreign travel (2-3 weeks) including location
- waterborne infection/farm animal exposure
- food intake (eg shellfish, chicken)
- recent antibiotic use
- other information (eg suspected food poisoning, viral gastroenteritis, contact with cases)

The history of the patient should identify risk factors for unusual causes of acute gastroenteritis, and non-infective and any extra-intestinal causes. It should be noted that the algorithms do not cover the following:

- investigation of *Helicobacter pylori, Mycobacterium* species, viral hepatitis or algal toxins
- investigation of overgrowth with *Clostridium perfringens* or *Candida* species
- further management of the patient with infective gastroenteritis
- faecal screening for antibiotic resistant bacteria

In addition to the point raised above National surveillance programmes for specific organisms should be taken into consideration when using the algorithm.

Viewing figures of the document on the UK SMI webpages during development and following issue are shown below in Figure 4. Following an initial spike post issue, visits to the S7 webpage has subsequently decreased. In March 2014 visits to the webpage were at around 150 per month, which although above the majority of it's associated documents, was well below B30 - Investigation of faecal specimens for enteric pathogens.

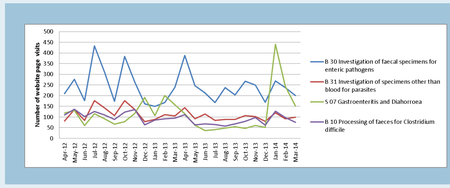


Figure 4. UK SMI Webpage Visits for S7 and associated documents

CONCLUSIONS

S7 is a useful diagnostic tool for the rapid and accurate investigation of gastroenteritis and diarrhoea, streamlining diagnosis, promoting time and cost efficiency. The algorithms rely on the receipt of accurate patient information, and submission of this to laboratories should be encouraged.

The algorithm should be presented to as wide an audience as possible, and its use on the website monitored over the coming year. It's viewing should, as an over arching algorithm, equal that of B30 – Investigation of faecal specimens for enteric pathogens. Ideally a clinical audit should be carried out to evaluate its uptake in laboratories across the UK.

To ensure that the algorithms are up to date and relevant, it will be reviewed in three years time.

ACKNOWLEDGEMENTS

UK SMIs are developed in equal partnership with PHE, the NHS, Royal College of Pathologists and professional organisations.

A list of partner organisations can be found via the following link.
http://www.hpa.org.uk/SMI/Partnerships

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