

## CPD study pack

**July/August 2021;265(1850)**

The study pack contains this month's CPD exercise plus all relevant articles:

- Multidisciplinary care is key in chronic pancreatitis
- Prevention, diagnosis and treatment of colorectal cancer
- Early recognition of hyperemesis gravidarum

### **Fillable PDF templates\***

- CPD exercise is a fillable PDF

### **CPD prompt and framework templates**

- Journal article ● Case review ● Audit

\* Adobe reader app needed for ipad etc  
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# Practitioner CPD exercise

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## Show impact

- Collection of data
- Practice audit to show improved care
- Case studies
- Implement a protocol
- Prescribing review
- Educational meetings
- Significant event audit
- Practice meeting
- Implement a new service
- Take on new role
- Significant event audits
- Change with feedback from patients and/or colleagues

## Further options for sessional GPs

- Self audit of own practice:
  - Record-keeping
  - Referrals for investigations
  - Prospective condition based reviews
  - Random case analysis with colleagues
  - Review of telephone triage outcomes
- Update drugs in emergency bag

## CPD Framework

Online all articles are associated with CPD prompts/frameworks to written reflection:

## Adobe fillable PDFs

- Article review framework
- Case review framework
- Audit framework

## Word documents

- Reflection on a journal article
- Stages of reflection on a situation
- Team reflection

## CHRONIC PANCREATITIS

### 1 Which of the statements are true?

**A** Smoking is an independent risk factor for chronic pancreatitis

True ☐ False ☐

**B** A diagnosis of chronic pancreatitis is usually confirmed by biopsy

True ☐ False ☐

**C** Screening for diabetes should include HbA<sub>1c</sub> and a fasting glucose measurement

True ☐ False ☐

**D** Pancreatic enzymes may be normal or only mildly elevated

True ☐ False ☐

**E** Most patients who are dependent on alcohol will develop chronic pancreatitis

True ☐ False ☐

### 2 List three potential complications of pancreatic pseudocysts.

### 3A List two investigations that should be carried out during an annual review in primary care.

### 3B Give three examples of lifestyle advice to reduce progression of the condition.

### 4 List any changes to your clinical practice that you may make having read this article.

## COLORECTAL CANCER

### 5 Which of the statements are true?

**A** High normal platelet counts in men are associated with a higher risk of colorectal cancer

True ☐ False ☐

**B** Patients presenting with symptoms that could be caused by colorectal cancer may recently have had a normal faecal immunochemical test (FIT)

True ☐ False ☐

**C** Patients with a positive FIT result during bowel screening will be invited for flexible sigmoidoscopy

True ☐ False ☐

**D** Type 2 diabetes and inflammatory bowel disease both increase the risk of colorectal cancer

True ☐ False ☐

**E** A diet low in fibre is a key risk factor for colorectal cancer

True ☐ False ☐

### 6A List three common presenting symptoms of colorectal cancer.

### 6B List three less obvious presentations.

### 7 Following sphincter preserving surgery for rectal cancer patients may develop low anterior resection syndrome. List four common symptoms.

Impact credits =

Impact credits =

**8 List any changes to your clinical practice that you may make having read this article.**

## HYPEREMESIS GRAVIDARUM

**9 Which of the statements are true?**

**A** Hyperemesis gravidarum is a diagnosis of exclusion  
True ☐ False ☐

**B** A history of hyperemesis gravidarum in a previous pregnancy is the strongest independent risk factor  
True ☐ False ☐

**C** Hyperemesis gravidarum is a recognised risk factor for VTE  
True ☐ False ☐

**D** Onset of symptoms generally occurs after 10 weeks' gestation  
True ☐ False ☐

**E** Acute kidney injury is a potential serious complication of hyperemesis gravidarum  
True ☐ False ☐

## 10 Complete the statement.

A non-urgent referral to an

should be made for all women with hyperemesis gravidarum to rule out a

or

pregnancy and confirm

Women who have persistent symptoms into the

trimester of pregnancy should have

antenatal care and serial fetal

**11 List three situations where urgent referral to secondary care is warranted.**

**12 List any changes to your clinical practice that you may make having read this article.**

## Answers

**HYPEREMESIS GRAVIDARUM**  
9 **A** True **B** True **C** True **D** False (between the 4th and 7th week) **E** True  
10 early pregnancy unit; molar; multiple; viability; second; consultant-led; growth ultrasound  
11 Persistent symptoms despite oral antiemetic treatment; weight loss < 5% of prepregnancy weight; medical comorbidities needing oral treatment and/or any clinical concerns needing specialist input  
12  
should be made for all women with hyperemesis gravidarum to rule out a  
or  
pregnancy and confirm  
Women who have persistent symptoms into the  
trimester of pregnancy should have  
antenatal care and serial fetal

**CHRONIC PANCREATITIS**  
1 **A** True **B** False **C** True **D** True **E** False (10%)  
2 Pain; bleeding; rupture; infection; obstruction  
3 **A** Blood tests to assess liver function and markers of malnutrition; DEXA scans  
3 **B** Abstinence from alcohol; quitting smoking; weight-bearing exercise to reduce the risk of osteoporosis  
4 **A** True **B** True **C** False (colonoscopy) **D** True **E** True  
5 **A** True **B** True **C** False (colonoscopy) **D** True **E** True  
6 **A** Persistent blood in faeces; persistent change in bowel habit; persistent lower abdominal pain  
6 **B** Unexplained weight loss; tiredness for no reason; iron deficiency anaemia detected on blood testing  
7 Increased bowel opening; urgency; incontinence; the feeling of incomplete emptying; fragmentation of bowel opening (small amounts little and often); difficulty in differentiating between gas and stool

## Multidisciplinary care is key in chronic pancreatitis

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# Multidisciplinary care is key in chronic pancreatitis

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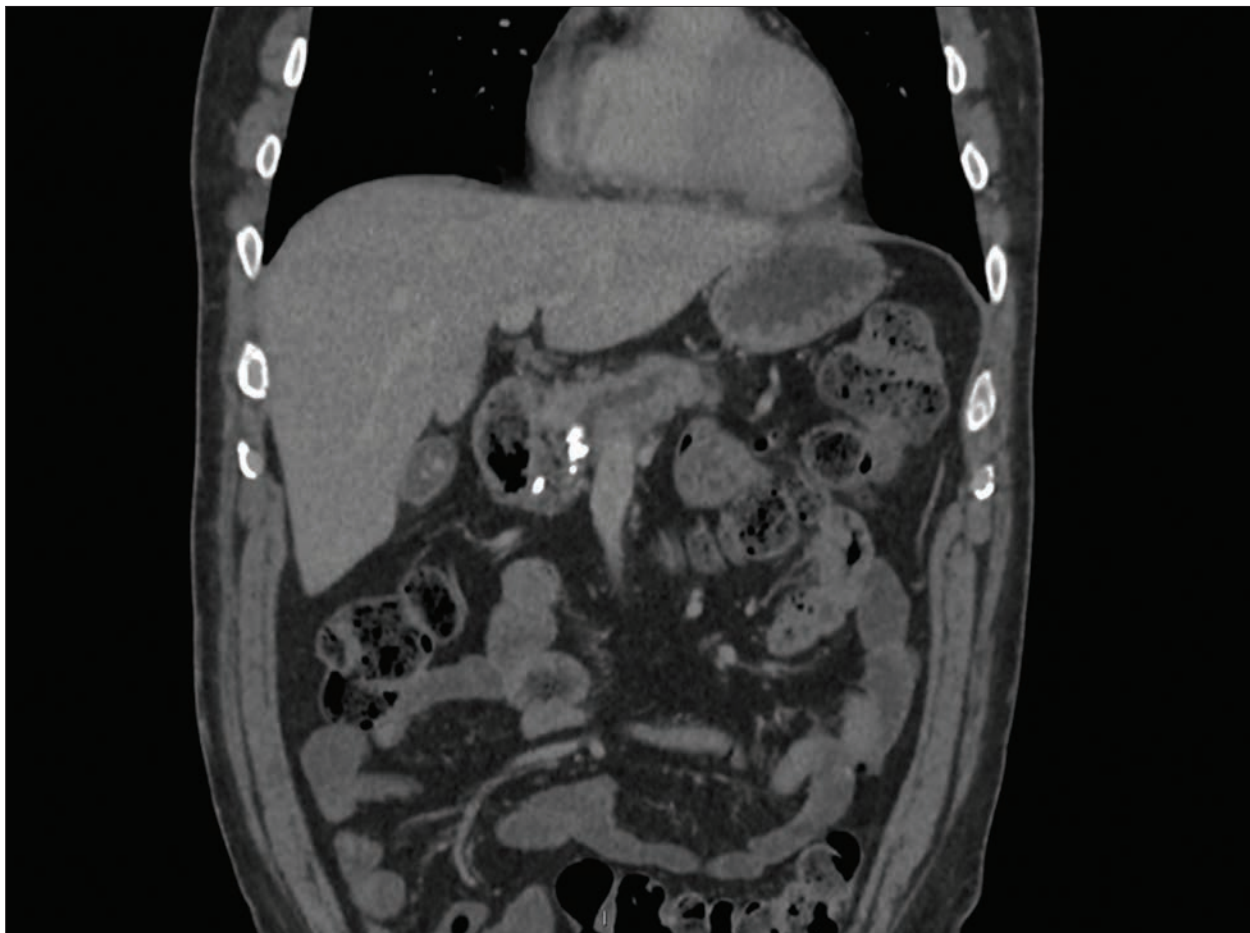
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## FIGURE 1

Coronal view of a contrast-enhanced CT scan demonstrating chronic calcific pancreatitis. Calcified stones are visible in the head of the pancreas

**What** are the common causes and risk factors?

**What** are the potential complications?

**How** should patients be followed up?



## IN CHRONIC PANCREATITIS CHRONIC INFLAMMATION OF THE PANCREAS RESULTS IN IRREVERSIBLE

injury and fibrosis. This can lead to local and systemic complications.

The annual incidence of chronic pancreatitis in Europe, based on estimates published in 2010, is 6 to 7 per 100,000 population per annum,<sup>1</sup> while NHS Hospital Episode Statistics data in England indicate that there are 8.6 hospital admissions per 100,000 population due to the condition.<sup>2</sup> In the UK, there are approximately 12,000 admissions due to chronic pancreatitis per year.<sup>3</sup> Mortality rates in patients with

chronic pancreatitis are five-fold greater than in the general population.<sup>4</sup>

Chronic pancreatitis can be difficult to recognise as its clinical features overlap with other gastroenterological disorders, and ineffective management can have significant effects on quality of life.<sup>5</sup>

The presenting features, diagnostic investigations and evidence-based management strategies for chronic pancreatitis have been detailed in recent NICE<sup>6,7</sup> and international guidelines,<sup>8,9,10</sup> to aid early recognition, prompt referral and appropriate follow-up in primary care.

## CAUSES AND RISK FACTORS

The diverse range of aetiologies and risk factors for chronic pancreatitis are summarised by the TIGAR-O classification system (see table 1, p12). For most of these aetiologies, the common pathological pathway is increased trypsin activation in the pancreas leading to inflammation, fibrosis and obstruction of pancreatic ducts.

The most common causal factor in chronic pancreatitis is excess alcohol consumption. In western populations, studies indicate it is a causal factor in 45-82% of cases.<sup>11,12</sup> However, only 10% of those dependent on alcohol develop >>

# SYMPOSIUM GASTROENTEROLOGY

## CHRONIC PANCREATITIS

chronic pancreatitis,<sup>12</sup> highlighting the complex interplay between alcohol and other genetic and environmental risk factors in disease development. NICE cautions against assuming chronic pancreatitis is alcohol-related in patients 'just because they drink alcohol.' Tobacco smoking is an independent risk factor for chronic pancreatitis.<sup>12</sup>

Genetic mutations, in the PRSS1, SPINK1 and CFTR (as part of cystic fibrosis) genes can lead to hereditary chronic pancreatitis, which is inherited in

a Mendelian manner. Idiopathic disease, where no clear associated cause can be identified, accounts for 20-30% of cases.<sup>13</sup>

### CLINICAL PRESENTATION

The typical presenting feature is upper abdominal pain which may radiate to the back.<sup>6</sup> Pain can be continuous with acute flares or episodic. The pain is commonly triggered or exacerbated by eating or alcohol consumption. The pain is caused by pancreatic inflammation and pancreatic duct obstruction due to strictures and stone formation (see figure 1, p11). Patients may also present with relapsing acute pancreatitis.

Inflammation of the pancreas can also lead to distal bile duct strictures resulting in biliary obstruction with jaundice. Disruption of the pancreatic duct from previous episodes of pancreatitis can lead to pseudocyst formation (see figure 2, p13), which may be asymptomatic but can result in pain, infection or gastric outlet obstruction. Pancreatic pseudocysts are fluid-filled sacs surrounded by granulation tissue which can bleed, rupture, become infected or cause obstruction of the biliary tree or duodenum.

Chronic pancreatitis is also a common incidental finding on routine imaging of the abdomen, and even with advanced radiological features of chronic pancreatitis the patient may be entirely asymptomatic.

Symptoms resulting from pancreatic exocrine insufficiency (PEI) include

weight loss and steatorrhoea, and patients may have other clinical signs of malnutrition. Steatorrhoea indicates a significant loss of exocrine function as it occurs only when lipase secretion is reduced by more than 90-95%.<sup>15</sup> Endocrine insufficiency will lead to diabetes mellitus and its associated symptoms.

On examination, patients may have signs of chronic liver disease (suggestive of excess alcohol consumption), upper abdominal tenderness or abdominal distention due to a pseudocyst.<sup>6</sup>

The presenting features of chronic pancreatitis are non-specific and overlap with other gastrointestinal conditions leading to a wide differential diagnosis (see table 2, below left).

A medical history including a thorough account of alcohol consumption, tobacco smoking, previous hospital admissions with abdominal pain and family history is invaluable in determining the index of suspicion for chronic pancreatitis.

Pancreatic cancer is difficult to distinguish clinically from chronic pancreatitis as there are overlapping features such as weight loss, change in bowel habit and jaundice. Chronic pancreatitis is also a risk factor for pancreatic cancer.

Patients aged 40 and over with jaundice and those aged 60 and over with weight loss and one other specified symptom related to pancreatic cancer should be referred along a suspected cancer referral pathway for investigation of pancreatic cancer.<sup>16</sup>

In those not meeting the criteria for referral along a suspected cancer pathway, but with evidence of a complication of chronic pancreatitis (e.g. biliary obstruction or malabsorption leading to weight loss and diarrhoea) NICE advises urgent referral to gastroenterology. This will facilitate timely investigation and help exclude malignancy promptly.<sup>6</sup>

### INVESTIGATIONS AND DIAGNOSIS

In patients with suspected chronic pancreatitis, the aims of investigations are to confirm the diagnosis, demonstrate any sequelae and to determine the underlying cause.

Biopsy is almost never undertaken owing to the risk of precipitating pancreatitis so imaging is used instead to provide evidence of characteristic features such as calcification, atrophy or pancreatic duct dilation.

CT is the first-line imaging modality for chronic pancreatitis.<sup>8</sup> It has similar

**Table 1**

#### TIGAR-O version 2 classification system for chronic pancreatitis risk factors and aetiologies (adapted from Whitcomb 2019)<sup>14</sup>

##### Toxic-metabolic

- Alcohol
- Tobacco smoking
- Hypercalcaemia
- Hypertriglyceridaemia
- Medications (e.g. azathioprine)
- Chronic kidney disease
- Metabolic syndrome
- Oxidative stress associated factors (post-irradiation/chemotherapy, ischaemia)
- Other toxins (scorpion venom, anticholinesterase pesticides)

##### Idiopathic

- Early onset (< 35 years of age)
- Late onset (≥ 35 years of age)

##### Genetic

- Autosomal dominant (e.g. PRSS1 mutations)
- Autosomal recessive (e.g. CFTR, SPINK1 mutations)
- Complex genetics (non-Mendelian, complex genotypes ± environment)
- Modifier genes
- Hypertriglyceridaemia syndromes
- Rare, non-neoplastic pancreatic genetic variant associated syndromes

##### Autoimmune pancreatitis (AIP)

- AIP type 1 – IgG4 related disease
- AIP type 2

##### Recurrent and severe acute pancreatitis

- Recurrent acute pancreatitis
- Severe acute pancreatitis

##### Obstruction

- Pancreatic divisum
- Ampullary stenosis
- Main duct pancreatic stones
- Widespread pancreatic calcifications
- Main pancreatic duct strictures
- Localised mass causing duct obstruction (e.g. tumour)

**Table 2**

#### Differential diagnosis of chronic pancreatitis (adapted from Jalal et al, 2018)<sup>8</sup>

##### Hepatobiliary

- Acute cholecystitis
- Biliary colic
- Acute pancreatitis
- Pancreatic cancer

##### Gastrointestinal

- Irritable bowel syndrome
- Peptic ulcer disease
- Gastroparesis
- Intestinal obstruction, ischaemia or infarction

##### Other

- Abdominal aortic aneurysm
- Thoracic radiculopathy
- Myocardial infarction
- Postherpetic neuralgia

diagnostic accuracy to MRI and endoscopic ultrasound (EUS), with a sensitivity of 75% and specificity of 91%,<sup>17</sup> and has the advantage of quantifying the presence of pancreatic calculi (which are usually calcified unlike gallstones), and parenchymal calcification.

MRCP (magnetic resonance cholangiopancreatography) has an advantage over CT in elucidating the pancreatic ductal anatomy in much greater detail than CT, which is useful in determining if there is pancreatic obstruction and anatomical anomalies such as pancreas divisum. Abdominal ultrasound can only diagnose chronic pancreatitis at an advanced stage<sup>9</sup> but can be useful to rule out differential diagnoses as well as eliciting the presence of gallbladder gallstones as a potential precipitant for previous acute pancreatitis.

PEI should be looked for in all patients using a stool sample for faecal elastase-1 (FEL-1) and by performing a nutritional assessment, measuring body mass index (BMI), prothrombin time, albumin, haematinics, calcium, phosphate, magnesium and fat-soluble vitamins (A,D, E and K).<sup>8,9</sup> Screening for diabetes mellitus should be considered in all patients and should include both HbA<sub>1c</sub> and a fasting glucose measurement as a normal HbA<sub>1c</sub> does not exclude diabetes in this patient group.<sup>9</sup> Pancreatic enzymes may be only mildly elevated or normal in chronic pancreatitis and so serum amylase is not a useful measurement in these patients.<sup>6</sup>

In cases where the aetiology is not clear from the history, calcium and triglyceride levels should be measured and serum IgG4 to check for autoimmune pancreatitis.<sup>9</sup> In patients under 35 years of age, clinical and genetic testing for hereditary causes

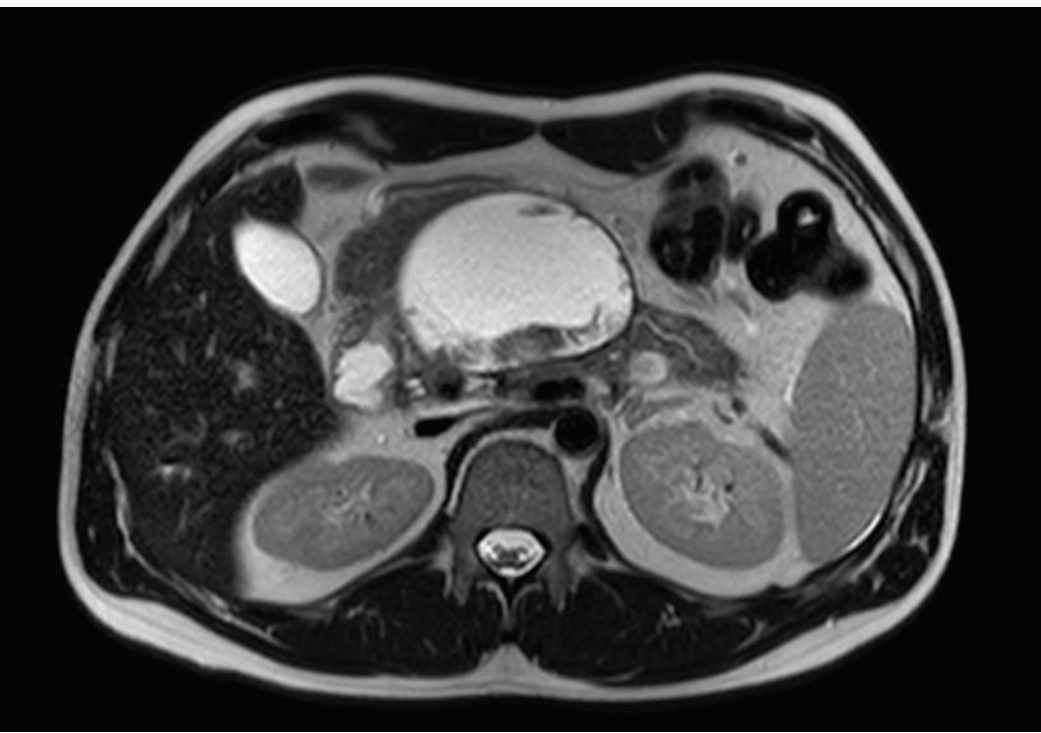


**FIGURE 2** Axial view of a T2-weighted MRI scan showing a pancreatic pseudocyst

including cystic fibrosis, PRSS1 and SPINK1 mutations should be carried out.<sup>8</sup>

NICE recommends urgent referral to gastroenterology if the patient presents with a complication of chronic pancreatitis (e.g. biliary obstruction). Otherwise, a routine referral is appropriate and GPs can conduct initial blood tests (e.g. liver function tests) and an abdominal ultrasound to rule out differential diagnoses while awaiting specialist input.<sup>6</sup> This may present an opportunity for GPs to perform the biochemical investigations for functional abnormalities, as above, and identify patients requiring input from diabetologists or dietitians.

**COMPLICATIONS**

The complications of chronic pancreatitis can be divided into local and systemic (see table 3, left). The risk of pancreatic cancer in chronic pancreatitis has been shown to be 4% at 20 years after diagnosis.<sup>18</sup> This risk is higher in those with a ≥ 60 pack-year smoking history, in those who are older at age of diagnosis and is much higher in those with hereditary pancreatitis.<sup>19,20</sup>

Pseudocysts < 4 cm in size are likely to regress spontaneously while larger ones are more likely to lead to further complications, as described earlier.<sup>21</sup>

Chronic pancreatitis leads to type 3c diabetes mellitus which is present in 5-10% of patients with the condition<sup>8</sup> and is difficult to control, often requiring insulin.<sup>22</sup>

Almost two-thirds of patients with chronic pancreatitis have osteoporosis or osteopenia and therefore this patient group has a high risk of fragility fractures.<sup>23</sup>

**MANAGEMENT**

The management of chronic pancreatitis requires a multidisciplinary team (MDT) approach involving GPs, gastroenterologists, surgeons, radiologists, dietitians and diabetologists. Treatment approaches aim to control pain, manage complications and target the underlying cause.

Pain has a significant impact on the quality of life of chronic pancreatitis patients.<sup>24</sup> NICE recommends initial treatment in primary care with paracetamol or ibuprofen, with progression to codeine if pain persists.<sup>6</sup> Additionally, abstinence from alcohol has beneficial effects on pain symptoms.<sup>25</sup> If these initial measures are unsuccessful referral to gastroenterology, pancreatobiliary surgery or a specialist pain clinic is required.<sup>6</sup>

Tricyclic antidepressants (e.g. amitriptyline) and neuropathic painkillers (e.g. pregabalin) can be started as further medical management in secondary care.

Psychiatric comorbidities in patients with chronic pancreatitis affect their level of pain and their quality of life. A recent study showed the prevalence of anxiety and depression (defined as

| Table 3                                               |  |
|-------------------------------------------------------|--|
| Complications of chronic pancreatitis                 |  |
| Local                                                 |  |
| ● Pancreatic cancer                                   |  |
| ● Pancreatic pseudocyst                               |  |
| ● Biliary obstruction                                 |  |
| ● Duodenal obstruction                                |  |
| ● Splenic vein thrombosis                             |  |
| Systemic                                              |  |
| ● Pancreatic exocrine insufficiency                   |  |
| ● Endocrine insufficiency (type 3c diabetes mellitus) |  |
| ● Metabolic bone disease                              |  |
| ● Ascites and pleural effusions                       |  |

## key points

### SELECTED BY

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**In chronic pancreatitis chronic inflammation of the pancreas results in irreversible injury and fibrosis.** This leads to local and systemic complications. The annual incidence in Europe is estimated to be 6-7 per 100,000 population. Mortality rates in patients with chronic pancreatitis are five-fold greater than in the general population. The most common causal factor is excess alcohol consumption, estimated to be responsible for 45-84% of cases. However, it is important not to assume that chronic pancreatitis is alcohol-related just because the patient drinks alcohol. Tobacco smoking is an independent risk factor. Gene mutations can lead to hereditary chronic pancreatitis, (autoimmune pancreatitis type 1 is associated with increased levels of IgG4), and idiopathic disease, where no clear cause can be identified, accounts for 20-30% of cases.

**Chronic pancreatitis can be difficult to recognise as its clinical features overlap with other gastrointestinal disorders.** The typical presenting symptom is intermittent or continuous upper abdominal pain which may radiate to the back. The pain is commonly triggered or exacerbated by eating or alcohol consumption. Distal bile duct strictures may cause biliary obstruction and jaundice. Disruption of the pancreatic duct from previous episodes of pancreatitis can lead to pseudocyst formation. Pseudocysts may be asymptomatic but can result in pain, infection or gastric outlet obstruction. Pancreatic exocrine insufficiency (PEI) may cause weight loss and steatorrhoea, and endocrine insufficiency will lead to diabetes mellitus and its associated symptoms.

**NICE recommends urgent referral to gastroenterology** if the patient presents with a complication of chronic pancreatitis such as biliary obstruction. Otherwise, a routine referral is appropriate; while awaiting specialist input, GPs can conduct initial blood tests and request an abdominal ultrasound to rule out differential diagnoses. Pancreatic cancer is difficult to distinguish clinically from chronic pancreatitis, and an urgent suspected cancer referral may be indicated if the NICE criteria are met.

**CT is the first-line imaging modality. MRCP has an advantage over CT in elucidating the pancreatic ductal anatomy in greater detail.** PEI should be looked for with a stool sample for faecal elastase-1 and a nutritional assessment. Screening for diabetes mellitus should include both HbA<sub>1c</sub> and fasting glucose as a normal HbA<sub>1c</sub> does not exclude diabetes in this patient group. Serum amylase measurement is not useful in chronic pancreatitis.

**Alcohol abstinence and smoking cessation are vital** to reduce progression of the disease. Weight-bearing exercise reduces the risk of osteoporosis. Patients should have 6 monthly diabetes screening and yearly DEXA scans. NICE recommends initial pain management with paracetamol or ibuprofen, with progression to codeine if pain persists. Tricyclic antidepressants and neuropathic pain medication may be prescribed in secondary care.

a HADS score  $\geq 7$ ) among chronic pancreatitis patients to be 47% and 39% respectively.<sup>26</sup>

Patients with these psychiatric comorbidities had significantly higher pain prevalence and pain severity and lower quality of life scores. Early recognition and management of comorbid anxiety and depression can improve pain management and quality of life in these patients.

Endoscopic or surgical approaches are used to treat pain resulting from pancreatic duct obstruction.

For uncomplicated chronic pancreatitis with an obstructed main pancreatic duct, most commonly due to stones or pancreatic duct strictures, endoscopic retrograde cholangiopancreatography (ERCP) is recommended.<sup>10</sup>

Extracorporeal shock-wave lithotripsy (ESWL), or more recently direct pancreatectomy and electrohydraulic lithotripsy, is recommended for calculi within the distal pancreatic duct where endoscopic extraction therapy has failed.<sup>10</sup>

EUS-guided coeliac plexus block can be used but its efficacy is short-lived with the majority of patients experiencing recurrent pain after 24 weeks.<sup>27</sup> Surgical options including decompression and resection can be undertaken for pain relief and have been shown to be superior to endoscopic therapy for long-term pain relief.<sup>28</sup> NICE guidance suggests surgery as a first-line treatment in painful chronic pancreatitis with obstruction of the main pancreatic duct.<sup>7</sup> However, comorbidities and surgical and anaesthetic risk need to be weighed up before a decision is made on surgery.

Chronic pancreatitis related pseudocysts should be treated if they are symptomatic or present with complications. Endoscopic drainage is used in preference to surgery for uncomplicated chronic pancreatitis related pseudocysts that are within endoscopic reach.<sup>10</sup>

For patients with chronic pain or symptomatic pseudocysts from chronic pancreatitis it is recommended that the imaging is reviewed in a hepatobiliary MDT meeting to determine the best strategy for management of pancreatic calculi and strictures: conservative management, endoscopic approaches or surgery.

Patients with PEI and clinical or laboratory evidence of malabsorption should be treated with pancreatic enzyme replacement therapy (PERT).<sup>29</sup> Oral PPIs can be used to improve PERT

efficacy.<sup>29</sup> NICE suggests considering assessment by a dietitian for all patients with chronic pancreatitis,<sup>7</sup> which can help improve patients' nutritional status and highlight patients requiring enteral tube feeding.<sup>9</sup> Guidelines have recently been published on PEI with useful advice on how PERT should be taken.<sup>30</sup> Diabetes in chronic pancreatitis is difficult to manage; up to 25% of patients have 'brittle diabetes' requiring specialist input.<sup>6,9</sup>

Abstinence from alcohol and smoking cessation are vital to reduce progression of the disease and these measures should be advised in primary care, alongside weight-bearing exercise to reduce the risk of osteoporosis.<sup>6</sup> These patients may require specialist alcohol or smoking services.

Metabolic disorders should be treated while drugs and other toxins should be removed as appropriate. Autoimmune pancreatitis is managed by a specialist hepatobiliary team with steroids or other immunomodulatory drugs.

## FOLLOW-UP

In primary care, patients should have an annual review with blood tests to assess liver function and markers of malnutrition.<sup>8</sup> Because of the high risk of osteoporosis in chronic pancreatitis, patients should have a bone density assessment by dual-energy X-ray absorptiometry (DEXA) at diagnosis followed by yearly follow-up DEXA scans.<sup>5,8</sup> If patients have no evidence of PEI at diagnosis, a FEL-1 can be repeated if symptoms attributable to PEI occur.<sup>9</sup> Patients with no endocrine dysfunction at diagnosis should have a HbA<sub>1c</sub> repeated every 6 months.<sup>7</sup> Pancreatic cancer screening should be considered only in those with hereditary pancreatitis and should occur annually with a pancreas protocol CT scan.<sup>30</sup>

## CONCLUSION

Chronic pancreatitis is a disease with a diverse range of causes, of which alcohol is the most common. Patients present primarily with abdominal pain and may have features of PEI or diabetes mellitus.

Diagnosis is achieved primarily with cross-sectional imaging and screening for complications should occur simultaneously.

Management of chronic pancreatitis requires a multidisciplinary approach to monitor and treat the complex range of problems that develop in these patients. Early recognition and referral to a hepatobiliary MDT is a priority in primary care.

## Competing interests

Dr Gavin Johnson has undertaken consultancy work for Boston Scientific, Olympus, Pentax and Cook Medical. The other authors have no competing interests.

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## Useful information

### For patients

#### Gut UK

Chronic pancreatitis factsheet

<https://gutscharity.org.uk/advice-and-information/conditions/chronic-pancreatitis>

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## Prevention, diagnosis and treatment of colorectal cancer

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# Prevention, diagnosis and treatment of colorectal cancer

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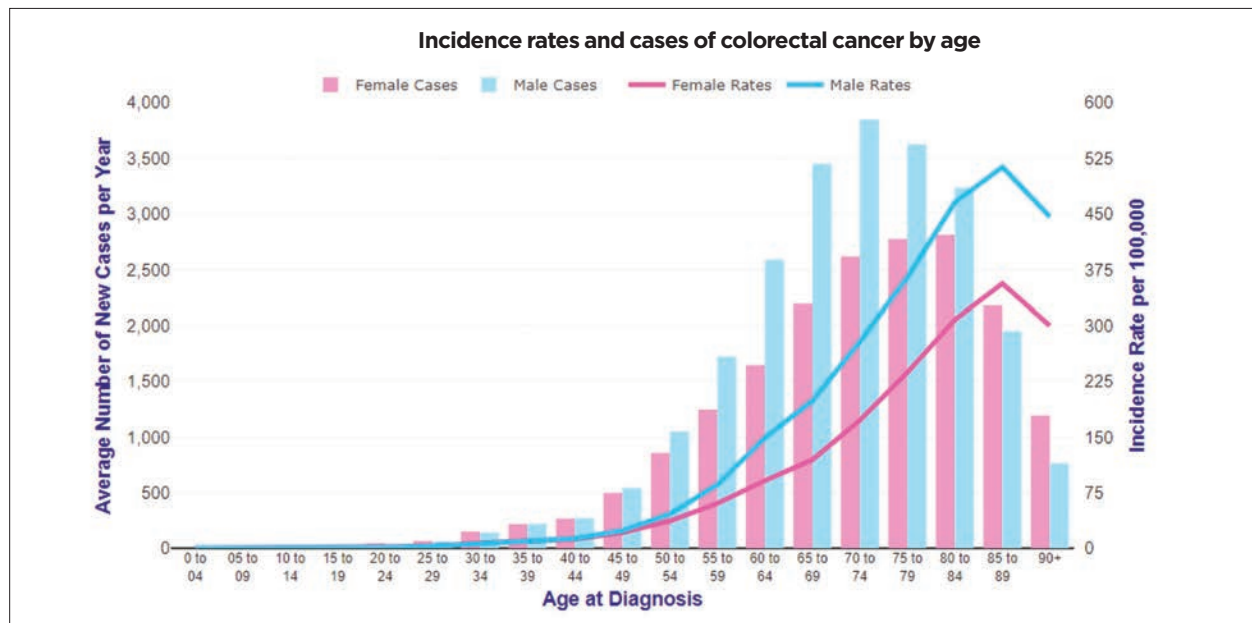
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## FIGURE 1

Incidence rates and cases of colorectal cancer by age<sup>2</sup>



**How** do patients present in primary care?

**What** are the management approaches?

**How** should patients be followed up?



**AROUND 42,300 CASES OF COLORECTAL CANCER ARE DIAGNOSED ANNUALLY IN THE UK.<sup>1</sup>**

Colorectal cancer is the third most common cancer in both women and men and is the second most common cause of cancer death in the UK, with around 16,600 recorded deaths per year.<sup>1</sup> The lifetime risk of developing colorectal cancer is 1 in 15 for men and 1 in 18 for women in the UK.<sup>1</sup>

## RISK FACTORS

The greatest risk factor for colorectal cancer, as with many other cancers, is increasing age. The incidence rate is highest in men in the 70-74 age range, and for women in those aged 80-84 years (see figure 1, above).<sup>2</sup>

Other risk factors include: family history, the risk of colorectal cancer more than doubles in people with a first-degree relative with the condition; a history of polyps (risk of advanced bowel cancer is increased by 80% in those with low-risk polyps seen on first colonoscopy compared with those

without);<sup>3</sup> inflammatory bowel disease (risk increased by 70%).<sup>4</sup> Individuals with type 2 diabetes have an increased risk of 22-30%.<sup>5-9</sup>

## Impact of lifestyle factors

Modifiable lifestyle factors are thought to be associated with the development of colorectal cancer in 54% of cases.<sup>1</sup> A diet with too little fibre is the main lifestyle risk factor implicated in 28% of cases.<sup>1</sup> There is a 10% decreased risk seen for every 10 g/day total dietary fibre consumed.<sup>10</sup> Processed meat consumption, obesity and overweight, smoking, alcohol and taking too little exercise are other modifiable risk factors.

## ROLE OF BOWEL SCREENING

Bowel screening detects both precancerous polyps (adenomas) and presymptomatic colorectal cancer. The screening programme was introduced in England in 2007 and has been estimated to save 2,400 lives per year.<sup>11,12</sup>

In areas of social deprivation bowel screening engagement is lower and colorectal cancer incidence is higher.

A quality improvement domain in the current Quality and Outcomes Framework in England gives general practices an opportunity to improve the uptake of bowel screening.<sup>13</sup> Direct contact with those who have not engaged with screening has been shown to increase engagement significantly.<sup>14</sup>

With the faecal immunochemical test (FIT) replacing the guaiac faecal occult blood test, the use of flexible sigmoidoscopy in patients aged  $\geq 55$  has been discontinued. Those patients with a positive FIT result are invited for a colonoscopy.

However, there is an increasing incidence of colorectal cancer in younger adults aged under 50<sup>15</sup> and the American Cancer Society has recently recommended reducing the age for starting bowel cancer screening in the USA to 45 years.

## PRESENTATION

The main three symptoms patients with colorectal cancer present with are:<sup>16</sup>

- Persistent blood in faeces



- Persistent change in bowel habit
  - Persistent lower abdominal pain
- Less obvious presentations are unexplained weight loss, tiredness for no reason, general malaise and iron deficiency anaemia found on blood testing. There is increasing interest in the role of thrombocytosis; it is recognised that lung, endometrial, gastric, oesophageal and colorectal cancers (LEGO-C) are associated with raised platelet counts.<sup>17</sup> It is also notable that high normal platelet counts in men are associated with increased risk of certain cancers, including colorectal cancer.<sup>18</sup>

### REFERRAL

The NICE recommendations for urgent referral of patients with suspected colorectal cancer are listed in table 1, below.<sup>19</sup>

The recommendations in the Scottish Referral Guidelines for Suspected

Cancer, published in 2019,<sup>20</sup> are very similar to those of the equivalent NICE guidelines (NG12).<sup>19</sup>

It is important to remember that patients presenting with symptoms that could be caused by colorectal cancer may recently have had a 'normal' screening FIT level (currently set at 120 µg/g in England, 80 µg/g in Scotland and 150 µg/g in Wales).<sup>21</sup>

Most areas in England now have Rapid Diagnostic/Rapid Investigation Services to address non-site specific symptoms, including raised platelet counts, where the symptomatic FIT level is in the normal range. NICE recommends a threshold for referral of 10 µg/g.<sup>22</sup>

Where symptom combinations do not 'qualify' for a two-week urgent referral, and if the clinician is concerned, many areas now offer an Advice and Guidance Service, which can facilitate a useful dialogue about how best to manage the

patient. There is also increasing evidence to support the use of FIT testing in symptomatic patients in order to help prioritise subsequent investigations<sup>23,24</sup> including those with rectal bleeding.<sup>25</sup>

### MANAGEMENT

#### Local disease

In January 2020, NICE published a clinical guideline on the management of colorectal cancer (NG151) which provides an evidence-based review of treatment options.<sup>26</sup> All patients should be discussed in an appropriate colorectal cancer multidisciplinary team (MDT) meeting.

In the management of non-metastatic colon cancer, surgical resection remains the treatment of choice for patients fit enough to be considered for surgery. Minimally invasive surgery (laparoscopic in most cases, robotic in the minority) is generally preferred, although some patients may still require a more traditional, open operation.

Systemic anti-cancer therapy (SACT) will be considered in certain patients after surgery when the tumour analysis shows the presence of high risk factors (e.g. cancer cells present in the lymph nodes or blood vessels).

For early rectal cancers, treatment options include:

- Transanal excision, which includes transanal minimally invasive surgery and transanal endoscopic microsurgery
- Endoscopic submucosal dissection, an advanced technique to remove rectal tumours endoscopically
- Surgery to remove the rectum (total or partial)

Preoperative radiotherapy with or without chemotherapy may be offered to patients with rectal cancer where preoperative MRI suggests the tumour is not at an early stage. Subsequently, laparoscopic excision is the technique of choice, unless an open operation is otherwise clinically indicated (e.g. multiple previous abdominal or pelvic surgery). Some centres are offering robotic surgery.

In those patients with low rectal cancer who appear to have had a complete clinical response (i.e. no tumour is evident) after radiotherapy with or without chemotherapy, the possibility of a watch and wait approach may be considered. In this situation, structured clinical, endoscopic and radiological surveillance is undertaken with the aim to reconsider surgery in the event that the tumour becomes apparent again following this treatment. This approach remains the subject of ongoing research.

**Table 1**

#### NICE (NG12) recommendations for referral of patients with suspected colorectal cancer<sup>19</sup>

##### 1.3.1 Refer adults using a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer if:

- They are aged 40 and over with unexplained weight loss and abdominal pain or
- They are aged 50 and over with unexplained rectal bleeding or
- They are aged 60 and over with:
  - Iron deficiency anaemia or
  - Changes in their bowel habit, or
- Tests show occult blood in their faeces

##### 1.3.2 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer in adults with a rectal or abdominal mass

##### 1.3.3 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer in adults aged under 50 with rectal bleeding and any of the following unexplained symptoms or findings:

- Abdominal pain
- Change in bowel habit
- Weight loss
- Iron deficiency anaemia

##### 1.3.4 Offer testing with quantitative faecal immunochemical tests (see the NICE diagnostics guidance on quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care) to assess for colorectal cancer in adults without rectal bleeding who:

- Are aged 50 and over with unexplained:
  - Abdominal pain or
  - Weight loss, or
- Are aged under 60 with:
  - Changes in their bowel habit, or
  - Iron-deficiency anaemia, or
- Are aged 60 and over and have anaemia even in the absence of iron deficiency



# key points

## SELECTED BY

**Dr Jez Thompson**  
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### Around 42,300 cases of colorectal cancer are diagnosed

annually in the UK. Colorectal cancer is the third most common cancer in both women and men and is the second most common cause of cancer death in the UK, with around 16,600 recorded deaths per year. The lifetime risk of developing colorectal cancer is 1 in 15 for men and 1 in 18 for women in the UK. The highest number of diagnoses in men are in the 70–74 age range, and for women in those aged 80–84 years.

### Modifiable lifestyle factors are thought to be associated

with the development of colorectal cancer in 54% of cases. A diet with too little fibre is the main lifestyle risk factor implicated in 28% of cases. There is a 10% decreased risk seen for every 10 g/day total dietary fibre consumed. Processed meat consumption, obesity and overweight, smoking, alcohol and taking too little exercise are other modifiable risk factors.

### The main symptoms patients with colorectal cancer

present with are: persistent blood in faeces; persistent change in bowel habit and persistent lower abdominal pain. Less obvious presentations are unexplained weight loss, tiredness for no reason, general malaise and iron deficiency anaemia found on blood testing. There is increasing interest in thrombocytosis; it is recognised that lung, endometrial, gastric, oesophageal and colorectal cancers (LEGO-C) are associated with raised platelet counts.

### In the management of non-metastatic colon cancer,

surgical resection remains the treatment of choice for patients fit enough to be considered for surgery. Minimally invasive surgery (laparoscopic in most cases, robotic in the minority) is generally preferred, although some patients may still require a more traditional, open operation. Systemic anti-cancer therapy (SACT) will be considered in certain patients after surgery when the tumour analysis shows the presence of high-risk factors (e.g. cancer cells present in the lymph nodes or blood vessels). For early rectal cancers, treatment options include: transanal excision, which includes transanal minimally invasive surgery and transanal endoscopic microsurgery; endoscopic submucosal dissection, an advanced technique to remove rectal tumours endoscopically; surgery to remove the rectum (total or partial).

### All clinicians should be aware of low anterior resection

syndrome (LARS), which will affect some of the 268,000 people living with, and beyond, colorectal cancer treatment. LARS is seen in some who have had sphincter preserving surgery for rectal cancer. The common symptoms with LARS are increased bowel opening, urgency, incontinence, the feeling of incomplete emptying, fragmentation of bowel opening (small amounts little and often) and difficulty in differentiating between gas and stool. A LARS questionnaire can be useful in patients who mention any of these symptoms.

number of preventable cases and enable stage shift at time of diagnosis to reduce both colorectal cancer incidence and mortality.

### Competing interests

Dr Richard Roope is the Cancer Research UK (CRUK) Primary Care Adviser, and receives funding from CRUK, and is a member of the Scientific Board for Oncimmune (an unremunerated role). Mr Justin Davies is an elected member of the NICE quality standards committee for colorectal cancer and was topic advisor for the NICE colorectal cancer guidelines (NG151).

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## Useful information

### Brief interventions

#### E-learning for healthcare

www.e-lfh.org.uk/programmes/making-every-contact-count/

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## Early recognition of hyperemesis gravidarum can prevent complications

Day A, Hollamby S, Girling J. Early recognition of hyperemesis gravidarum can prevent complications.  
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# Early recognition of hyperemesis gravidarum can prevent complications

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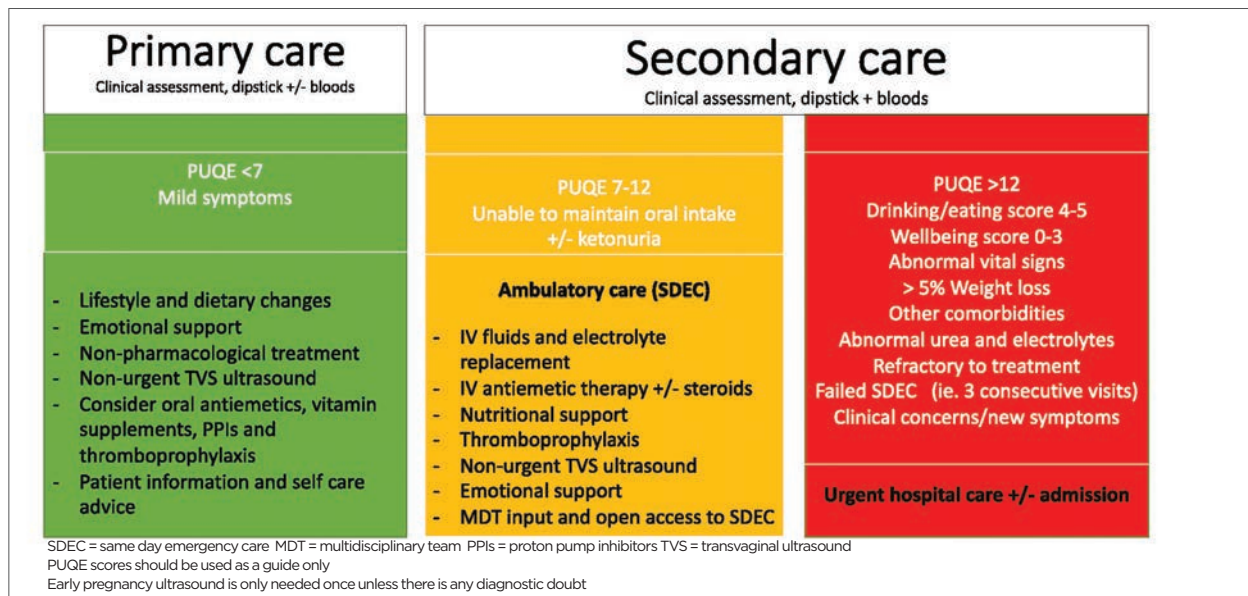
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## FIGURE 1

Recommended place of care and action plan for women with nausea and vomiting in pregnancy and hyperemesis gravidarum



**How** should women be assessed?

**What** are the potential complications?

**Which** women should be referred?



## NAUSEA AND VOMITING IN PREGNANCY IS VERY COMMON AND AFFECTS UP TO 80% OF WOMEN.

It is usually mild and resolves during the first half of pregnancy. However, in a small proportion of women (0.3-3.6%) symptoms are so severe that they lead to dehydration, electrolyte imbalance and weight loss.<sup>1</sup> This condition is known as hyperemesis gravidarum. As well as affecting the woman's physical and mental health it can also cause fetal morbidity.

Traditionally, women with severe symptoms were referred to the emergency department and often required admission to hospital for parenteral treatment. As part of the Urgent and Emergency Care transformation programme within the NHS Long Term Plan, most women with hyperemesis gravidarum can now bypass the emergency department and receive immediate treatment in an ambulatory care setting without the need to stay in hospital overnight.

Early recognition in primary care and appropriate escalation to secondary care can prevent complications and improve quality of life.

The aetiology and pathogenesis of hyperemesis gravidarum remain unknown. However, it is well recognised that the following factors and medical disorders are associated with the condition:

- A history of hyperemesis gravidarum in a previous pregnancy. This is the strongest independent risk factor with a recurrence rate of 26%<sup>2</sup>
- Increased pregnancy hormone levels present in a multiple pregnancy or molar pregnancy<sup>3</sup>
- Preexisting medical conditions such as diabetes, hyperthyroidism, gastrointestinal disorders (specifically being seropositive for *Helicobacter pylori*) and psychiatric illness<sup>3,6</sup>

Young maternal age, Asian or Black ethnicity, nulliparity and carrying a female fetus may also be associated with an increased likelihood of hyperemesis gravidarum.<sup>2,4,5</sup>

## ASSESSMENT

Most women usually complain of nausea, inability to swallow saliva, gagging, retching, dry heaving, vomiting, and odour and/or food aversion. These symptoms typically start between the fourth and seventh weeks

of gestation, peak around the ninth week and resolve by the 20th week in 90% of women.

Hyperemesis gravidarum is a diagnosis of exclusion. If the onset of symptoms occurs after ten weeks' gestation, the symptoms are unremitting or the presentation is atypical with or without other symptoms, a different clinical condition needs to be considered. Table 1, below, outlines the most common differential diagnoses. »

## Table 1

### Differential diagnoses to consider when assessing women with nausea and/or vomiting in pregnancy

- Peptic ulcers
- Cholecystitis
- Gastroenteritis
- Hepatitis
- Pancreatitis
- Appendicitis
- Genitourinary conditions
- Metabolic conditions
- Neurological or ENT conditions
- Hyperthyroidism
- Drug-induced

# SPECIAL REPORT

## HYPEREMESIS GRAVIDARUM

A full history, examination and targeted investigations are essential to exclude other diagnoses and also to establish severity of hyperemesis gravidarum. It is always important to:

- **Enquire** about the onset, duration and frequency of symptoms, dehydration symptoms (urine volume and colour) as well as response to any antiemetic treatment if used.

- **Exclude** other causes, especially if women present with vaginal bleeding, symptoms of systemic infection, severe abdominal pain, haematemesis, urinary or bowel symptoms, late onset of vomiting or significant headache or confusion.

- **Assess** the woman for any coexisting conditions in which the efficacy of oral medications can be reduced (i.e. epilepsy) or where dehydration could cause complications (i.e. sickle cell disease, diabetes).

- **Measure** vital signs (consider using maternity specific warning scores) including lying and standing blood pressure.

- **Look** for signs of significant dehydration and/or muscle wasting, sepsis, hypokalaemia (muscle weakness), hypocalcaemia, thyrotoxicosis or abdominal pathology. Perform a symptom guided examination if required (i.e. neurological examination if headache is present).

- **Classify** the severity and quantify the ability to tolerate food/fluids using objective and validated measures (see table 2 and table 3, below).

- **Evaluate** mental health status and the effects on quality of life. This can be done using the Edinburgh Postnatal Depression Scale.<sup>7</sup>

- **Monitor** weight at initial presentation and then weekly and escalate care if weight loss > 5% when compared with prepregnancy weight.

- **Test** the urine, for evidence of infection ( $\pm$  MSU) and ketonuria. The presence of ketones does not always correlate with severity of symptoms and more commonly reflects a state of starvation rather than dehydration, and

therefore should not be used as a sole marker of severity of symptoms.<sup>8,9</sup>

- **Calculate** venous thromboembolism (VTE) risk using the maternity VTE assessment tool (note hyperemesis already scores 3 points) and prescribe antiembolism stockings or low molecular weight heparin as indicated.<sup>10</sup>

- **Organise** an ultrasound in the early pregnancy unit to exclude multiple pregnancy and trophoblastic disease and confirm viability.

- **Prescribe** antiemetics (see details on page 23).

- **Consider** the need for outpatient parenteral treatment and/or hospitalisation (see figure 1, p21).

- **Signpost** to self-help resources and support groups (see Useful information box, p25)

- **Monitor** progress and arrange follow-up to prevent hospital admission and complications.

In primary care, laboratory investigations are generally not required and are usually reserved for cases where

### Table 2

The 24-hour Pregnancy-Unique Quantification of Emesis (PUQE-24) score that can be used to classify severity<sup>19</sup>

| Question                                                                                                                     | Points (in brackets) |                      |                     |               |                       |
|------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|---------------------|---------------|-----------------------|
| <b>PUQE score Q1:</b> In the past 24 hours for how long have you felt nauseated?                                             | Not at all (1)       | 1 hour or less (2)   | 2-3 hours (3)       | 4-6 hours (4) | More than 6 hours (5) |
| <b>PUQE score Q2:</b> In the past 24 hours how many times have you vomited?                                                  | None (1)             | 1-2 (2)              | 3-4 (3)             | 5-6 (4)       | 7 or more times (5)   |
| <b>PUQE score Q3:</b> In the past 24 hours, how many times have you had retching or dry heaves without bringing anything up? | None (1)             | 1-2 (2)              | 3-4 (3)             | 5-6 (4)       | 7 or more (5)         |
| <b>Severity according to PUQE-24 score</b>                                                                                   | <b>Mild &lt;7</b>    | <b>Moderate 7-12</b> | <b>Severe 13-15</b> |               |                       |

### Table 3

Drinking, eating and wellbeing scores that can be used in conjunction with PUQE-24

| Question                                                                                                              | Points (in brackets)                                           |                     |                      |                       |             |
|-----------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|---------------------|----------------------|-----------------------|-------------|
| <b>Drinking score:</b> In the past 24 hours have you been drinking?                                                   | Normally (1)                                                   | Nearly normally (2) | Less than normal (3) | Virtually nothing (4) | Nothing (5) |
| <b>Eating score:</b> In the past 24 hours have you been eating?                                                       | Normally (1)                                                   | Nearly normally (2) | Less than normal (3) | Virtually nothing (4) | Nothing (5) |
| <b>Wellbeing score:</b> How would you rate your overall sense of wellbeing over the past 24 hours on a scale of 0-10? | 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10<br>(0 = awful 10 = wonderful) |                     |                      |                       |             |

intravenous hydration is needed. However, if an alternative diagnosis is considered these may be indicated.

POTENTIAL COMPLICATIONS

Persistent vomiting can cause serious complications, both for the woman and the baby,<sup>11</sup> see table 4, right.

REFERRAL

Figure 1, p21, outlines the recommended criteria and place of treatment for women with nausea and vomiting in pregnancy and hyperemesis gravidarum. Urgent referral to secondary care should be considered for those women with:

- Persistent severe symptoms despite oral antiemetic treatment (with or without ketonuria), PUQE score > 7
- Weight loss > 5% of prepregnancy weight
- Medical comorbidities needing oral treatment (such as disease modifying drugs in rheumatic or inflammatory bowel disorders, blood pressure control, antibiotics, antiepilepsy drugs) and/or any clinical concerns needing specialist input.

Hospital assessment and treatment is currently provided in two settings: ambulatory care, i.e. at an ambulatory emergency care unit, where women receive prompt intravenous replacement treatment and usually can be discharged after 2-4 hours with open access to reattend as needed, or the emergency department (usually out of hours), where women may need brief admission to an observation unit to receive similar treatment. Both settings have provision for multidisciplinary team (MDT) care (pharmacists, endocrinologists, dietitians, medical and surgical specialists and mental health professionals) with the option of relocation for inpatient care if indicated, a typical length of stay is 2-3 days.

Nausea and vomiting in pregnancy or hyperemesis gravidarum has a substantial emotional impact and can significantly affect a woman's ability to carry out daily tasks. Signposting to support groups, self-help resources or a referral to the mental health team should be considered.

A non-urgent early pregnancy unit referral should be made for all women with hyperemesis gravidarum to rule out a molar or multiple pregnancy and confirm viability.

MANAGEMENT

Most women with mild nausea and vomiting in pregnancy should be advised to avoid foods, odours and activities that exacerbate symptoms,

discontinue iron supplements, drink adequate amounts of fluids, eat small meals frequently and snack on carbohydrate-rich foods.<sup>12,13</sup>

Pharmacological treatment and psychological support (psychotherapy and possible involvement of the mental health team) may need to be considered in certain patients.

Choosing the best antiemetic drug presents challenges as there is a lack of evidence from controlled trials and a concern about potential teratogenesis in the first trimester.<sup>14</sup> Regimens recommended are usually guided by the approach for treatment of nausea and vomiting secondary to chemotherapy or postoperative care with consideration of safety data in pregnancy and the side effect profile.

Women should be given the necessary information to make an informed decision, weighing the potential harm from pharmacological interventions against the harm of the complications resulting from dehydration, weight loss, nutritional deficiencies, metabolic imbalance, and the potential impact on mental health.

Figure 2, p24, reflects the Royal College of Obstetricians and Gynaecologists' (RCOG) advice illustrated in a stepwise approach. Previous efficacy, adverse reactions and route of administration should be considered in the decision making. If a woman does not respond to a single antiemetic, an incremental approach adding a second agent that has a different mode of action is advocated. Prescribing 'as needed' may be required together with appropriate counselling.

The RCOG recommends using antihistamines (cyclizine, promethazine) and phenothiazines (prochlorperazine and chlorpromazine) as first-line treatment. These agents are thought to be effective, have few and mild side effects, and are not known to be associated with any fetal malformations. A delayed release tablet containing doxylamine succinate (an antihistamine) and pyridoxine hydrochloride (vitamin B6) was licensed in the UK in 2018 for use in pregnancy and has been recommended in a NICE evidence summary document published in 2019.<sup>15</sup> It is recommended only after conservative measures have failed.

Second-line medications include the dopamine antagonists (metoclopramide and domperidone) and a serotonin 5-HT<sub>3</sub> antagonist (ondansetron). The safety profile of metoclopramide is well established<sup>16</sup> but the risk of short-term extrapyramidal disorders and tardive

dyskinesia limits its use to a maximum dose of 30 mg in 24 hours and a maximum recommended duration of treatment of five days.

Ondansetron is very commonly used and usually well tolerated. However, an American observational study<sup>17</sup> »

Table 4

Maternal and fetal complications secondary to hyperemesis gravidarum

Maternal complications

Electrolyte imbalance

- Hyponatraemia: (lethargy, headache, confusion and seizures). Quick and exaggerated correction of hyponatraemia can lead to central pontine myelinolysis<sup>6</sup>
- Hypokalaemia (muscle weakness and cardiac arrhythmias). Measure potassium and do an ECG (inverted T wave, ST segment depression and prominent U wave). Measure magnesium levels to rule out deficiency as a contributing factor for hypokalaemia
- Hypochloraemia
- Hypercalcaemia or hypocalcaemia (Chvostek's or Trousseau's sign)

Nutritional deficiencies

- Vitamin B1 (thiamine) deficiency can lead to Wernicke's encephalopathy. It is important to note that dextrose-containing solutions can precipitate Wernicke's encephalopathy in thiamine-deficient states
- Vitamin B12 (cobalamin) and vitamin B6 (pyridoxine) deficiency can cause anaemia and peripheral neuropathies
- Folic acid

Metabolic disturbances

- Metabolic hypochloraemic alkalosis
- Transient biochemical thyrotoxicosis. Resolves as the hyperemesis gravidarum improves and treatment with antithyroid drugs is not usually indicated.<sup>13</sup> Present in up to 60% of women with hyperemesis gravidarum<sup>20</sup>
- Acute kidney injury
- Liver function tests may be abnormal in up to 40% of women with hyperemesis gravidarum, mostly transaminitis

Gastrointestinal complications

Oesophageal reflux disease, oesophagitis or gastritis, Mallory-Weiss tear of the oesophagus

Other

Depression,<sup>21,22</sup> anxiety and thromboembolism

Fetal complications<sup>23</sup>

It is suggested that the increased risk of fetal complications is probably due to the low pregnancy weight gain (< 7 kg during the pregnancy) and nutritional deficiencies. Complications include:

- Fetal growth restriction
- Prematurity
- Low birthweight
- Low 5 min Apgar scores
- Anomalies of the central nervous system and skeletal malformations

## key points

### SELECTED BY

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### Nausea and vomiting in pregnancy is very common and

affects up to 80% of women. It is usually mild and resolves during the first half of pregnancy. However, in a small proportion of women (0.3–3.6%), symptoms are so severe that they lead to dehydration, electrolyte imbalance and weight loss. This is known as hyperemesis gravidarum. A history of hyperemesis gravidarum in a previous pregnancy is the strongest independent risk factor with a recurrence rate of 26%. Increased pregnancy hormone levels caused by a multiple or molar pregnancy and preexisting medical conditions such as diabetes, hyperthyroidism, gastrointestinal disorders (specifically being seropositive for *H. pylori*) and psychiatric illness also increase risk.

### Symptoms typically start between the 4th and 7th weeks

of gestation, peak around the 9th week and resolve by the 20th week. If the onset of symptoms occurs after 10 weeks' gestation, the symptoms are unremitting or the presentation is atypical, the possibility of a different clinical condition needs to be considered. An alternative diagnosis may also be suggested by vaginal bleeding, symptoms of systemic infection, severe abdominal pain, haematemesis, urinary or bowel symptoms, significant headache or confusion.

### It is important to enquire about the onset, duration and

frequency of nausea and vomiting, symptoms of dehydration (e.g. oliguria, dark urine), and the response to antiemetic treatment if used. Check for signs of significant dehydration and/or muscle wasting, sepsis, hypokalaemia (muscle weakness), hypocalcaemia, thyrotoxicosis and abdominal pathology. Monitor weight weekly, test the urine for evidence of infection, calculate VTE risk and organise an ultrasound in the early pregnancy unit.

### Urgent referral to secondary care, for intravenous fluids,

electrolyte and vitamin replacement, should be considered for those women with: persistent severe symptoms despite oral antiemetic treatment; a PUQE score >7; weight loss > 5% of the prepregnancy weight; medical comorbidities requiring oral treatment and/or any clinical concerns needing specialist input. Hyperemesis scores 3 points on the maternity VTE assessment tool, so any further risk factor is an indication to consider thromboprophylaxis.

### Most women with mild nausea and vomiting should be

managed with lifestyle and dietary modifications. If these are ineffective and symptoms are persistent, antiemetic treatment should be considered. The RCOG recommends using antihistamines (cyclizine, promethazine) or phenothiazines (prochlorperazine, chlorpromazine) first line. Second-line medications include dopamine antagonists (metoclopramide and domperidone) and ondansetron. If polytherapy with second-line agents is ineffective and symptoms are severe, steroids can be considered. Women who have persistent symptoms into the second trimester of pregnancy should have consultant-led antenatal care and serial fetal growth ultrasound.

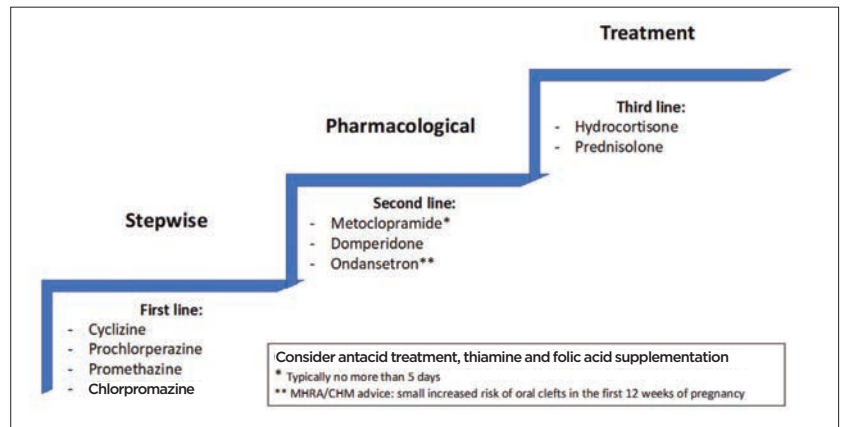


**FIGURE 2**

Stepwise pharmacological treatment of women with nausea and vomiting in pregnancy and hyperemesis gravidarum (adapted from the RCOG guideline)<sup>1</sup>

reported in 2018 that its use was associated with an additional 3 cases of oral clefts per 10,000 births (14 cases vs 11 per 10,000 births in the unexposed population). The European Medicines Agency Pharmacovigilance Risk Assessment Committee then responded by banning ondansetron in the first trimester of pregnancy. However, the UK Teratology Information Service in collaboration with the European Network of Teratology Information Service reviewed all available evidence and issued a joint statement in September 2019 advocating that ondansetron can be used (with adequate counselling) as a second-line agent for the treatment of nausea and vomiting in pregnancy (as currently recommended by the RCOG Green-top Guideline).<sup>1</sup>

If polytherapy with second-line agents is not effective and symptoms are severe, steroids can be considered, usually prednisolone or hydrocortisone which do not cross the placenta. However, yet again, evidence for efficacy is weak. The side effects include hyperglycaemia and hypertension, and steroids are only recommended when other treatment combinations have been exhausted.<sup>18</sup>

Hyperemesis gravidarum is a recognised risk factor for VTE as dehydration and reduced mobility aggravate the prothrombotic risk already imposed by pregnancy.<sup>10</sup> Any further risk factor increases the threat considerably which in early pregnancy includes any of the following: age ≥ 35 years, BMI ≥ 30, smoking, parity ≥ 3, gross varicose veins, personal or family history of VTE, thrombophilia or medical comorbidity, multiple pregnancy, conception by assisted reproductive technology, ovarian

hyperstimulation syndrome, infection, hospitalisation and reduced mobility.

All women with hyperemesis gravidarum should have a documented risk assessment which should be repeated in any change of circumstances, such as an admission. Once hyperemesis resolves the risk should be reassessed and thromboprophylaxis stopped if appropriate.

### FOLLOW-UP

Priority appointments should be given to women suffering from nausea and vomiting in pregnancy and hyperemesis gravidarum as they can deteriorate quickly if treatment is not started promptly. This should include patient information leaflets, advice on tracking food, fluid and medication intake at home, the option of providing a fit note and clear guidance on how to stop medication using a pragmatic approach is vital.

Women who have persistent symptoms into the second trimester of pregnancy should have consultant-led antenatal care and serial fetal growth ultrasound.

### CONCLUSION

Assessment of women with nausea and vomiting in pregnancy and hyperemesis gravidarum should be holistic, recognising that no one measure can reliably indicate severity or guide management.

Early intervention with a stepwise approach allowing patients to make an informed decision is essential to avoid maternal and fetal complications.

Women with severe symptoms should have a prompt and appropriate referral (ideally before 5pm) for same day emergency care which

expedites treatment and allows patients to self-refer for ongoing treatment. Primary care has a vital role including supporting emotional wellbeing.

**Competing interests:** None

#### Acknowledgements

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## Useful information

**For healthcare professionals**  
**Advice on medicines in pregnancy**  
UK Teratology Information Service (UKTIS)  
UKTIS helpline: 0344 892 0909  
Mon-Fri 9am to 5pm  
<https://www.medicinesinpregnancy.org/Medicine--pregnancy/NV/>

**MHRA drug safety advice**  
[www.gov.uk/drug-safety-update/ondansetron-small-increased-risk-of-oral-clefts-following-use-in-the-first-12-weeks-of-pregnancy](http://www.gov.uk/drug-safety-update/ondansetron-small-increased-risk-of-oral-clefts-following-use-in-the-first-12-weeks-of-pregnancy)

**NICE Clinical knowledge summaries**  
**Nausea and vomiting in pregnancy**  
<https://cks.nice.org.uk/topics/nausea-vomiting-in-pregnancy/>

**For patients**  
**Pregnancy Sickness Support**  
[www.pregnancysicknesssupport.org.uk](http://www.pregnancysicknesssupport.org.uk)

**RCOG patient information leaflets**  
[www.rcog.org.uk/en/patients/patient-leaflets/pregnancy-sickness](http://www.rcog.org.uk/en/patients/patient-leaflets/pregnancy-sickness)

**Chelsea and Westminster NHS Foundation Trust**  
**Hyperemesis treatment in AEC:**  
patient information video  
[www.chelwest.nhs.uk/services/medicine/ambulatory-care](http://www.chelwest.nhs.uk/services/medicine/ambulatory-care)

## We welcome your feedback

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### Show impact

- Collection of data
- Practice audit to show improved care

- Case studies
- Implement a protocol
- Prescribing review
- Educational meetings
- Significant event audit
- Practice meeting
- Implement a new service
- Take on new role
- Significant event audits
- Change with feedback from patients and/or colleagues

### Further options for sessional GPs

- Self audit of own practice:
  - Record-keeping
  - Referrals for investigations
  - Prospective condition based reviews
  - Random case analysis with colleagues
  - Review of telephone triage outcomes
- Update drugs in emergency bag

### Time credits

### Impact credits

Quick impact

Later impact

Later impact=

### Total credits

## Title and reference

Date

What have you learned?

How will this change your practice?

What research/actions will you take that will have further impact on practice?

Draft of your action plan

|                                                                                           |  |                                                                                               |  |
|-------------------------------------------------------------------------------------------|--|-----------------------------------------------------------------------------------------------|--|
| <div>CPD prompt and framework</div> <div>Case review</div>                                |  | <div></div> |  |
| <div>Clinical case for review</div>                                                       |  | <div>Summary of any discussion of the case with peers</div>                                   |  |
| <div>Reason for selection of the case for reflection</div>                                |  | <div>What changes/actions have resulted to your personal practice?</div>                      |  |
| <div>Evidence base used to reflect on your practice</div>                                 |  | <div>What changes/actions have resulted to the practice?</div>                                |  |
| <div>What went well?</div>                                                                |  | <div>How/when will you review these changes?</div>                                            |  |
| <div>What could have been done better?</div>                                              |  | <div></div>                                                                                   |  |
| <div>What were the causes of the condition/event?</div>                                   |  | <div></div>                                                                                   |  |
| <div>What learning needs arise from this case for (a) you and (b) for the practice?</div> |  | <div></div>                                                                                   |  |
|                                                                                           |  | <div>Time creditsImpact creditsTotal credits</div>                                            |  |

Title

Reflection on Table 1 results

Reason for the audit (target to improve or implement)

Define criterion (or criteria) to be met

What changes were implemented to improve results?

Set the standard and its basis

Reflection on Table 2 results and review with peers

Plan the audit process and any involvement of peers

Time credits

Impact credits

Total credits

| Table 1                    |                |                          |              |
|----------------------------|----------------|--------------------------|--------------|
| Results of data 1 analysis |                | Date of data collection: |              |
| Criterion                  | Number sampled | Achievement (%)          | Standard (%) |
| A                          |                |                          |              |
| B                          |                |                          |              |
| C                          |                |                          |              |

| Table 2                               |                       |                        |                          |                        |              |
|---------------------------------------|-----------------------|------------------------|--------------------------|------------------------|--------------|
| Results of data 1 and data 2 analyses |                       |                        | Date of data collection: |                        |              |
| Criterion                             | Number sampled Data 1 | Achievement (%) Data 1 | Number sampled Data 2    | Achievement (%) Data 2 | Standard (%) |
| A                                     |                       |                        |                          |                        |              |
| B                                     |                       |                        |                          |                        |              |
| C                                     |                       |                        |                          |                        |              |