The Christie NHS
NHS Foundation Trust

Colorectal and peritoneal oncology centre

Information for health professionals - pseudomyxoma peritonei

What is it?
Pseudomyxoma Peritonei (PMP) is often a slowly progressive disease that produces extensive mucus accumulation within the abdomen and pelvis. There are two clinically distinct groups of peritoneal mucinous lesions. The first can be described as having an essentially histologically benign origin from an appendiceal adenoma known as a LAMN (low grade appendiceal neoplasm). When there is no histological evidence of perforation and there is no evidence of extra-appendiceal mucin, it is termed as a LAMN I. When there is microscopic evidence of appendiceal perforation, the lesion is termed a LAMN II. The second group can be described as an appendiceal carcinoma and represents approximately 20% of all appendiceal neoplasms. The treatment options and outcomes are dependent on the type of appendiceal tumour.

PMP is often referred to as being a 'borderline malignant' condition in the absence of a clearly malignant lesion. These tumours are not biologically aggressive as they do not metastasise via the lymphatics or blood stream like gastrointestinal adenocarcinomas; however, they can still be a fatal process. The space required within the abdomen and the pelvis for nutritional function eventually becomes replaced by mucinous tumour.

Most of these tumour cells are surrounded by fluid of varying consistency. Bulky cellular deposits are usually found within the omentum and beneath the right hemidiaphragm. Gravity creates a further accumulation of adenomucinous cells within the pelvis where the peritoneum reflects over the pelvic organs.

Common sites involved in tumour dispersion also include the stomach, the area around the terminal ileus and the rectosigmoid colon within the pelvis. All three of these sites are fixed to the retroperitoneum and are not free to move as a result of peristaltic activity. The peristaltic activity of the small bowel may prevent mucinous tumour implantation on these surfaces resulting in relative sparing of the small bowel.

What causes PMP?
For the majority of people with true PMP an adenoma is found in the appendix. Like many other tumours, PMP can occur in people who lead healthy lifestyles. There is no known evidence of inheritance of this condition unlike colorectal cancer.

Signs and symptoms
For women and men the most predominant feature is a gradual increase in abdominal girth. The increase in abdominal girth increases pressure on the gut and prevents the patient from eating normally. Despite this the patient often notes an increase in body weight. The symptoms can be non-specific and are often misdiagnosed.

How is it diagnosed?
The diagnosis of PMP can be difficult. It is often an unexpected finding during investigations of non-specific abdominal symptoms, either on USS/CT scan or the patient has undergone an

abdominal operation. The diagnosis of PMP can confused with other mucinous tumours from elsewhere in the gastrointestinal tract, gallbladder or in the ovaries. Women with both low-grade mucinous carcinoma peritonei and high-grade mucinous carcinoma peritonei often have ovarian involvement by mucinous tumour. The ovarian tumour is often the presenting clinical symptom or sign and is often assumed to be the primary site, therefore no attempt is made to identify the appendix as a possible source of mucinous tumour.

In some cases the primary tumour in the appendix can be quite inconspicuous in the context of abundant mucinous peritoneal tumour. In addition, rupture and fibrosis can obliterate the appendix. Other problems are that ovarian tumours are often interpreted pathologically as primary mucinous borderline malignant tumours. This happens particularly when the appendix has not been removed but even occurs when an appendiceal adenoma is identified. There is evidence that the ovarian mucinous tumours in PMP are on the surface of the ovary and secondarily derived from the associated appendiceal mucinous tumour.

Treatment options

There are 4 approaches in the management of PMP:

1. Watch and wait
Monitor the situation closely. This is commonly used in patients with a diagnosis of LAMN I (ie appendiceal adenoma with no evidence of rupture). Over the past 10 years we have not observed any patient with this type of lesion progressing to widespread mucin deposition/PMP.

2. Debulking surgery
The traditional surgical approach is debulking to remove as much of the tumour as possible and generally includes removal of the uterus and ovaries in women and often the right colon and the omentum. Disease recurrence is almost inevitable due to residual and recurrent disease around the peritoneal cavity. Repeat debulking surgery may be possible on a number of occasions but each attempt becomes more difficult and dangerous. The small bowel becomes increasingly involved due to adhesions and eventually surgery is fraught with severe complications such as small bowel fistulae.

In patients with extensive PMP at presentation this may be the only surgical option and can still be helpful in a palliative setting but should only be performed after thorough assessment and consultation with the patient.

3. Cytoreductive surgery and heated intra-peritoneal chemotherapy (HIPEC)
Cytoreductive surgery refers to the complete removal or destruction of all visible tumours present throughout the peritoneal cavity. Peritonectomy procedures include stripping the parietal peritoneum and resecting structures at fixed sites that contain adenomucinosis. This can be accomplished by removal of or by destruction of the tumour using a combination of surgical techniques that include organ resection and tumour destruction using electro-evaporation. The operation **may** comprise a number of different procedures including:

- Right hemicolectomy, colectomy, removal of rectum and sigmoid (anterior resection)
- Greater and lesser omentectomies
- Splenectomy
- Cholecystectomy
- Pelvic peritonectomy, which sometimes includes the rectum by anterior resection and in the female includes removal of the ovaries and uterus
- Stripping of the peritoneum from the left hemidiaphragm
- Stripping of the peritoneum from the right hemidiaphragm
- Stripping of disease from the surface of the liver.

The long-term results depend upon the extent to which the tumour can be removed at surgery. The smaller the size of the residual tumour deposits the greater the chance the tumour will respond to the chemotherapy. Cytoreductive surgery is an extensive, lengthy procedure that may take several hours. If complete tumour removal has been possible, intraperitoneal chemotherapy (HIPEC) has been given and the tumour is at the benign end of the spectrum, up to 80% will have 10 year disease free survival.

When chemotherapy is administered directly into the peritoneal cavity, the peritoneum-plasma barrier allows for a high concentration of drugs directly to the abdominal and pelvic surfaces where the tumour is located. The chemotherapy used is based on the drug's ability to produce a cytotoxic effect over a short time period (90 minutes in theatre) and to have an increased response with heat. The use of heated intra-operative intraperitoneal chemotherapy after complete dissection of adhesions and before anastomoses are completed allows optimal perfusion of the chemotherapy to the peritoneal surfaces and organs. Mitomycin C has a slow clearance from the peritoneal cavity. Pharmacokinetic studies of intra-operative intraperitoneal chemotherapy report an absorption of 75-90% of Mitomycin C within the first hour.

Heating chemotherapy to 41.5 degrees celsius not only improves drug distribution but also improves the drug cytotoxicity penetration into tissue compared to chemotherapy administration at room temperature. Similarily the physical process of circulating the fluid around the abdomino-pelvic cavity allows filtration to remove cellular debris and improves the efficacy of the treatment.

4. Chemotherapy
Based on results from a study carried out at The Christie, we sometimes offer a combination of Mitomycin C and Capecitabine (MCap) to patients with inoperable or recurrent PMP. Approximately 40% of patients benefit from this treatment, which is given over a 3 to 6 month period. It is generally well-tolerated and if it becomes necessary, we will provide more detailed information on the side-effects of this therapy.

Post-operative mortality and morbidity
Complete cytoreduction carries a mortality risk of 2-5%, which means 1/30 to 1/20 patients die as a direct result of surgical complications. The main complications are cardio-respiratory (lung infections and heart failure). There is also a risk of clots in the main leg veins, which can result in pulmonary embolus.

Surgery also has significant morbidity (serious complications) of around 30%. Approximately 20% (1 in 5) patients require further surgery to deal with the complications of the primary operation during the same admission. Approximately 20% of patients require a stoma. A permanent stoma is required if all or most of the colon has to be removed. A temporary stoma is usually used when the rectum has to be removed and the join, although appearing intact at the time of surgery, has a very high risk of leakage due to the particular position of the anastomosis or join, and the fact that intraperitoneal chemotherapy is used. The temporary stoma is usually closed between 3 and 6 months after the primary operation.

The colorectal and peritoneal oncology centre
The colorectal and peritoneal oncology centre has an international reputation for treating advanced and early colorectal cancer, appendix tumours, peritoneal tumours, anal cancer and tumours within the pelvis.

If you have a query regarding our service or would like to refer a patient, please contact **0161 446 8051.**

The service will provide:

- ongoing advice and support for patients, their partners and families
- information and advice about treatment and treatment options
- a point of contact should problems arise
- a link with other health care professionals involved in care at home and in hospital
- referral to specialist services

Who can contact us?

Any health care professional who requires information or advice and any patient coming for assessment or treatment for cytoreductive surgery and intraoperative intraperitoneal chemotherapy can contact the service themselves or by referral from another health care professional. We are also happy to speak to partners, friends and family, providing the patient has given consent.

If you know the name of your consultant, please contact their secretary directly:

Consultants:	**Contact:**	
Miss S T O'Dwyer	Eve Kennerley	**0161 446 8311**
Mr M S Wilson	Gill Harrison	**0161 446 3366**
Mr P E Fulford	Rebecca Brown	**0161 918 7352**
Prof A Renehan	Bev Tyrrell	**0161 918 2189**
Mr C R Selvasekar	John Lupea	**0161 918 2310**
Mr O Aziz	Laura Elliott	**0161 918 2057**
Miss A Minicozzi	Marion McKenna	**0161 918 2391**
Clinical Nurse Specialists:	**Contact:**	
Rebecca Halstead	**0161 918 7096 / 07766 780952** **rebecca.halstead@christie.nhs.uk**	
Rachel Connolly	**0161 918 7859 / 07785 725629** **rachel.connolly@christie.nhs.uk**	
Lisa Wardlow	**0161 918 7183 / 07826 892213** **lisa.wardlow@christie.nhs.uk**	
Sarah Wemyss	**0161 918 2097 / 07824 373 785** **sarah.wemyss@christie.nhs.uk**	
	Fax: **0161 918 7078**	
Service Manager: Hannah Rogers		

Further information

For information about the colorectal and peritoneal oncology centre visit **www.christie.nhs.uk/cpoc**

Other useful websites

www.pmpawareness.org (support network)

What would we like you to do?
The diagnosis of PMP is often difficult, particularly in women. Equally the effective treatment of it can be made harder by inappropriate initial surgery.

If a case appears to have the potential diagnosis of PMP, please feel free to contact the service and we will be happy to discuss the individual case. If there is a clinical need to operate before contacting us, try to avoid performing widespread resection – in particular avoiding peritonectomies and omental surgery other than a simple biopsy. This is because the resulting adhesions will sometimes prevent a complete cytoreduction being performed and can render a patient inoperable who would have otherwise been potentially curable.

It is common that patients require emergent surgery in which case a simple appendicectomy with or without oophorectomy (but avoiding a hysterectomy) and possibly with the release of mucinous ascites should suffice and will allow for an accurate histological diagnosis. If this is done laparoscopically, it is optimal if all the port sites can be kept in the midline so that they can be easily excised subsequently.

If you need information in a different format, such as easy read, large print, BSL, braille, email, SMS text or other communication support, please tell your ward or clinic nurse.

We try to ensure that all our information given to patients is accurate, balanced and based on the most up-to-date scientific evidence. If you would like to have details about the sources used please contact **patient.information@christie.nhs.uk**

For more information about The Christie and our services, please visit **www.christie.nhs.uk** or visit the cancer information centres at Withington, Oldham or Salford.

Contact The Christie Hotline for urgent support and specialist advice

The Christie Hotline: 0161 446 3658

Open 24 hours a day, 7 days a week

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The Christie Patient Information Service
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Health & care information you can trust
The Information Standard Certified Member

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