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GASTRO-INTESTINAL UPDATE

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FOLLOW-UP OF COLORECTAL CANCER

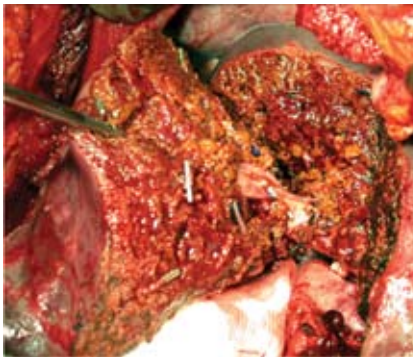
Colorectal cancer (CRC) is one of the commonest cancers, and its diagnosis, investigation and management are important components of both general practice and specialist surgery. One area frequently neglected is long term postoperative follow-up.

Up to 70% of patients will develop metastases. CRC is generally a slowly progressive cancer. This coupled with the often step-wise nature of spread (colon→lymph nodes → liver → lung → systemic) provides an opportunity to identify and treat metastatic disease successfully.

There are no universally agreed guidelines for follow-up of CRC. Considerations include benefit versus cost-effectiveness of intensive follow-up regimens. Meta-analyses generally favour more intensive follow-up. As the cure rates for metastatic disease, especially liver resection, continue to rise, intensive follow-up becomes more worthwhile.

LIVER RESECTION

Approximately 50% of patients with CRC develop liver metastases, and approximately 50% of these are amenable to curative resection. Continuing technical advances in the resection of liver metastases combined with new adjuvant therapies, are yielding 5 year survival rates of 40-50%. The indications for resection are expanding, and the number and distribution of metastases are no longer an absolute limitation, providing that adequate liver volume and perfusion remains following resection. Metasectomy remains the cornerstone of treatment, supplemented with adjuvant therapy (radio-frequency ablation, chemotherapy and new microwave technology).



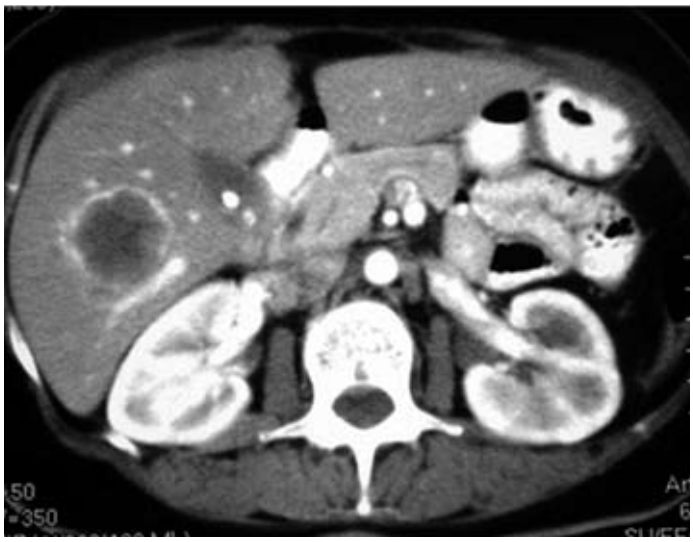
Segment 5 and 6 liver resection for a colorectal metastasis.

LUNG AND OTHER RESECTIONS

Lung resections for CRC metastases, either alone or in addition to liver resection, can be performed for cure. However the pulmonary disease must be limited to a small area of the lung and there must be no evidence of systemic spread. Only 10% of lung metastases are amenable to curative resection. Extra-hepatic recurrence within the abdominal cavity is usually a grave prognostic sign, although curative resections may still be performed if the recurrence is isolated, and a considerable time out from the original colorectal surgery.

CARCINO-EMBRYONIC ANTIGEN (CEA)

CEA is produced by some 80% of colorectal cancers. It has a limited role in the initial diagnosis of CRC, but its role in follow-up is more established. The CEA should be tested prior to resection of the colorectal primary. If it is elevated initially, the level would be expected to drop following resection in the absence of metastases. If the level then increases in the follow-up period, imaging investigations (CT chest, abdomen and pelvis) should be carried out to look for metastases that may be amenable to curative resection. If the CEA is not elevated prior to resection of the primary, there is no benefit to subsequent CEA testing. In this instance imaging with CT and Ultrasound should be relied upon instead.



Large right lobe liver metastasis amenable to curative excision

ABDOMINAL IMAGING

CT, Ultrasound, and MRI scanning all have a role in the evaluation of CRC liver metastases. They all have a sensitivity of approximately 90% for metastases of >1cm. CT is the preferred method as it provides information regarding resectability, in addition to having a slightly higher sensitivity for the identification of small tumours. Ultrasound can be used in addition if suspicion is high, or a CT has been performed recently. MRI is reserved for use in planning of surgical resections, as its cost is prohibitive for use as a screening follow-up investigation.

SEARCHING FOR METACHRONOUS COLORECTAL DISEASE

10-20% of patients who have had a colorectal carcinoma will develop a second primary CRC tumour during their lifetime. All patients with a CRC primary should have a full colonoscopy to exclude a synchronous tumour prior to the initial surgery. If this shows no evidence of polyps then a colonoscopy should be repeated at 5 yearly intervals. The presence of polyps would require earlier colonoscopy depending on the number and size of the polyps.

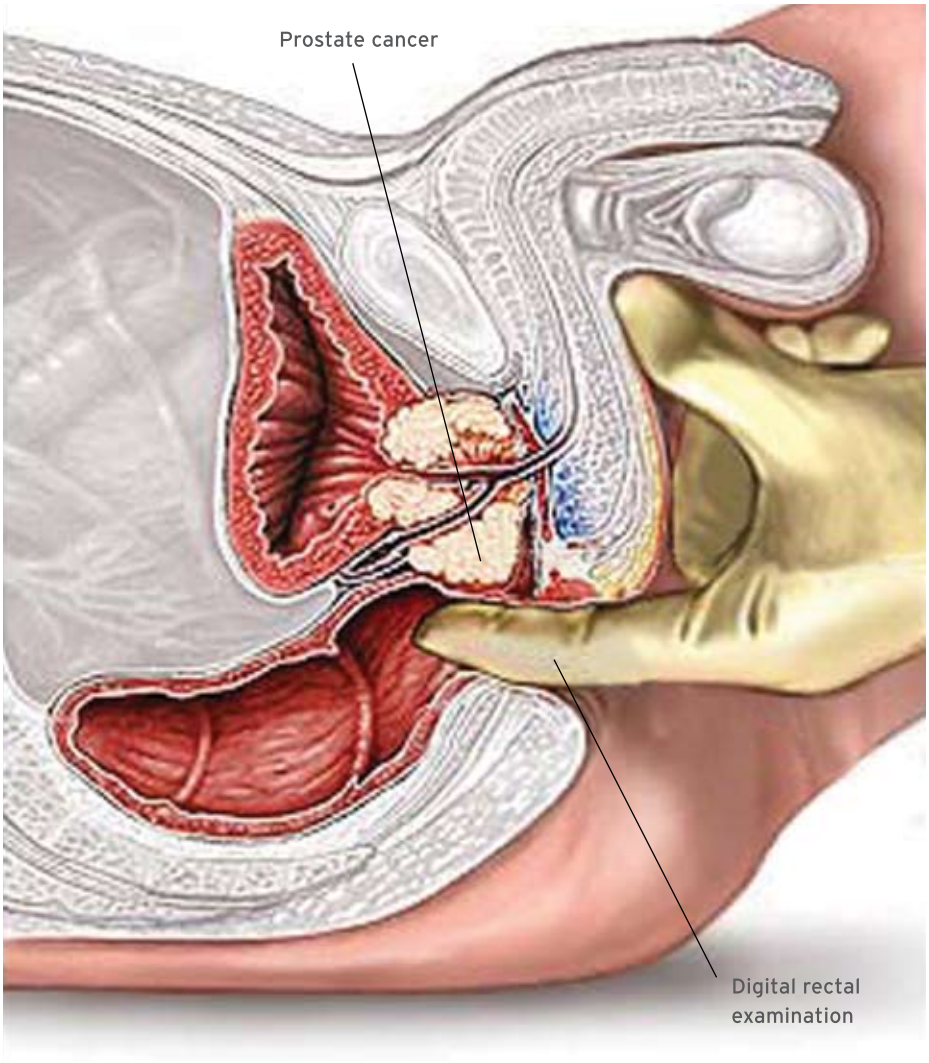
SUMMARY

- :: Repeat colonoscopy at 5 years (earlier if polyps present).
- :: CEA producers:
  - Regular CEA monitoring. CT if level rises.
  - CT at 2 years.
- :: Non-CEA producers:
  - Abdominal CT at 1 year and at 2 years.
- :: Follow-up for 5 years.
- :: Additional investigations as indicated by symptoms.

PSA – 20 YEARS ON – WHAT WE NEED TO KNOW

Prostate cancer incidence has increased over the last 20 years, and is the commonest cancer in older men. It is the second leading cause of cancer related death (after lung) in the USA. The goal of cancer screening is to find clinically detectable cancers at a curable stage. Widespread use of PSA has lead to a dramatic stage migration – whereas previously about 80% of men were diagnosed with incurable advanced prostate cancer, now 80% of men are diagnosed with localized (potentially curable) cancer. PSA testing has, however, created new risks for both over and under diagnosis. For patients there is a risk of over-diagnosis and over-treatment of insignificant prostate cancer, incurring costs and complications without significant benefit

It is more important to diagnose early prostate cancer in younger men, because it is more likely to be the cause of death than in older men. PSA is prostate specific, but not cancer specific. An increased PSA can be associated with non-malignant conditions such as benign hyperplasia, infection or chronic inflammation. Digital rectal examination (DRE) plus PSA doubles the detection rate compared to PSA alone. Normal PSA range is 0,0 to 4,0 ngs/ml. Using this threshold, about 25% of prostate cancers are not detected (false negative rate) whereas about 65% of biopsies will not show cancer (false positive rate).



WHO SHOULD BE OFFERED PSA TESTING?

Prostate cancer is rare in men younger than 50 years (0,1%). 85% of cases are diagnosed after 65 years. Testing is recommended from 50 years, and from 45 years for higher risk (family history, Black Africans). The recommended upper age limit is 70 – 75 years.

Screening of asymptomatic men should be limited to those with a life expectancy of more than 10 years. Early-stage prostate cancer is unlikely to cause the patient's death in < 10 years. Some protocols suggest biennial screening for a PSA <2 ngs/ml and annually for a PSA > 2 ngs/ml or above.

However, in 2009 the largest ever screening study, of 182 000 men screened since 1990, found that a 4 year screening interval was reasonable. It also showed 1,400 men need to be screened and 48 cases treated to prevent one death. (Reference: Screening and prostate-cancer mortality in a randomized European study. N Engl J Med. 2009)

DIGITAL RECTAL EXAMINATION

Detection rates are significantly higher using both PSA and DRE. Abnormal DRE is a predictor of high-grade cancer, independent of PSA. In a symptomatic men examination of the external genitalia and DRE are mandatory.

THE MESSAGE TO MEN WHO CONSIDER UNDERGOING SCREENING HAS CHANGED.

Early detection of prostate carcinoma decreases mortality by 25 – 30%. But the subject may have a non-aggressive cancer that would remain subclinical in his lifetime. Thus, screening may bring all the worries and side effects of treatment with no survival benefit.

Dr Peter Nicolle–Consultant Urologist

SUMMARY

- **PSA testing can be offered every 2-4 years to all men after 50 years (45 if high risk)**
- **Stop PSA testing in asymptomatic men over 75 years or with less than 10 years life expectancy, and in those aged over 65 years with a PSA of less than 0,5 – 1 ngs/ml.**
- **PSA screening reduces the death rate by 20% but is associated with a high risk of over diagnosis**

CONSTANTIABERG GIT WARD

We are pleased to announce that the long-awaited GIT ward at Constantiaberg Hospital will open on March 1st 2010. The advances and complexities in managing GIT conditions together with the shortage of quality, trained nursing staff across all hospitals in South Africa has been the driving force behind the creation of the specialised GIT ward at Constantiaberg Hospital. We will manage the full spectrum of surgical and medical GIT conditions from oesophageal, gastric, hepato-biliary, pancreatic and colorectal conditions.

Dr Ravi Oodit has been instrumental in setting up the ward that now has a complete multidisciplinary team. The team includes dedicated laparoscopic, hepato-pancreatic-biliary and colorectal surgeons, an experienced gastroenterologist, and specialised nutritional and physiotherapy support. This expertise, combined with fully trained and supportive GIT nurses, will allow us to provide high quality care for all patients with GIT related illnesses.

CHARCOT'S BILIARY TRIAD

Jean-Martin Charcot was born in Paris in 1825 and became regarded as the Father of Modern Neurology, his Neurology Clinic at Salpetriere being the first of its kind in Europe. He was the first to describe Multiple Sclerosis and his "Other Triad" of nystagmus, intention tremor, and staccato speech is associated with this condition. Other neurological associations are Charcot's joints and Charcot-Marie-Tooth disease.

He retained his interest in General Medicine and was the first to describe intermittent claudication (1858) and his Biliary Triad (1877) of jaundice, abdominal pain and fever, due to cholangitis.

Jean Martin Charcot

Charcot's Mausoleum in Paris

His son, Jean-Baptiste, much against his will, studied Medicine. But as soon as his father died he used his inheritance to buy a vessel, Francais, and from 1901 to 1903 did pioneering scientific research in Antarctica. He returned in 1908 with a new ship, Porquoi Pas? (Why Not?), and named Charcot Island off the Antarctic Peninsula in honour of his father. In 1935 he drowned off the coast of Iceland and lies with his father in the Charcot mausoleum in the Montmatre Cemetary in Paris.

MARK HEWAT

MBCHB (UCT), FCS(SA), CERTIFICATE OF SURGICAL GASTROENTEROLOGY(SA)

We are pleased to announce that Mark Hewat joins our partnership in February 2010.

Mark grew up in Durban and matriculated in the top 30 in Natal. He completed his medical training at the University of Cape Town in 1998, where he was the elected class rep. for five years. He won the Family Medicine class medal, and Frank Foreman prize for the greatest contribution to student affairs. He then spent a year at Edendale Hospital in Pietermaritzburg for his internship followed by a year at various secondary hospitals in Cape Town for his community service. Mark then spent a year working as a GP in Manitoba, Canada.

In 2002 Mark returned to Cape Town to begin specialist surgical training at Groote Schuur hospital. He completed this training in 2006, being awarded the ASSA prize for surgical research, and the Swann-Morton prize for the best surgical registrar.

Mark continued at Groote Schuur for a further two years in a sub-specialist fellowship training position in the Hepato-biliary unit. This provided training in ERCP, GI endoscopy, and complex liver, pancreatic and biliary surgery. At the end of these two years Mark passed the sub-specialist exam in surgical gastroenterology.

Mark and his family moved to Newcastle, UK, for 2009, where he completed a one year fellowship at the Freeman Hospital. This year, in a leading Hepato-biliary and transplant unit, exposed him to a high volume of liver and pancreatic surgery as well as ERCP. This unique training experience was directly supervised by established experts in the UK Hepato-biliary surgical community.

Mark is an accomplished general surgeon, with special interests in HPB and laparoscopic surgery, endoscopy and ERCP. We look forward to benefiting from his experience and expertise when he joins us on the new surgical gastroenterology unit at Constantiaberg.

Mark and his wife Tanya are the proud parents of Rebecca. His hobbies include golf, fly-fishing, cricket and scuba diving.

OBSTRUCTIVE JAUNDICE IN THE ADULT PATIENT

The causes of biliary obstruction are best divided into pathologies in the lumen, in the wall, or outside the wall.

Intra-luminal obstruction is most commonly caused by gallstones. Cholelithiasis (gallbladder calculi), is a common finding in adult patients, but does not account for jaundice. Jaundice indicates obstruction of the biliary tree by stones that have migrated through the cystic duct into the common bile duct (Fig 1) (choledocholithiasis). Cholangitis occurs if the obstructed bile becomes infected. This life-threatening complication requires urgent biliary decompression, best achieved by ERCP.

Lesions in the wall include tumours arising from the bile duct epithelium (cholangiocarcinoma) (Fig 3) or invading into it (pancreatic Ca, gallbladder Ca). Survival rates for these malignancies are poor when they are advanced, so early detection and specialist assessment are essential. Benign inflammatory strictures typically follow chronic pancreatitis. The presence of jaundice with acute pancreatitis usually occurs as a result of a residual gallstone in the CBD, rather than as a result of the pancreatitis itself.

Lesions outside the wall (extrinsic compression) include enlarged portal lymph nodes from metastatic carcinomas or lymphoma. Occasionally HIV lymphadenopathy can cause obstruction, though these nodes tend to be softer and smaller and less likely to obstruct the CBD.

TAKE HOME MESSAGE

- Look out for Charcot's Biliary triad
- LFTs to determine conjugated vs unconjugated bilirubin
- Conjugated >50% of total bilirubin = obstruction
- U/S to determine level of obstruction and presence or absence of gallstones
- Surgical referral to determine further investigations and plan definitive treatment

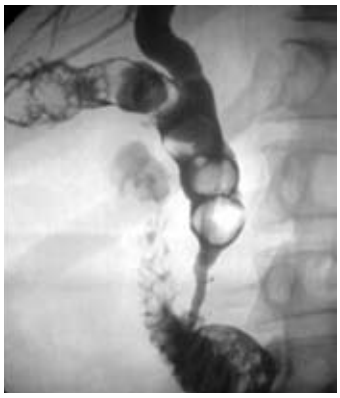


Fig 1: CBD stones on ERCP

Fig 2 Gallstones

CLINICAL PRESENTATION OF JAUNDICE

Patients with jaundice may present with a range of symptoms, from an incidental finding to life-threatening disease. This follows the wide variety of underlying causes and their rate of onset.

The acute presentation is characterised by fever, rigors, abdominal pain, and flu-like symptoms. For these patients, the change in skin colour is usually of secondary concern. It is usually caused by infection (viral hepatitis, cholangitis).

Patients with non-infectious jaundice may complain of weight loss or pruritus. Abdominal pain is uncommon, even in patients with pancreatic or biliary cancers. Significant weight loss and chronic back pain are often poor prognostic signs.

Physical Examination

Classical signs of liver disease such as bruising, spider naevi, gynaecomastia, testicular atrophy, and palmar erythema reflect chronic cellular damage and cirrhosis, and are not seen in acute infection or obstruction. Ascites may be associated with cirrhosis and portal hypertension as well as advanced malignancy. The presence of jaundice, RUQ pain, and fever/rigors (Charcot's Biliary triad) is diagnostic of cholangitis, and is an emergency.

INVESTIGATIONS

Blood tests should include liver function tests, a full blood count, and an INR. Further investigation depends on whether the hyperbilirubinaemia is conjugated (direct) or unconjugated (indirect). Intrahepatic jaundice usually leads to a mixed picture with elevation in both unconjugated and conjugated bilirubin. As a rough guide, if the conjugated bilirubin is greater than the unconjugated (i.e. >50% of the total) this most likely represents obstruction (posthepatic). The reverse indicates intrahepatic or hepatocellular disease. AST and ALT are markers of hepatocellular injury. ALP and GGT are the ductal enzymes, and indicate obstruction.

Imaging is indicated when an obstructive (posthepatic) cause of jaundice is suspected. The preferred initial investigation is an ultrasound, as it is relatively inexpensive, and accurate for evaluating biliary dilatation, and has the highest sensitivity for detecting gallstones. Further investigations such as CT, ERCP, MRCP (magnetic resonance cholangiopancreatogram) and PTC (percutaneous transhepatic cholangiogram) depend on the level of obstruction, likely diagnosis and planned therapy (See table). *RO*

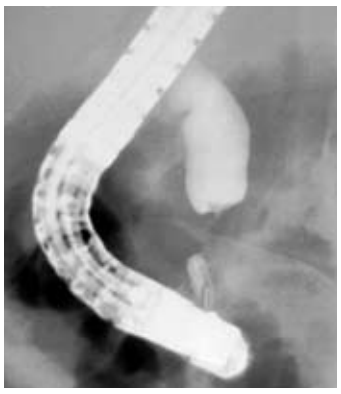


Fig 3. Malignant biliary stricture

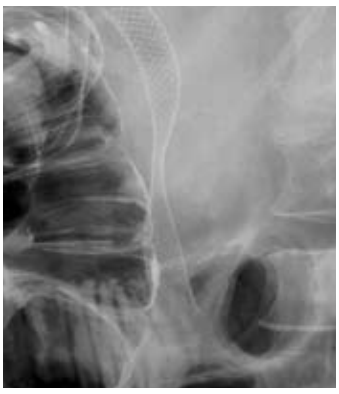


Fig 4. Metal stent inserted into CBD for palliation of irresectable pancreatic Ca

LEVEL OF OBSTRUCTION	U/S FINDINGS	COMMON DIFFERENTIAL DIAGNOSIS
Ampulla	Dilated intra-hepatic ducts Dilated cbd Dilated pancreatic duct	Ampullary tumour Small cbd stone Chronic pancreatitis Some pancreatic ca
Distal cbd	Dilated intra-hepatic ducts Dilated cbd Pancreatic duct usually not dilated	Cbd stone Pancreatic ca Distal cholangioca Chronic pancreatitis
Biliary hilum	Dilated intra-hepatic ducts Normal cbd Normal pancreatic duct	Cholangioca (klatskin tumour) Gallbladder ca Mirizzi syndrome Portal lymphadenopathy