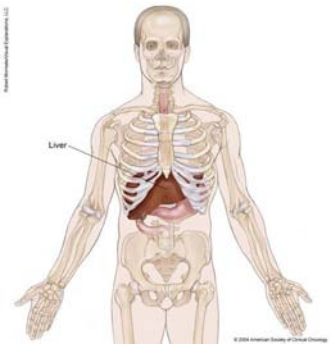
Liver Cancers

Dimensions in Oncology 2019

LIVER~Where and what is it?

- Located under the ribs on the right side of the body
- It is both the heaviest internal organ and the largest gland in the human body
- There are 2 lobes and 8 segments
- It is connected to 2 large blood vessels that filter all of the blood
- It is the only internal organ capable of regeneration! You need as little as 25 % of your liver to survive!
- The biliary tract/tree secretes bile which stored in the gallbladder or released into the duodenum

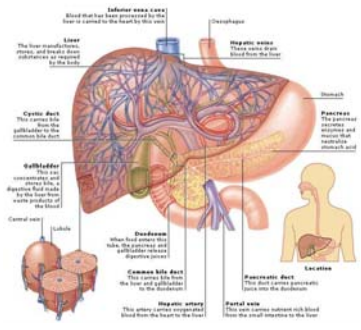


Functions – up to 500 of them

- Collecting and filtering blood from the intestines
- Processing and storing needed nutrients absorbed in the intestines
- Removing toxins from the body
- Producing some of body's blood clotting factors
- Converting nutrients into energy or into substances need to repair and build tissue
- Helps to maintain the proper sugar levels in the body

MORE…

- Plays a major role in carbohydrate, protein, amino acid and lipid metabolism
- Key role in break down of toxic substances like alcohol
- Stores Vitamins
- Produces albumin which is the most abundant protein in the blood and is essential to maintain oncotic pressure
- Synthesized hormones that are responsible for raising the blood pressure



Risk Factors

- Viral hepatitis is the LARGEST risk factor for Primary Liver Cancer
- Cirrhosis- develops when liver cells are damaged and replaced by scar tissue
- Obesity/ NASH/Diabetes- this is becoming the largest concern
- Age: most often over the age of 60
- Gender : Men higher risk
- Race and ethnicity : In the US highest in Asian Americans and Pacific Islanders
- Hereditary hemochromatosis
- Life style and environmental exposure

Statistics

- Statics (American Cancer Society's publication, Cancer Facts & Figures 2016.)
- This year, an estimated 39,230 adults (28,410 men and 10,820 women) in the United States will be diagnosed with primary liver cancer.
- It is estimated that 27,170 deaths (18,280 men and 8,890 women) from this disease will occur this year.
- Liver cancer is the 10th most common cancer
  - the 5th most common cause of cancer death among men
  - the 8th most common cause of cancer death among women.

Screening

- Hepatitis C Screening Best Practice Alert at wellness checks started at Allina in Nov 2013, CDC (Center for Disease Control) recommendation 2012, USPSTF(U.S. Preventive Services Task Force)2013, AASLD (American Association for the Study of Liver Diseases) 2014
- With documented risk factors
  - Annual labs
  - Annual Liver US

Diagnostic work up

- Labs/Fab 5 (CBC,basic panel,LFT,INR, AFP)
  AFP alpha feta protein tumor marker (HCC and testicular cancer)In the United States, Alpha feta protein tumor marker (AFP) is found in elevated levels in the blood of about 50% to 70% of people who have HCC.
- Diagnostic imaging of a Multiphasic Liver CT or Liver MRI with gad
- Initial chest CT if normal repeat annually
- Bone scan if documented bone pain or is excessively high AFP
- NO PET scan as HCC is not PET avid (cholangio and met cancers are)
- Biopsy may be required IF …….including lesion/tumor and back ground liver

Algorithm for liver masses

- There is currently set language in the radiology reports if identified or suspicious liver mass/lesion recommending ordering provider to have case reviewed at the Multidisciplinary Liver Conference at Abbott
- Pending those findings/recommendations referral to VPCI/Liver Clinic
  - Hepatobiliary and pancreas surgery service
  - Interventional Radiology
  - Oncology
  - AND MORE

Liver Conference and Cancer Care Team

- Hepatologist (Dr. Jack Lake and Dr Ibrahim Hanouneh)
- Hepatobiliary surgery team (Dr. M. Hill and Dr A. Kamath, Jenell Gilman PA)
- Cancer Care Coordinator Nurse (Jill May, RN BSN OCN)
- Interventional Radiology (Team of 6 at ANW)
- University of MN Liver Transplant Program
- Hepatobiliary Pathology
- Oncology (MNOncology attends conference)
- General GI for surveillance endoscopy
- Palliative Care
- Cancer Rehab
- Oncology social worker (Sarah Johnson)
- Cancer Mental Health Services
- Primary Care Provider

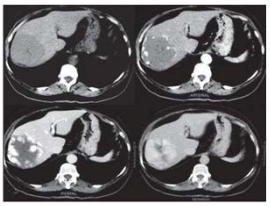
Types of liver lesions/tumors

Malignant tumors of the liver
- HCC/Primary Liver cancer- 80%
- Cholangiocarcinoma – 10-20%
- Angiosarcoma 1-2%
- Metastatic lesions (any kind of cancer possible)

Benign tumors of the liver
- Hemangiomas
- FNH (focal nodular hyperplasia
- Hepatic adenomas

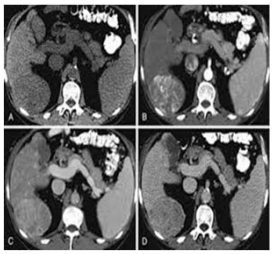
Hepatic Hemangioma

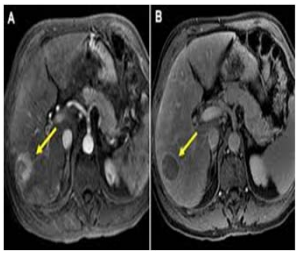
Peripheral nodular enhancement that fills in delayed venous phase



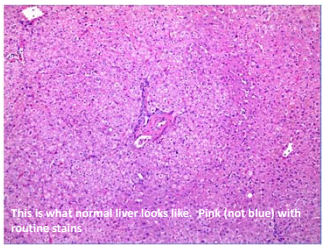
Hepatocellular Carcinoma

Two cases of that demonstrate diagnostic findings for HCC (no biopsy needed).
On the left CT scan and on the right MRI that shows arterial enhancement with delayed venous washout.

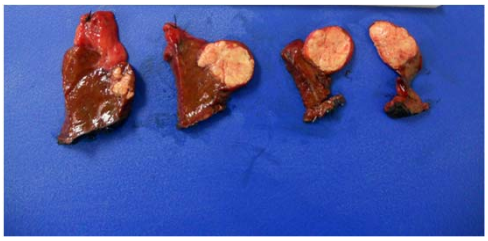




Normal Liver

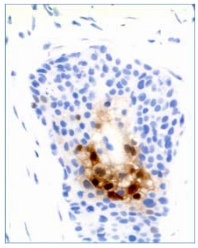


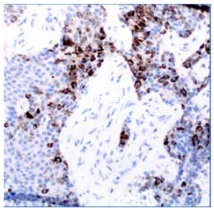
Hepatocellular Carcinoma – Resection Specimen



Hepatocellular Carcinoma – Microscopic Appearance

Hepatocellular Carcinoma - Immunohistochemistry

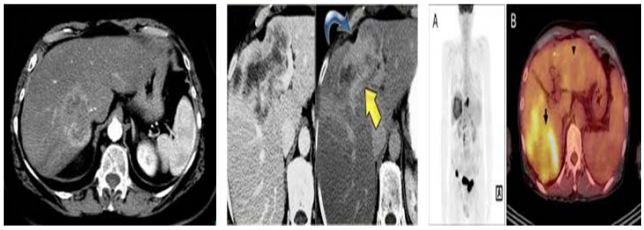




In difficult cases, antibodies against proteins only found in liver can help diagnose the tumor as HCC.

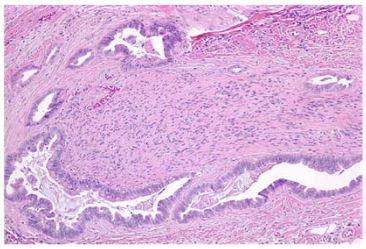
Cholangiocarcinoma.

Arterial enhancement or delayed venous enhancement as seen on the case on the right. Usually FDG (glucose) avid as seen on third Case.



Cholangiocarcinoma- resection

Cholangiocarcinoma- microscopic appearance



Staging of Primary Liver Cancer

BCLC (Barcelona Clinic Liver Cancer) staging system. The BCLC system categorizes HCC based on characteristics of the tumor, liver function, performance status, and cancer-related symptoms.

TNM staging that is used in most cancers is not used with HCC as it does not include liver function and cirrhosis which are critical in the decision making for any treatment.

BCLC stage groupings

- Very early stage. The tumor is smaller than 2 cm. There is no increased pressure in the portal vein. Bilirubin levels are normal. Surgery is usually recommended.
- Early stage. The tumor is smaller than 5 cm. Liver function varies. There may be no increased pressure in the portal vein, increased portal vein pressure and normal bilirubin levels, or increased portal vein pressure and increased bilirubin levels. People with early-stage disease may be candidates for a liver transplant, surgery, or radiofrequency ablation (RFA).
- Intermediate stage. The tumor may be large or there may be multiple tumors. Doctors usually recommend regional liver directed therapies
- Advanced stage. The tumor has invaded the portal vein or spread to other parts of the body, such as the lungs and bones. Doctors usually recommend targeted therapy.

Treatment options

- Liver resection
- Liver transplant
- Liver directed therapy
- Chemotherapy
- Immunotherapy/ Hormonal therapy
- Clinical trials

Surgery

Most patients are NOT a candidate for a liver resection for many reasons

- Abnormal LFT
- Portal Hypertension
- Fatty liver disease
- Cirrhosis
- Varices
- Plts >100K, history of bleeding
- History of hepatic encephalopathy
- In addition to size and location of tumor/tumors

Liver Transplant

- General facts:
  - Human liver transplants were first performed by Thomas Starzl in the United States and Roy Calne in Cambridge, England in 1963 and 1967, respectively.
  - Liver allografts for transplant usually come from donors who have died from fatal brain injury.
  - Living donor liver transplantation is when a portion of a living person's liver is removed and used to replace the entire liver of the recipient
  - More recently, adult-to-adult liver transplantation has been done using the donor's right hepatic lobe, which amounts to 60 percent of the liver. Due to the ability of the liver to regenerate, both the donor and recipient end up with normal liver function if all goes well
  - Pts are typically listed for 1 ½ before donor liver is available and the reach a MELD score in the 30's
  - Pts can have live donor transplant which can move up to time line but does not change the requirements for transplant

Criteria for Listing for Liver Transplant

- Liver transplantation is the only for those who meet Organ Procurement and Transplantation Network (OPTN) criteria
- 1 tumor between 2-5 cm or up to 3 tumors the largest of which can be no bigger than 3 cm
- If a pt has a tumor/tumors less than 2 cm they are assessed for surgery or liver directed therapy (MWA) for curative intent. If reoccur then could be assessed for transplant.
- No portal vein invasion
- No metastatic disease
- AFP below 400
- Age rare to be transplanted if age beyond early 70's
- If history of ETOH or drug abuse must complete chemical dependency evaluation and have ongoing documented sobriety

Liver directed therapy

These are treatments that provide direct treatment to the liver tumor by an Interventional Radiologist

- Microwave ablation: a special cath is placed into the tumor sending microwave energy into the tissue
- RFA/Radiofrequency ablation: a special cath is placed directed at the tumor, then very thin flexible electrodes are extended in the tissue dispensing heat
- Bland embolization: particles are released by hepatic angiogram into the vascular of the tumor
- Chemoembolization: chemotherapy (Adriamycin)saturated particles are released by hepatic angiogram into the vascular of the tumor
- Radioembolization: millions of tiny glass beads containing Yttrium-90 are released by hepatic angiogram into the vascular of the tumor

Chemotherapy

- Currently no good options for systemic IV chemotherapy
- Nexavar/Sorafenib: Protein kinase inhibitor
  - Median survival 10.7 vs. 7.9 months
  - Response of disease control ~ 20% of patients
  - Wide range of side effects many significantly affecting QOL
  - can be prescribed by Hepatologist or Oncologist
- Stivarga/Regorafenib/Erbitux: Multikinase inhibitor
  - Similar to Nexavar
- New FDA approved Opdivo/Nivolumab: anti PD-1 monoclonal antibody

Clinical Trials and other treatment options

- Currently 1 trial/study available within the Allina system

  Mayo clinic is collecting samples as a one-time blood draw for patients with HCC, IHC and gallbladder. It is a biomarker study, non-treatment.
  The purpose of this study is to create a registry that can be used to improve the ability to diagnose and treat liver and bile duct cancers.

- Clinical Trials.gov is an excellent resource for clinical trials that will allow you to search by disease or region of country
- Additional Treatment options in the future may include Immunotherapy or hormonal therapy

Symptoms with HCC

- Jaundice or itching
- Fluid retention: ascites and edema
- Pain
- Anorexia, weight loss
- Nausea/vomiting
- Constipation/Diarrhea
- Hepatic encephalopathy
- Excessive fatigue
- Bleeding: easily bruising, blood in emesis or stool

Nutrition

- Low salt diet less than 2 grams daily
- High calorie High Protein – including protein supplements
  - 80- 100gms a day
- Fluid restriction 1.5 liter daily if Na level in 120's
- Vitamins

Activity

- Better balance lowers risk of falls and broken bones
- Improves circulation to lower extremities
- Improves fatigue
- Strengths muscles and lessens wasting with inactivity
- Improves overall mental health and independence with ADL's
- Weight management

Prevention

- Screening for Hepatitis B,C and at risk pt populations for liver disease
- Vaccinating for Hepatitis B and treating those with chronic Hep B viral loads
- Assess chronic Hep C patients for possible treatment
- Education on sexually transmitted diseases and risk for hepatitis
- Screening by blood banks of donated blood products for hepatitis
- Ongoing education on obesity, chemical/ETOH dependency and diabetes in correlation to decrease risk of cirrhosis
- Annual monitoring for pts with identified cirrhosis including labs and liver US

Survivorship: "Count no day lost"

- The 5-year survival rate tells you what percent of people live at least 5 years after the cancer is found. Percent means how many out of 100. The general 5-year survival rate is 18%. Survival rates depend on several factors, including the stage of the disease.
  - 43% of people who are diagnosed at an early stage, the 5-year survival rate is 31%.
  - If liver cancer has spread to surrounding tissues or organs and/or the regional lymph nodes, the 5-year survival rate is 11%.
  - If the cancer has spread to a distant part of the body, the 5-year survival rate is 3%.

Patient Education Book Resources

- 100 Questions and Answers about Liver Cancer by Ghassan K. Abou-Alfa and RonaldDeMatteo
- Grant Me Serenity by Janalee Card Chmel
- The Official Patient's Sourcebook on Adult Primary Liver Cancer by James Parker and Phillip M. ParkerResources

Patient Education on line and phone resources

- American Cancer Society www.cancer.org 1-800-227-2345
- Cancer Care www.cancercare.org 1-800-813-4673
- Medline Plus-U.S. National Institutes of Health www.nlm.nih.gov
- National Cancer Institute www.cancer.gov 1-800-422-6237
- Navigating Cancer www.navigatingcancer.com/explore/liver 1-800-925-4456
- Cancer Support Community www.cancersupportcommunity.org 1-888-793-9355
- American Liver Foundation www.liverfoundation.org1-800-GO-LIVER
- National Center for Biotechnology Information www.ncbi.nlm.nih.gov
- Radioembolization/Liver-directed therapy www.Nordion.com/Theraspheres
- RadiologyInfo.org www.radiologyinfo.org