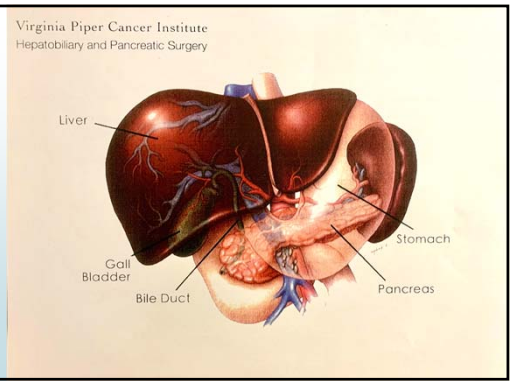
Dimensions in Oncology 2019

Pancreatic Cancer

Pancreas- Where and what is it?

- It is a gland, about six inches long, that is located deep in the abdomen toward the back.
- It is surrounded by the stomach, small intestine, liver and gallbladder.
- The widest end of the pancreas is called the head.
- The middle sections of the pancreas are the neck and body.
- The end of the pancreas is called the tail.
- Three are 3 very important blood vessels
  - superior mesenteric artery, superior mesenteric vein and the portal vein that cross behind the pancreas.



Functions

- The pancreas functions as both an Exocrine gland and an Endocrine gland.
  - **Exocrine cells** produce the enzymes that help with digestion. This process starts when food enters the stomach the pancreas releases enzymes in to the system through small ducts that lead to the main pancreatic duct (PD duct)
  - The pancreas duct runs the length of the pancreas, carrying enzymes and other secretions called pancreatic juice.
  - The main pancreas duct connects with the common bile duct which carries bile from gallbladder connecting into the duodenum at the Ampulla of Vater.
  - The mixture of bile and pancreas enzymes aid in the digestion of fats, carbohydrates and proteins within the duodenum

...continued

- The endocrine cell of the pancreas produce hormones.
  - Hormones help control and regulate functions of the body
  - Hormones are usually made in one part of the body then carried through the blood to work at another location.
  - The pancreas produces 2 main hormones
    - Insulin: lowers blood sugars
    - Glucagon: raises blood sugars
    - Islet cells are a type of endocrine cells that produce and secret insulin and glucagon into the blood

Risk factors for pancreas cancer

- Obesity: 20% more likely to have pancreas cancer
- Smoking: risk twice as high as non smokers. 25% cancer patients have history of smoking
- Diabetes: the reason is not understood but there is some correlation
- Chronic pancreatitis: which is a condition of inflammation of the pancreas
  - often but not always associated with heavy alcohol use and smoking
- Work exposure: Heavy exposure at work to certain chemicals used in the dry cleaning and metal working industries

Risk factors that can't be changed

- Age: most older than 45. 2/3 of patients are over 65 and the average age is 70
- Gender: men slightly higher incidence ? Related to higher use of ETOH and smoking
- Race: slightly higher occurrence of pancreas cancer in the African American population
- Family history: most often no relation, however there are some inherited genetic syndromes that increase risk

Inherited Genetic Syndromes

- Hereditary breast and ovarian cancer syndrome, caused by mutations in the BRCA1 or BRCA2 genes
- Hereditary breast cancer, caused by mutations in the PALB2 gene
- Familial atypical multiple mole melanoma (FAMMM) syndrome, caused by mutations in the p16/CDKN2A gene and associated with skin and eye melanomas
- Familial pancreatitis, usually caused by mutations in the PRSS1 gene
- Lynch syndrome, also known as hereditary non-polyposis colorectal cancer (HNPCC), most often caused by a defect in the MLH1 or MSH2 genes
- Peutz-Jeghers syndrome, caused by defects in the STK11 gene. This syndrome is also linked with polyps in the digestive tract and several other cancers.
- Chronic pancreatitis due to a gene mutation: People with this inherited (familial) form of pancreatitis have a high lifetime risk of pancreatic cancer

Risk Factors with unclear effect

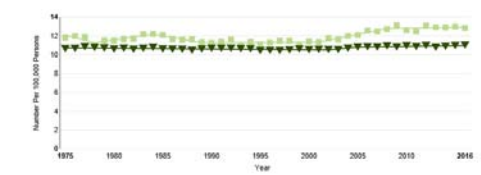
- Diet: diets that are high in red and processed meats (such as sausage and bacon) and low in fruits and vegetables ? Higher risk.
- Physical inactivity: Some research has suggested that lack of physical activity might increase pancreatic cancer risk. Not all studies have found this.
- Coffee: Older studies have suggested that drinking coffee might increase the risk of pancreatic cancer, but more recent studies have not confirmed this. (thankfully!)
- Alcohol: Some studies have shown a link between heavy alcohol use and pancreatic cancer. This link is still not certain but as mentioned in prior slide pancreatitis which can be 2' heavy alcohol use is a risk.
- Infections: There have been limited studies that question the link between infection of the stomach with the ulcer-causing bacteria Helicobacter pylori (H. pylori) or infection with Hepatitis B may increase the risk of getting pancreatic cancer.

Statistics

- Pancreatic cancer is the 12th most commonly occurring cancer in men and the 11th most commonly occurring cancer in women in the world. There were 460,000 new cases in 2018. (World Cancer Research Fund)
  - Hungary had the highest rate of pancreatic cancer in 2018
- National Cancer Institute: Estimated New Cases in 2019 56,770
  - 3.2% of All New Cancer Cases 3.2%
  - Estimated Deaths in 2019 45,750
  - 7.5%
  - of All Cancer Deaths

Statistics about the last 40 years in pancreas cancer

- New cases come from SEER 9 Incidence. Deaths come from U.S. Mortality. 1975-2016, All Races, Both Sexes. Rates are Age-Adjusted.



Screening for pancreatic cancer

- Unfortunately there is not a screening for pancreas cancer like a mammogram, colonoscopy or PSA
- This is one of the focuses within the research community
- Of note though for those patients that have inherited genetic syndromes there are recommendations for screening
  - MRI
  - EUS (will discuss further)
- Currently there are no blood tests available for routine surveillance of pancreas cancer development
- NCI does not have evidence-based information about prevention or screening of pancreatic cancer.

Symptoms of pancreatic cancer

although it is called the silent disease because symptoms are rarely present in the early stages

- Ascites: abnormal fluid collection in the abdomen, usually representing advanced cancer
- Blood clots: DVT/deep vein thrombosis or PE. Cancer causes changes in the blood that can increase clotting.
- Changes in bowels: constipation, diarrhea or both.
  - Diarrhea: loose, watery, oily, very foul smelling stools 2' lack of pancreas enzymes in system causing malabsorption of food and therefor passing quickly through the GI tract
  - Constipation: often related to pain medications that are being used.
  - Diabetes: sudden onset Type 2 diabetes after the age of 50 and if have low BMI. Also if established diabetic with well controlled blood sugars and a sudden change.

MORE…

- Digestive difficulty: poor appetite, indigestion, early satiety, N/V maybe caused by the tumor invading or pressing up again the duodenum causing a blockage.
- Jaundice: yellowing of the skin or eyes. Also resulting in very dark urine and pale stools. This occurs because of a blockage of the bile duct causing excel bilirubin in the blood. Pt may experience severe pruritus.
- Pain: may occur in the upper abdomen or more commonly the mid back caused by the tumor pressing against or invading nerves and organs near the pancreas.
- Unexplained weight loss: Cancer induced weight loss or cachexia is a complex problem that affects the way the body uses calories and protein. Cancer causes the body to use more calories than normal, breaking down muscles and decreasing appetite.

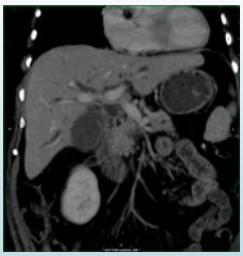
Symptoms of pNET/Neuroendocrine tumors

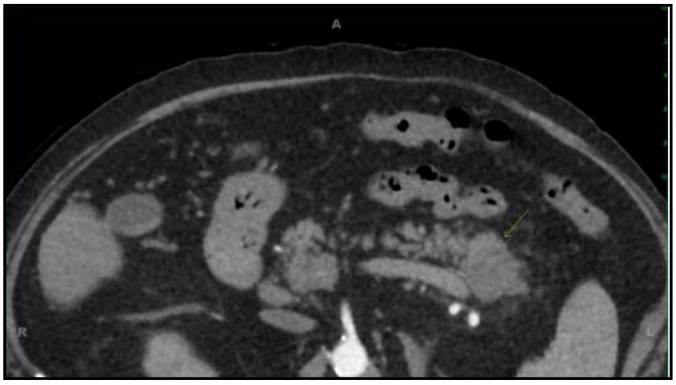
- Type of cancer Steve Jobs had unlike Alex Trebek who has adenocarcinoma (more to come on the difference)
- These types of tumors cause an overproduction of hormones like insulin and glucagon. The high levels of hormones can cause weight loss, N/V, muscle wasting and a skin rash. The overproduction of hormones do not cause jaundice or pain.

Diagnosis

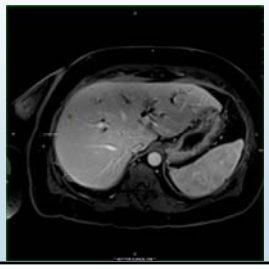
- Because of the location of the pancreas it can make diagnosing difficult and delayed. In addition since the symptoms usually develop gradually pancreas cancer might not be in the initial equation for a provider.
- Imaging:
  - MRI: can aid in visualizing the tumors when not visible on CT or if there is a contrast allergy. MRI is also extremely helpful in staging if concern of liver metastasis
    - MRCP: Magnetic Resonance Cholangiopancreatography is a special MRI that allows for specific imaging of the pancreatic and bile ducts. It can be done as part of standard MRI
  - CT: using IV contrast and multiphasic imaging related to the timing of contrast administration. If can is suspected scan should include the chest, abdomen and pelvis. Preferable a pancreas protocol that is a higher resolution imaging.
  - PET/Positron Emission Tomography scan: Imaging that is produced based on metabolic activity. Radioactive glucose is injected in to the body to measure the metabolic function of a cancer. PET helps delineate between benign and malignant tumors.

Tumor in the body of the pancreas

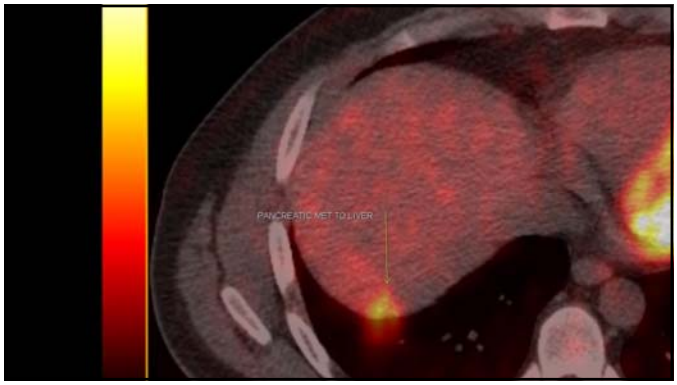




Metastatic cancer to the liver



Metastatic pancreas cancer to the liver



Additional work up

- EUS/Endoscopic Ultrasound: a procedure using an endoscope with a small ultrasound probe built into the tip. It is used to obtain immediate real time detailed imaging of the digestive tract, bile and pancreas duct and pancreas. This is typically done as an outpatient.
  - During this procedure a thin needle can be passed through the scope to allow for a fine needle aspirate/FNA. Cells collected during this procedure will then be examined by pathology to determine a diagnosis.
- ERCP/ Endoscopic Retrograde Cholangiocarciopancreatography: a procedure using a special endoscope that uses a narrow tube or catheter is inserted through the scope into the bile and pancreas ducts from the small intestine. Contrast is injected through the catheter into the ducts. Pictures are then taking to determine if there is a blockage or narrowing and why. May require overnight observation.
  - During this procedure if a blockage is seen, especially if patient is jaundice, a stent can be placed. The stent may be plastic/temporary or permanent/metal depending on the findings.
  - Biopsy or brushing of ducts can also be completed
- Both of these procedures have small risk for complications: bleeding, pancreatitis

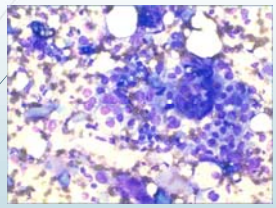
MORE…

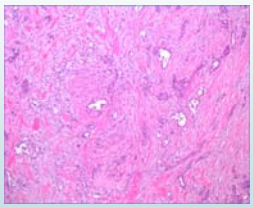
- If patients present with findings concerning for metastatic disease ie liver masses a percutaneous biopsy will be completed of the liver masses to obtain tissue.
- Laproscopic surgery is infrequently used for initial diagnosis. If there is a concern for malignant ascites or other findings in the abdomen that are not reachable by EUS this intervention may be used.

Types of pancreatic cancer

- Pancreatic tumors are classified in two groups
  - Exocrine tumors: which is ~ 94% of pancreas cancers
    - Adenocarcinoma: accounts 90% of all pancreas cancers. It begins in the lining of the pancreatic duct
    - Acinar Cell Carcinoma: is very rare. They cause excessive production of lipase the enzyme that is secreted to digest fats.
    - IPMN/Intraductal Papillary Mucinous Neoplasm: is a cystic tumor that grows from the main pancreatic duct or the side branches of the ducts. They may be benign and progress to cancer. The highest risk is with tumors that arise in the main duct and may be in many areas throughout the pancreas
    - Mucinous cystadenocarcinoma: is a rare malignant cystic tumor. Like the IPMN the cysts are filled with a thick fluid called mucin. They most often occur in the tail of pancreas and are mostly seen in women.
  - Endocrine tumors/Neuroendocrine tumors/NET: ~ 6 % of pancreas cancers
    - Which would include Gastrinomas, Glucagomas, Insulinomas and a few others
    - The majority of the information today will focus on the Exocrine type of pancreas cancer

Pancreas cancer up close





Lab tests

- No simple blood test exists for detecting or diagnosing pancreatic cancer however patients may have elevated liver function tests that direct additional work up to be completed
- High levels of certain hormones may be a sign of pNET such as insulinomas or gastrinomas
- Ca 19-9 is a blood test that measures the level of tumor associated antigens found in the blood. They are released by some pancreatic tumor cells. The normal range in a healthy person is 0-37U/ml however in 30% of patients there isn't an abnormal finding.
  - This can not be used as a means of detecting pancreas cancer as it may also be abnormally elevated by non cancerous conditions like gallstones, biliary infections, liver disease, pancreatitis and jaundice.

Genetic or germline testing

- Genetic testing looks for changes or mutations in genes that may have been inherited from the patients parents.
- If a mutation is found it may have options for additional targeted therapies
- If a mutation is found it may help determine the risk to other family members who may then have surveillance to monitor for cancer.
- Who should have genetic testing? Patients with a family history of cancers including melanoma, pancreas, colorectal, ovarian or breast cancer or digestive diseases. Additionally patients under 50 or of Asheknazi Jewish ancestry should be tested.

Staging

Tumor description	Extent of tumor
STAGE IA limited to the pancreas and mass is 2 cm or less	Localized
STAGE IB limited to the pancreas and mass is greater than 2 cm	Localized
STAGE IIA extends directly beyond the pancreas but does not involve the major arteries for local lymph nodes	Locally advanced
STAGE IIB may or may not extend beyond the pancreas but does no involve major local arteries. Local lymph nodes are involved	Locally advanced
STAGE III involves major local arteries. Local lymph nodes may or may not be involved	Locally advanced
STAGE IV Primary tumor may be any size. Disease has spread/metastasized to another part of the body including liver, lungs, abdominal wall and distant lymph nodes	Metastatic

Surgical resection category related to staging

- Resectable: tumors that can be removed. The tumor may be contained or extend just beyond the pancreas without involving major arteries or veins.
- Borderline resectable: tumors that may or may not be resectable at time of diagnosis. These tumors may or may not involve the celiac or superior mesenteric artery or veins but has not metastasized.
  - These patients will undergo neoadjuvant chemotherapy and possible chemo/radiation prior to surgery.
  - If blood vessels are affected neoadjuvant therapies improve the chances of an R zero or cancer free resection.
  - Some centers included ANW have surgical specialists that will use advanced techniques of vein resections
- Unresectable: tumors that can not be surgically removed either because of spread to other organs or can not be completely removed with surgery.

Treatment options for pancreatic cancer

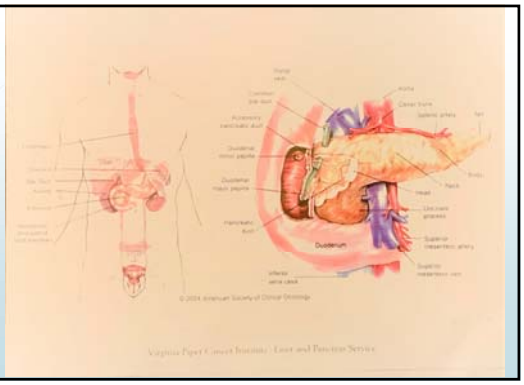
- Treatment of pancreatic cancer depends on the stage of the cancer and the patients overall health
- Stage I: surgery, chemotherapy with or without radiation before and or after surgery
- Stage II: same as Stage I
- Stage III: chemotherapy and chemo/radiation, surgery (occasionally)
- Stage IV: chemotherapy, targeted therapy
- Clinical trials can be available for all stages

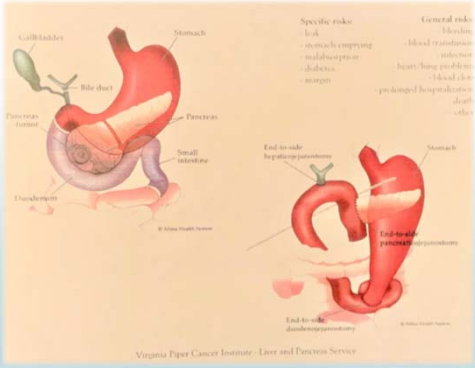
Surgery in general

- Surgery is the best chance for long term survival
- Approximately 20% of patients with adenocarcinoma are surgically resectable
- Vascular involvement does not preclude surgery
- Determining eligibility of a patient for surgery regardless of before treatment or after neoadjuvant therapy involves all facets of their whole person
  - Emotional and psychological health
  - Overall condition
  - Comorbidities including cardiac and pulmonary
  - Social picture

Whipple

- The Whipple or pancreaticoduodenectomy was first performed by Dr A Whipple in 1935 at Columbia University. It has changed very little over the past 84 years.
- This surgery is for when the cancer is located in the head of the pancreas or grand central station of your gi system
- It involves removing the lower part of the stomach/antrum, the top part of the small intestine or duodenum, head of the pancreas, gallbladder.
- This surgery takes 6-10 hours depending if vascular resection is required. The first Whipple surgeries were done over 2 days.
- Surgery is started by laparoscopically thoroughly assessing the inside of the abdomen for metastatic disease which may be the size of a sesame seed. If metastatic disease is found at any time during the initial dissection and mobilization up until the primary organ resections surgery will be aborted.





General risks of surgery

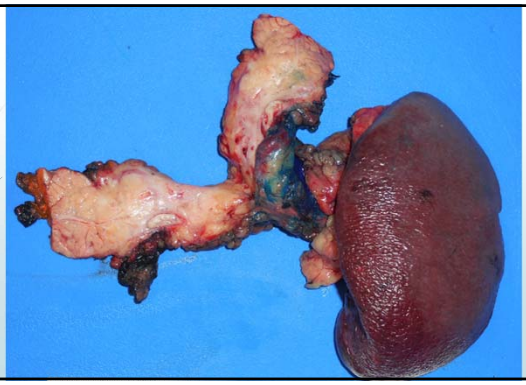
- Bleeding, possibly requiring blood transfusion
- Infection
- Heart/lung problems
- Blood clots
- Prolonged hospitalization
- Death

Specific surgery risks related to Whipple

- Leak from any of the surgical anastomosis/connections
- Delayed gastric emptying
- Malabsorption including pancreatic insufficiency
- Diabetes
- Positive surgical margin of unresected cancer

Distal pancreatectomy

- The distal pancreatecomy is when the tumor located in the body or tail of the pancreas is removed.
- This surgery also always entails the removal of the spleen. The spleen is attached to the tail of the pancreas and shares its blood supply.
- Vaccinations are given 2 weeks prior to surgery. These immunizations against encapsulated bacterial pathogens decrease the incidence of post-splenectomy sepsis. Pneumococcal, meningococcal, and Haemophilus influenzae (Hib) vaccinations are the standard vaccinations.
- This surgery typically takes ½ the time of the Whipple
- The most common complication is the leakage of pancreatic justice.



Other pancreas surgeries

- Total pancreatectomy: the removal of the entire pancreas. This is rarely done in the setting of cancer. You can live without your pancreas but will deal with severe diabetes and pancreatic insuffiency
- Laparoscopic or Robotic surgeries: these minimally invasive surgery techniques are not often used in the setting of pancreas cancer
- Palliative surgery: surgical interventions that are performed to alleviate symptoms like jaundice, N/V 2' duodenal obstruction. These procedures are typically bypass procedures rather than cancer resecting surgeries.

Chemotherapy

- There are currently 4 drugs approved by the FDA for the treatment of pancreatic cancer.
  - Fluorouracil- used before Gemcitabine became front runner
  - Gemcitabine- approved in 1996 for unresectable pancreas cancer
  - Paclitaxel-approved in September 2013 to be used in combination with Gemcitabine as first line treatment for metastatic cancer.
  - Irinotecan- approved in October 2015 in combination with Fluoruracil and Leucovorin for treatment of metastatic cancer if progression on Gemcitabine.
  - The 4 drugs, Folfirinox (Fluorouracil, Irinotecan, Leucovorin, Oxaliplatin) now standard depending on patients performance. They call it the "big guns"
  - Gemcitabine alone or Gem Paclitaxel are also standard
  - Capecitabine is used as a sensitizer during radiation

Side affects of chemotherapy and management

- Alteration in taste: food may taste bland or have metallic taste. Tart or bitter tasting food may help with metallic taste. Cold food often betted than hot.
- Constipation: drink plenty of fluids, Caffeine free is better. High fiber diet with moderate exercise
- Diarrhea: over the counter medications or if need prescription anti-diarrheals. Changes in nutrition may help improve
- Fatigue: some medications can help boost red blood cell production. Energy conservation and activity moderation.
- Hair loss/Alopecia: be gentle! Shampoo, drying and tools. Protect scalp when outside.
- Hand/foot syndrome: redness, tenderness, peeling of palms and soles. May also be accompanied by numbness and tingling. Wear gloves/socks. Keep well moisturized.
- Loss of appetite: eat every couple of hours throughout the day. Make it count for nutritional value. Medications are options to stimulate appetite.

More side effects

- Low blood counts
  WBC,Plt, Hgb: may require medication to stimulate new WBC or chemo reduction
- mouth sores: avoid spicy or acidic foods. Caffeine and alcohol may irritate. High protein foods and hydration will help heal faster. Use mild tooth paste and mouth wash, soft tooth brush.
- Nail changes: avoid chemicals and nail treatments. Wear gloves for household duties. Moisturize frequently. May require antifungal treatment.
- Nausea and vomiting: scheduled anti emetics of which there are many options. Acupuncture and acupressure.
- Neuropathy: numbness and tingling in hands and feet. Avoid temperature extremes, tight fitting shoes. Medications may be of help.
- Skin rashes: Erlotinib is often associated with acne like rash that will not respond to acne treatments. Other medications can also affect the skin. Avoid harsh soaps, sun exposure and alcohol.

How to mange…

- Encourage patients to journal
  - Symptoms
  - Activity
  - Nutrition
  - Thoughts and Feelings
- Encourage patients to report changes in their symptoms: new, worse, changed to allow for candid conversations with providers to improve, maintain or improve their quality of life during their cancer journey. Journaling remains a very helpful tool even from a reflective prospective in addition to the historical narration which can provide better insight to symptom management.

Radiation

- Radiation therapy is used to either prevent the tumor from growing or to shrink it. It can be used at different times and for all stages of pancreatic cancer.
- Radiation prior to surgery is neoadjuvant therapy and is done with oral chemo to boost the affects of the radiation. The goal is to reduce the tumor often away from critical vasculature.
- Radiation after surgery is adjuvant therapy to help prevent cancer from locally returning and to kill microscopic cancer cells that may have been left behind after surgery.
- There are different kinds of radiation
  - External beam (5 days a week for 4-6 weeks)
  - Internal radiation/brachytherapy: rarely used
  - Steroetactic/SBRT: very focused high dose radiation (1-5 treatments over 1-2 weeks)
  - Proton beam: external radiation that used proton beam which are charged particles of energy that allows for a higher more conformed dose of radiation.
- Radiation is painless but it can cause skin irritation and in rare cases abdominal pain.

Immunotherapy

- Immunotherapy is a treatment that stimulates the body's immune system to fight against cancer.
- Currently there are no FDA approved immunotherapies for pancreatic cancer.
- Studies and reviews for clinical trails are ongoing.

Clinical trials

- Allina active enrolling trials
- PANCREATIC CANCER
- Geistlich GP-2250 1001 Pancreas Cancer Study: Phase 1/ 2 trial of GP-2250 + gemcitabine in metastatic pancreatic cancer who have progressed on FOLFIRINOX
- University of Minnesota Tissue Procurement Study: Development of Oncolytic Adenovirus targeting cancer stem cells: Tissue procurement from pancreatic or esophageal cancer surgery, tx naïve patients.
- LAM 001-2018 ELITE Protocol: Collection of blood from Healthy Patients, Patients with Benign Disease, and Patients with Cancer. LAM is only looking for patients with active disease at this time.
- Clinicaltrials.gov is a service of the U.S. National Library of Medicine that provides access to anyone looking for additional information regarding clinical trials.

May 2019: Allina Health news release

Abbott Northwestern Hospital has enrolled the first human participant in a Phase 1 drug trial for a medication to fight pancreatic cancer. We are one of only two institutions in the world recruited by Geistlich Pharma AG, an international medical device and pharmaceutical manufacturer, to conduct trials for this groundbreaking cancer treatment. The fact that the manufacturer selected Abbott Northwestern Hospital speaks to the outstanding reputation we have in the research community, particularly in the treatment of pancreatic cancer.

Our Virginia Piper Cancer Institute research team enrolled and treated the patient on a Phase 1 pancreatic cancer study at the Abbott Northwestern Hospital Infusion Center. Everything went smoothly thanks to our research team, investigators, pharmacy, infusion center and laboratory staff members working together. This is a great example of how we are working on new and innovative ways to treat those with complex care needs. This is what distinguishes us from other hospitals in the area.

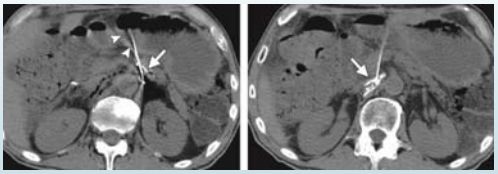
Nutrition(post surgery)

- Eat a well balanced diet of frequent smalls. Goal for protein intake 60-80 grams daily to aid in healing and prevent muscle wasting
- Stay hydrated but fluids should be taken in small amounts during or after meals to prevent filling quickly and feeling of fullness
- Light exercise can stimulate appetite and also increase the bodies need for calories.
- Recommend not eating prior to sleeping to minimize possible heartburn.
- Enzymes to assist in digestion of fats may be required.
- Insulin is sometimes needed at least during the initial post op recovery.

Activity

- Almost all of the pancreas patients seen through VPCI are referred to Cancer Rehab to prevent debility and deconditioning that can happen related to the cancer, treatments or with surgery.
- Research has shown that exercise during and after cancer diagnosis and treatment is safe and it can improve and extend survivorship.
- The 3 components of the fitness program focused on through VPCI Cancer Rehab are Cardiorespiratory exercise, strength or resistance training and flexibility exercises.
- Regular activity will improve circulation, lessen bone weakening, strengthens the immune system, lowers risk of falls and improves balance, improves quality of life.

Celiac plexus block: an injection performed by IR or via EUS. A neurolytic is injected into the nerve causing neurolysis which can significant decrease or completely remove pain and decrease the use of opiods and overall improving quality of life.



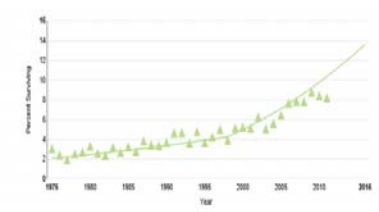
Supporting therapies

- Acupuncture
- Massage
- Aroma therapy
- Meditation
- Energy healing
- Biofeedback
- Traditional Chinese medicine
- Resilience training
- Cancer mental health service.

There are countless ways to support patients (and their families and care teams) to improve their quality of life during their journey.

Statics about survivorship over the past 40 years

SEER 9 5-Year Relative Survival Percent from 1975-2011, All Races, Both Sexes.



5-year Relative Survival Rate
(Based on people diagnosed with pancreatic cancer between 2008 and 2014)

SEER Stage
(SEER= Surveillance, Epidemiology, and End Results)

Localized: 34%

Regional:12%

Distant: 3%

All SEER stages combined: 9%

Pancreas team Allina

Dr Mark Hill, HPB surgery
Dr Ashwin Kamath, HPB surgery
Jenell Gilman, PA
Jill May RN Cancer Care Coordinator, Navigator

Books

- 100 questions & Answers about Pancreatic Cancer (2010) by Eileen O'Reilly MD & Joanne Franklel Klein RN
- My Journey with Pancreatic Cancer(2006) by Calvin Rains, Sr
- Pancreatic Cancer: Current & Emerging Trends in Detection and Treatment (2009) by Amy Steriling
- Pancreatic Cancer: "It's a Family Affair" (2010) by Lida Sthras-Lorene
- A Patient's guide to Pancreatic Cancer(2012) by Nita Ahuja and Joann Coleman
- The Last Lecture (2008) by Randy Pausch
- Pancreatic Cancer: A Patient and His Doctor Balance of Hope and Truth (2011) by Michael J ILipp and Dung T Le

Online and phone resources

- Pancreatic Cancer Action Network/PANCAN www.pancan.org 1-877-272-6226
- Pancreatica www.pancreastica.org 1-813-658-0600
- 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

"I've learned that people will forget what you said, people will forget what you did, but people will never forget how you made them feel."

— Maya Angelou

Disclosures

I have no disclosures related to this presentation