

SEMINAR-TUTORIAL CASE STUDIES

STUDENT EDITION

Mechanisms of Disease II

Spring, 2004

Mechanisms of Disease II
Seminar-Tutorial Case Study Schedule
Spring, 2004

Microscopic slide assignments are included after the last ST case of each session

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Jan 13	Jan 15	1A 1B 1C	Bloody stools, weight loss Fatigue and heme-positive stools Diarrhea and epigastric burning	2
Jan 27	Jan 22	2A 2B 2C	Nausea, vomiting, jaundice Hematemesis, ascites, and confusion Abnormal LFT's	9
Feb 03	Feb 05	3A 3B 3C	Edema and dark urine Fruity breath and stupor Fever, CVA tenderness	15
Feb 25 8-8:50	Feb 25 9-9:50	Congenital Heart Disease Lab		20
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SEMINAR-TUTORIAL CASE #1A

“Bloody stools, weight loss”

Y.M. was a 63 year old white male who presented to a local outpatient clinic with the chief complaint of "blood in my bowel movements".

The initial interview revealed that Mr. M. had a similar problem approximately three years earlier. At that time, he reported that physicians at an outside hospital "put a black hose up my rear and took something out.". When asked what exactly what was removed, the patient replied that it was a "plop". Previous pathology records could not be found.

In further trying to define the current problem, it was learned that Mr. M. first noticed bright red blood on his toilet paper approximately 5 months ago, and his stools were increasingly bloody. He denied having black or tarry stools,

The patient also reported a recent 15 pound weight loss mainly because he just wasn't hungry anymore. He denied fever, chills or night sweats.

Past Medical History: Remarkable for tonsillectomy during childhood.

Social History: One to two packs of cigarettes per day since 17 years of age. He also reported "occasional" alcohol use of no more than a six-pack a day during weekdays. He was increasingly vague with his attempts at quantification during weekend periods.

Family Medical History: His mother is alive and doing reasonably well living with his sister in Abilene. His father died 10 to 15 years ago from something. He did report, though, that his father had some kind of intestinal operation that required him to "...wear, you know, one of those plastic bag things on his stomach.".

Hospital Course: Physical exam showed a slightly obese white male appearing the stated age of 63 years. His appearance was somewhat disheveled. Pulse 78, respirations 18, blood pressure 180/92, temperature was not recorded.

The neck was supple and without masses. The chest diameter was slightly enlarged with hyperresonance to percussion. The heart had a regular rate and rhythm with a grade II/VI systolic ejection murmur. The abdomen was somewhat protuberant. The liver edge was 4 to 6 cm. below the right costal margin. A large mass was found in the right upper quadrant near the midline. This mass was fixed and rather firm. A digital rectal exam noted a normal rectal tone with no hemorrhoids. The stool was guaiac positive. Examination of the extremities was remarkable for nicotine stains between the right second and third fingers.

Laboratory: CBC: WBC 9800 with a normal differential. H & H of 10.2/27.1.

A colonoscopy was performed which identified a large ulcerating and fungating mass in the transverse colon. Surgery was scheduled for the following morning when a 12 inch portion of his colon including the mass was removed. The mass was noted to ulcerate through the colon wall. In addition, four mesenteric lymph nodes were noted to be positive for tumor. No distant metastasis was noted at the time of surgery.

Following surgery, the patient initially was doing well. However, on the third postoperative day, he spiked a temperature. A chest x-ray demonstrated bilateral pneumonia. Blood cultures were remarkable for E. coli. Despite aggressive therapy, the patient continued a downhill course and expired on the 8th hospital day. When explaining the situation to the decedent's family, the intern said "I'm sure you don't want an autopsy, do you?". The decedent was buried without benefit of a postmortem examination.

Study Questions for Students

Case #1A

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. Review Images ST1A-1 (gross colon), ST1A-2 (low power, colon), ST1A-3 (medium power, colon) and ST1A-4 (medium power, colon). What is the patient's diagnosis? What is the patient's stage and prognosis?
2. What is CEA? Would a CEA level have been useful in the diagnosis of this disorder? What is the role of CEA in the management of this disease?
3. What risk factors does this patient have for the development of colon cancer?
4. What are the potential screening tests for colon cancer. Who should be screened and when?
5. What is the adenoma – carcinoma sequence?
6. Could there have been a better way to ask the family's permission for an autopsy? Even in the face of supposed clear-cut diagnosis, what questions could have been answered by an autopsy.

SEMINAR-TUTORIAL CASE #1-B

“Fatigue and Heme-positive stools”

W. R is a 37 year old female who presents with fatigue and dizziness. She has had a “nervous type of stomach” and diarrhea all her life with 2 to 3 bowel movements per day that are “semi-formed, loose”.

Past Medical History: Cervical biopsy with cervical dysplasia. A benign cyst removed from her back last year.

Social History: Married, does not smoke, quit approximately 3-4 years ago. Alcohol use on rare occasions.

Current Medications: Ortho-Novum, multivitamin 1 p.o. q.d. No over the counter agents.

Family History: Grandmother with colon cancer diagnosed in her 90's. Grandmother and great aunt with breast cancer in their 70's. Father has Crohn disease.

Physical Exam: BP 144/85, HR 114, Temp 100.1, Weight 132.6 lb. She is an alert female who appeared her staged age. Skin is remarkable for a subcutaneous nodule just below the right clavicle. Eyes are non-icteric. Lungs are clear to auscultation. Heart has a regular rate and rhythm without murmur. Abdomen has active bowel sounds with no organomegaly, masses or tenderness. Heme occult blood test is positive on rectal exam.

Laboratory: WBC 7.0, RBC 3.56, Hb 8.4, MCV 76, MCH 23.7, MCHC 31.2, RDW 23.1, PT 13.4 APTT 26.7. Blood chemistries are normal

Outpatient work-up: Due to the heme positive stools the patient had an upper and lower endoscopy. Upper endoscopy was normal except for multiple small polyps in the body and fundus of the stomach, biopsies were taken (ST1B-1). No abnormality of the ampulla of Vater was identified. Lower endoscopy (colonoscopy) revealed multiple colonic polyps, too numerous to count. The polyps were present in the entire colon from rectum to cecum. Intubation of the terminal ileum revealed no polyps in the distal small intestine. Biopsies of some representative polyps were taken (ST1B-2).

Hospital course: The patient was taken for total abdominal colectomy. Findings in surgical pathology were an entire colon and terminal ileum. On opening the bowel, multiple polyps both sessile and pedunculated were identified (ST1B-3). The polyps ranged in size from 0.2 cm to 5 cm. One lesion in the sigmoid colon measuring 3.0 cm was fixed to the underlying submucosa. Representative sections of the polyps, (including the fixed polyp ST1B-4) and lymph nodes were taken. A total of 22 lymph nodes were identified (ST1B-5).

Study Questions for Students Case #1B

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. Review Images ST1B-1 (low power, stomach), ST1B-2 (medium power, colon polyp) ST1B-3 (gross picture, colon), ST1B-4 (medium power fixed polyp), and ST 1B-5 (medium power lymph node). What is the patient's diagnosis? What is the patient's stage and prognosis?
2. What is the inherited genetic defect in this disease and what other syndromes also have the same inherited genetic defect?
3. What is the difference between Familial Adenomatous polyposis (FAP) and Hereditary Nonpolyposis Colon Carcinoma (HNPCC) with respect to gross findings, microscopic findings, age of onset, and underlying inherited genetic abnormality?
4. What is the natural history of the disease and what is the treatment?
5. How should the family be counseled?

SEMINAR-TUTORIAL CASE #1-C

“Diarrhea and epigastric burning”

A.F is a 48 year old with a long-standing history of inflammatory bowel disease initially diagnosed at age 20. She had a partial colectomy with an ostomy at age 25. This was revised seven years later with an ileocolonic anastomosis. She has been treated over the years with multiple medications including Prednisone and Azulfidine. She has been intolerant to Azulfidine and had to stop taking this medication. She has had multiple flares over the years. Two years ago Remicade was tried on two different occasions with good results. Currently she is experiencing diarrhea and epigastric burning. The epigastric burning is severe and she is able to eat very little food. Even water exacerbates the esophageal discomfort. She has lost 40 lbs of weight over the last few months. She is also having abdominal pain and bloating in addition to the diarrhea.

Past Medical History: She has had left and right hip replacement secondary to avascular necrosis from her Prednisone.

Family History: She has a sister and nephew with inflammatory bowel disease.

Social History: She smokes one pack of cigarettes per day for the past 30 years. Social alcohol.

Physical Exam: Thin female in no apparent distress. Heart rate 93, BP 131/61, weight 101 lb, temp 98.2. The skin is normal to inspection, eyes non-icteric. Heart with regular rate and rhythm and a 2/6 systolic murmur. The lungs were clear bilaterally. The abdomen was non-distended with hyperactive bowel sounds. She has mid-epigastric tenderness on palpation. There are no hepatosplenomegaly or masses. Rectal exam revealed normal tone, no fissures identified. Heme occult stool is positive. Extremities displayed no edema or rashes.

Laboratory: WBC 6.6, RBC 5.08, Hb 9.78, Hct 32.7%, MCV 64.4, MCH 19.2, MCHC 29.9, RDW 17.3, Plt 520. Iron 12, UIBC 360, TIBC 372, % sat fe/TIBC 3%. Sed rate 32. Metabolic panel within normal limits.

Hospital course: A small bowel follow through radiologic exam revealed a stricture at the ileosigmoid anastomosis. The patient was admitted for surgical excision of the strictured region. Surgical pathology received an 18 cm portion of bowel (ST1C-1). The average diameter of the bowel is 4 cm. The specimen is opened to reveal three distinct areas of stricture. The mucosa is normal except for the strictured areas which have irregular mucosal ulceration. No polyps or masses are identified. Representative sections are taken (ST1C-2 to 4).

Study Questions for Students

Case #1C

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. What is the diagnosis in this case?
2. What are the differences between Ulcerative colitis and Crohn disease with respect to macroscopic, microscopic, and clinical findings?
3. Is there an increased risk of colonic adenocarcinoma for this patient?

Microscopic Slide Assignment

SLIDE 4: Sections of adipose tissue with supporting stroma, probably from omentum, in which there are large areas of enzymatic fat necrosis and associated calcification. In some areas recognizable macrophages may be present as well as nuclear debris. The yellow pigment is hematoidin.

SLIDE 18: This is a section of lymph node and adjacent fibrofatty tissue. They are largely replaced by a malignant neoplasm of epithelial origin which tends to reproduce gland-like structures. Particularly near the periphery there are numerous vascular structures. Some of these are blood vessels and others are lymphatics. Many of these contain plugs of these cancer or neoplastic cells and these represent **tumor emboli to lymph node**.

SLIDE 20: This section of colon demonstrates a transition from normal glandular mucosa into atypical and neoplastic gland forming epithelial cells which infiltrate the fibromuscular wall. This is an **adenocarcinoma of the colon**.

SLIDE 42: **Cystic fibrosis of pancreas**. A four year old male diagnosed at age three months. Death due to pulmonary complications. Slides show loss of acini with preservation of ducts and islets which are surrounded by fibrous tissue. Lobular outlines are still seen. Some ducts are dilated and may be filled with eosinophilic material (inspissated secretion). This material has formed some concretions and may show calcification.

SLIDE 85: Sections of ileum from a case of **regional enterocolitis** or **Crohn disease** (S78-15131). Sections of ileum demonstrate a tremendous thickening of the wall with a focal and relatively small area of mucosal necrosis and ulceration. The thickness of the wall is due to extensive chronic inflammatory changes with appreciable fibrosis. The inflammatory exudate, which is chronic in type, also reveals a somewhat nodular or granulomatous characteristic and many of these consist of large numbers of histiocytes and occasionally a multinucleated giant cell. This full thickness inflammatory change extending from the mucosa to the serosal surface with resultant extensive thickening of the wall of the intestine and the granulomatous foci are characteristic of this disease.

SLIDE 86: **Chronic ulcerative colitis** (S78-9158). Sections of colon reveal numerous areas of mucosal necrosis and ulceration and active chronic inflammatory cellular reaction involving the mucosa and submucosa with occasional spreading of the inflammatory process into the muscle and subserosal fibrofatty tissue. Involvement of the muscle and serosal tissue, however, is focal and not the dominant feature. The remaining mucosa protrudes above the surface in a pseudopolypoid fashion and an occasional gland contains inflammatory exudate in the lumen (crypt abscess) and a few remaining crypts reveal similar necrosis and acute inflammation with occasional lateral progression of this process.

SEMINAR-TUTORIAL CASE #2-A

“Nausea, vomiting, jaundice”

This 18 y.o. white male was admitted to the MUH because of progressive hepatic failure, two weeks after being seen by his local physician for a one-week history of nausea, vomiting, headache, and developing jaundice. At that time a diagnosis of hepatitis was made and Phenergan was prescribed. Ten days later he returned to his physician, unable to keep fluids down. There had been an approximate 10 lb. weight loss and one episode of hematemesis. He was admitted to the local hospital that same day and became progressively encephalopathic over the next three to four days.

Significant past history included a long history of heavy beer drinking. Through a detoxification program, the patient had been taking Antabuse daily (administered by his mother) for the past three months. According to his mother, the patient had earlier consumed alcohol only once, and had a hives-like reaction. The Antabuse was discontinued on the day of his initial visit to his physician. The patient's mother denied knowledge of any illicit drug use, although the patient had been staying for the past six weeks to three months at a friend's house where there was little parental supervision. Other medications used during this time were over-the-counter headache preparations, especially Tylenol (supposedly less than 30 tablets during the past month).

Past Medical History: There had been no travel outside of the community, and no past blood transfusions (Moped accident at age 13 with head lacerations). The patient drank city water. No allergies.

Family History: No family history of liver disease. Maternal history of hypertension and diabetes. Paternal history of stroke and diabetes.

Medications at the time of admission: Phenergan, vitamin K and lactulose.

Physical Exam: Temperature 99.6, pulse 112, blood pressure 150/60 and respirations 18. General appearance: A heavy, young, white male, who was comatose and displayed occasional posturing movements. His skin was noted to be very jaundiced. There was no lymphadenopathy. HEENT exam: Atraumatic head. The pupils were dilated widely, but briskly reactive. Sclerae were very icteric. He was noted to have some papilledema bilaterally. The oral cavity was without lesions. Chest exam revealed clear breath sounds anteriorly. Cardiovascular exam revealed tachycardia, a regular rate and rhythm without murmurs, rubs, or gallops. The abdomen was soft with hypoactive bowel sounds. The liver edge was not palpated, although his liver span was percussed to 10 cm. No masses were palpated. His external genitalia were normal. Neurologic exam revealed the patient to open his eyes and exhibit decerebrate posturing with stimulation. He was unable to follow any verbal commands. He did move all extremities spontaneously. Deep tendon reflexes could not be obtained. Babinski reflexes were negative.

Labs: Hematocrit 48, white blood cell count 14,000 and platelets 420,000. Sodium 143, potassium 3.7, chloride 107, bicarb 28, BUN 4 and creatinine 1.4 with glucose 143. AST 345; ALP 465; Direct bilirubin 29.7, Total bilirubin 40.2; Ammonia 119. PT 30.4, APTT 56.3. Total protein 5.6; albumin 3.6. Chest x-ray was clear and EKG revealed sinus tachycardia without ischemic changes.

Hospital Course: The patient was immediately admitted to the Medical Intensive Care Unit. He was felt to be in Grade IV encephalopathy. Based on the patient's likelihood of having cerebral edema, the patient was treated aggressively with fresh frozen plasma and IV mannitol. His neurologic status continued to deteriorate and he was intubated for airway protection. He was left on T-bar that night, but the next day, was placed on a ventilator. He subsequently became anuric. His AST rose to 1,034; ALT to 1,480. Hepatitis profile was negative for hepatitis A and B. The patient developed left-sided seizures in the early AM of the fourth hospital day which required IV Dilantin, IV Valium and IV phenobarbital to control them. CT scan was obtained which was very suggestive of a subarachnoid hemorrhage. The patient's neurologic exam, as he continued to deteriorate, was significant for pupils which were found to be fixed and dilated. The Neurology Consult Service evaluated the patient and he was felt to fit the criteria for irreversible brain death. The patient was subsequently disconnected from the ventilator on the sixth hospital day and shortly thereafter died. The post-mortem examination was limited to the liver.

Autopsy Findings: The body of the patient appeared the stated age, with a body weight of 180 lbs. and a body length of 170 cm. The skin, sclera, and conjunctivae were extremely jaundiced. Scars were present over the left knee. Urinary bladder catheter, nasogastric and endotracheal tubes, and intravenous catheters were present.

180 cc. of serosanguineous fluid were present in the peritoneal cavity.

The liver was small, weighing 910 gms. The liver was a dark red to green organ with a wrinkled capsule covering most of the liver. The right lobe was somewhat nodular. Cut surface displayed a dark red to focally green soft parenchyma interspersed with lighter, green nodular areas of regenerating liver. The gallbladder was described as normal.

Study Questions for Students

Case #2-A

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. Name some infectious, drug and chemical causes of fulminant hepatic failure. Which ones might reasonably be suspected in this case?
2. List the features (clinical signs and symptoms, laboratory values) of this patient's course which pointed toward profound liver failure. What is hepatic encephalopathy?
3. Describe the histopathologic changes present in Images ST2A-1 (gross), ST2A-2 (low power), ST2A-2 (medium power), and ST2A-3 (high power) of the liver. Identify the expanses of liver wherein no hepatocytes survive. What is there? What are the narrow cords of epithelial cells next to areas of necrosis? Are there any viable hepatocytes in this section? Any sign of regeneration? What would be the likely outcome of the liver if the patient had recovered neurologically and had been successfully supported for several months?

SEMINAR-TUTORIAL CASE # 2-B

“Hematemesis, ascites, and confusion”

A fifty-two year old male is admitted to the Emergency Room. The history indicates chronic alcoholic abuse with sporadic episodes of heavy drinking. In the last 2-3 days, he has been nauseated, has vomited small quantities of bright red blood and has been progressively confused.

Examination confirms his confusion, notes mild tachycardia, hypotension, and yellowing of the conjunctivae. On abdominal examination, there are occasional spider nevi. Percussion and palpation suggests abdominal ascites. The liver is not palpable.

Laboratory Data:

Blood	Bilirubin total	- 2.0 mg/dL
	Glucuronide bound (direct bilirubin)	- 0.6 mg/dL
	Total Protein	- 5.3 G/dL Protein
	Albumin	- 1.8 G/dL
	Globulin	- 3.5 G/dL
	Prothrombin Time	- 18 seconds
	Aspartate Amino Transferase (AST)	- 161 U/L
	Alanine Amino Transferase (ALT)	- 80 U/L
	Alkaline Phosphatase	- 140 U/L
	Gamma glutamyl transferase (GGT)	- 80U/L
	Urine Dipstick	- Bilirubinuria Urobilinogen increased
	Electrophoresis	notes Beta - Gamma bridging

Liver Biopsy: Trichrome stain (ST2B-1). H&E stain (ST2B-2 to 4)

Study Questions for Students Case #2-B

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. What is the diagnosis? Explain the laboratory findings in conjunction with this case.
2. Describe the histopathologic changes present in Images ST2B-1 (low power, trichrome stain), ST2b-2 (low power, H&E), and ST2B-3-4 (high power, H&E) of the liver. Identify the Mallory bodies.
3. What is the mechanism of the liver damage in this patient?

SEMINAR-TUTORIAL CASE #2-C

“Abnormal LFT’s”

A forty-two year old female is referred for increased LFT’s at the time of a routine blood draw for an insurance physical exam. The patient is currently asymptomatic. She has no fever, chills, nausea or vomiting. There is no history of jaundice, increased abdominal girth or bright red blood per rectum. She has no shortness of breath or anorexia.

Past Medical History: No travel outside the community. Was in a car accident 20 years ago and received a blood transfusion at that time. Otherwise has never been in the hospital.

Social History: “Occasional” alcohol use, primarily in social occasions. Has a history of a DUI 20 years ago. She has been married for 12 years, but has no children. Admits to a remote history of IV drug use in her late teens, nothing for the last twenty years.

Family History: Has an aunt with pancreatic cancer. Her mother is in her 70’s and in good health. Her father died 10 years ago from alcoholic liver disease.

Physical Exam: 42 year old female who appears her stated age in no apparent distress. Temp 98.8, BP 136/70, HR 61, respirations 18. Weight 210 in this 5’ 2” woman. Sclera are anicteric. Heart: regular rate and rhythm. Lungs are clear to auscultation bilaterally. Abdomen is obese, soft, non-tender, non-distended, with normal bowel sounds. Liver edge and spleen are not palpable.

Laboratory Data:

Blood	Bilirubin total	- 1.3 mg/dL
	Glucuronide bound (direct bilirubin)	- 0.6 mg/dL
	Total Protein	- 7.1 G/dL Protein
	Albumin	- 4.6 G/dL
	Prothrombin Time	- 13 seconds
	Aspartate Amino Transferase (AST)	- 90 U/L
	Alanine Amino Transferase (ALT)	- 87 U/L
	Alkaline Phosphatase	- 140 U/L
	Hepatitis A AB	- Negative
	Hepatitis B surface AB	- Positive
	Hepatitis B surface Ag	- Negative
	Hepatitis B core AB	- Positive
	Hepatitis C AB	- Positive
	Hepatitis C viral load	- 331000 IU/mL
	Hepatitis C genotype	- 1a
	Hepatitis B DNA	- Negative
	AMA	- Negative
	ANA	- Negative
	Alpha fetoprotein	- 5.0

Liver Biopsy: Trichrome stain (ST2C-1). H&E stain (ST2C-2 to 4)

Study Questions for Students

Case #2-C

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. What is the diagnosis? Explain the laboratory findings in conjunction with this case.
2. Describe the histopathologic changes present in Images ST2C-1 (low power, trichrome stain), ST2C-2 (low power, H&E), and ST2C-3 and 4 (high power, H&E) of the liver.
3. What risk factors does this patient have for her disease?

Microscopic Slide Assignment:

SLIDE 1: Sections show liver in which the cytoplasm of most of the hepatic cells is distorted or replaced by a clear vacuole. These vacuoles are rather sharply outlined and in hematoxylin-eosin prepared sections, this is the characteristic picture produced by fat. This is an example of **fatty change of the liver**.

SLIDE 11: This is a section of liver. This liver was diffusely, coarsely nodular. Patient's age was 52. He was a known alcoholic for many years, consuming large quantities of alcohol per day. At autopsy the liver weighed 2100 gms. Under low power the hepatic cells are arranged in nodules of varying size and separated by broad bands of fibrous and collagenous scar tissue, within which single to multiple bile ducts may be observed together with a fine scattering of chronic inflammatory cells, mostly lymphocytes in type. The lobules of liver cells are sometimes oriented with a central vein but often this is not readily demonstrable or not present. In the latter case, these are regenerating liver cells producing pseudolobules. The liver cells individually show varying amounts of vacuolization of the cytoplasm. These clear vacuoles represent fat which is one of the features seen in the liver in cases of alcohol abuse. The fibrosis, which is noted, is the feature related to the term "cirrhosis", and this is variously called **alcoholic cirrhosis, nutritional cirrhosis, portal cirrhosis and Laennec cirrhosis**.

SLIDE 39: A section of liver. There are somewhat distorted lobules of hepatic cells, many of which show evidence of fatty change separated by thin bands of scar tissue. If one searches throughout the lobules of liver cells in a properly stained area, one may find numerous intracytoplasmic roughly circular bright pink bodies. These are so called Mallory bodies or hyaline bodies frequently found in severely damaged livers of chronic alcoholics. **Alcoholic fatty liver with Mallory bodies**.

SLIDE 79: AIDS (A85-602). This is a section of liver from a 5 year old who died with AIDS. The immediate cause of death was an esophagopleural fistula secondary to Candidiasis. During life, cultures of the bone marrow were positive for Mycobacterium avium intracellulare complex. This is a section of liver with MAI. The liver contains multiple small granulomas, chiefly in the portal areas. The macrophages in these granulomas have many acid fast bacilli within them on special staining. Some fatty change and minimal centrolobular necrosis can also be identified.

SEMINAR-TUTORIAL CASE #3-A

“Edema and dark urine”

History of present illness: B.R is a 36 year old white female who was in her usual state of health until three weeks prior to admission when she developed fever, night sweats, and chills. This was followed by generalized progressive edema. Coincident with the onset of edema the patient noticed the onset of dark urine. No other GU symptoms were noted. The patient has a chronic mildly productive cough and has noted streaky hemoptysis along with the physical illness but no gross hemoptysis. She denies rash, arthritis or arthralgias but has some myalgias.

Past Medical History: G7, P6, A1. Questionable pyelonephritis 14 years ago.

Medicines: Anacin 8 tabs daily for 10 to 20 years, Alka Seltzer 1 or 2 tabs daily for several years.

Social History: 8-10 pack year history of cigarette smoking. Social alcohol and has had moonshine in the past.

Family History: Positive for hypertension, M.I., and "Bright Disease".

Admission Physical Examination: Obese white female in no acute distress, blood pressure 155/105, pulse of 96 supine. Significant findings included normal fundoscopic exam, pharynx without exudate or erythema. Neck was supple, chest clear. Cardiac exam revealed a II/VI systolic injection murmur at the left sternal border. Abdomen was soft with minimal tenderness in the right upper quadrant and suprapubic area. Extremities revealed 2+ pitting edema. There was 1+ pre-sacral edema.

Admission Laboratory Data: Bun 24, Cr 2.4, albumin 2.5. Hemoglobin 8.4, hematocrit 24.5; WBC 10.9 with 80% polys, no bands, 17% lymphs. Urinalysis: 2+ protein, 2+ blood, 11-20 WBCs, many RBCs and RBC casts. Gross hematuria noted. EKG showed non-specific ST wave changes. Chest x-ray was normal. ASO titer 480, ANA negative, C3 9.9, C4 less than 90.

A percutaneous kidney biopsy was performed. The images show an H&E-stained (Image ST3A-1, medium power, kidney) and a silver stained (Image ST3A-2, high power, kidney) section of the biopsy. The image (ST3A-3) of the immunofluorescence shows a glomerulus stained with fluorescein labeled anti-human IgG antibody. The staining for C3 was similar. Two photographs (Images ST3A-4 and ST3A-5) of the renal electron micrographs are included.

Study Questions for Students

Case #3-A

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. What clinical syndrome does the patient have? What are the components of this clinical syndrome?
1. What is your differential diagnosis based on the clinical history alone?
3. What is the significance of red cell casts?
4. Describe the light microscopic, immunofluorescent, and electron microscopic findings. What is your diagnosis according to these findings?
5. What is this patient's prognosis? What are the possible outcomes of this disease?

SEMINAR-TUTORIAL CASE #3-B

“Fruity breath and stupor”

A forty two year old male is seen in the Emergency Room. He is stuporous.

He lives alone in an apartment complex where he was found, last seen apparently well, 2 days ago. A friend who has no historical knowledge of the patient's previous health says that he has had a flu like illness for the past week. You are informed that the patient does not drink liquor, use drugs and no prescription items have been found in the apartment. He is said to be a salesperson in a department store.

On examination he is rousable only to severe painful stimuli. Breath odor described as "fruity". No physical evidence of head trauma noted.

Temperature 40°C
Pulse 160
Blood pressure = 100/60 mm Hg (hypotensive)
Respiratory Rate 36/min.

Laboratory Data:

Blood	K	5.7 mEq/L
	Na	140 mEq/L
	Chloride	104 mEq/L
	HCO ₃	12 mEq/L
	Creatinine	2.7 mg/dL
	Glucose	620 mg/dL
Arterial Blood Gases	pH	7.25
	PO ₂ (room air)	= 90 mm Hg
	PCO ₂	= 28 mm Hg
	HCO ₃	14 mEq/L
Urine (Fresh)	pH	5.2
	Protein	++
	Glucose	++++
	Ketones	+++

Study Questions for Students Case #3-B

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. What is the most obvious diagnosis? Upon what findings do you base this?
2. What is the acid base abnormality?
3. Explain the elevated creatinine.
4. Are there other types of hyperglycemic coma?
5. What is the follow up investigation of this patient?

SEMINAR-TUTORIAL CASE 3-C

“Fever, CVA tenderness”

A previously healthy 25 year old white female visits her physician with a major complaint of high fever accompanied by shaking chills. She reports that the fever has been present for 2 days. She denies any cough, nausea, vomiting or diarrhea. Her last menstrual period was 14 days ago.

Physical examination reveals a febrile (103°F) young woman with right costovertebral angle (CVA) tenderness.

Initial work-up of this patient should included:

1) The following laboratory investigation:

WBC	15.6 x 10 ³	Polys	84%
RBC	4.8 x 10 ⁶	Bands	8%
Hgb	12.6 gm/dL	Lymphs	8%
Hct	36.2%		
MCV	87.2u ³	RBC morphology	– within reference ranges
MCH	30.3uu		
MCHC	34.8%	Platelets	- 250,000

2) Urinalysis:

Color	- yellow	Protein	- 2+	WBC	- 21-50/HPF
Clarity	- cloudy	Glucose	- Neg	RBC	- 2-5 HPF
S.G.	- 1.010	Ketones	- Neg	Bact.	- Moderate numbers
pH	- acid	Bile	- Neg	Hyaline Casts	- 5-10/LPF
		Blood	- Neg	Granular Casts	- 1-5/LPF
				WBC Casts	- 1-5/LPF

Study Questions for Students

Case #3-C

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. What do the results of the hematology panel suggest?
2. What do the results of the urinalysis suggest? What is the significance of WBC casts?
3. Which organism is most like to grow from the urine culture?
4. The patient’s plasma creatinine is 2.5 mg/dL and the urine creatinine concentration is 100 mg/dL. The urine volume is 1000 mL/24 hours. Calculate the creatinine clearance. The patient’s weight is 55 kg. Calculate the creatinine clearance using the approximation formula:

$$\frac{(140 - \text{age}[\text{yrs}])(\text{weight}[\text{kg}])}{72 (\text{serum creatinine})} \quad (\text{values for women are } 0.85 \text{ of this formula})$$

5. The patient’s blood urea nitrogen (BUN, actually more properly serum urea nitrogen) is 25 mg/dl. If the BUN were significantly higher than this, what might it suggest? If the BUN were significantly lower than this, what might it suggest?

MICROSCOPIC SLIDE ASSIGNMENT

SLIDE 2: Sections of kidney show a sharply outlined area within which there is a complete loss of cellular structure and detail and merely a ghost-like outline of anatomical structure showing a configuration of tubules, glomeruli and vessels. This area is literally bleached out, containing few, if any, blood cells with, however, evidence of hyperemia at the periphery of this zone. This represents another example of ischemic necrosis due to vascular occlusion and grossly would appear as a so-called anemic **infarct of the kidney**.

SLIDE 64: This is a section of kidney (A68-173) in which there is extensive glomerular damage, many of which appear as balls of pink hyalinized material, with others showing evidence of a transition from epithelial proliferation, so-called demilunes or crescents, into completely scarred glomeruli. There are variable associated changes of interstitial scarring, tubular dilatation and focal accumulations of exudate within tubular lumens. Other dilated tubules contain homogeneous pink masses of apparent proteinaceous debris. This is an example of **chronic glomerulonephritis**.

SLIDE 66: (A69-274) **Cortical necrosis of kidney**. Ischemic infarction involving the midcortex. Subcapsular with juxtamedullary zones are generally spared.

SLIDE 68: (VA 30-79) Kidney showing **arterio- and arteriosclerosis**. These are essentially end stage or nonfunctioning kidneys. The primary disease process is not conclusively known but it may well be vascular. The interlobar and intralobular arteries are uniformly thickened by fibrous and hyalinized fibrous tissue as well as some showing an increase in ground substance. The arterioles show thickened walls which are almost totally hyalinized. In addition the renal parenchymal (primarily cortex) is markedly diminished. Many glomeruli are partially to totally scarred. The tubules are largely atrophic with focal areas of dilatation and filled with inspissated proteinaceous material, some of which is calcified. The interstitial tissue reveals increased fibrosis and scattered inflammatory cells.

SLIDE 24: This specimen consists of a well outlined mass of normal adult mature adipose tissue. This is a typical histological picture of a **lipoma**.

SLIDE 25: This is a section of skin and underlying fibrofatty tissue. The subsurface tissue is partially replaced by loose fibrillar material and cells tending to have a fusiform shape intermingled with giant cells, some of which have single nuclei and others more than one nucleus and the nuclei are atypical. Occasionally, large cytoplasmic vacuoles are present. This is an infiltrating mesenchymal malignancy, classified as a **liposarcoma**.

CONGENITAL HEART DISEASE LAB - 2004

A. GENERAL INFORMATION

1. The objective of this congenital heart disease lab is to give you an opportunity to examine heart defects as they actually exist (or existed in cases of surgical repair) and to understand some of the pathophysiologic effects of abnormal structures.
2. Most of the nine groups of hearts displayed around the classroom contains examples of the more common congenital heart defects as discussed in lecture. Look at several of these tables first and you will be able to observe each of the 10 defects (or combinations thereof) illustrated in class:

VSD	PS	T of F
ASD	AS	TGV
PDA	Coarct. of aorta	Hypoplastic left heart syndrome
ECD		

Booklets with information about the cases are present at each table.

Study questions are listed below. Answer these as completely as you can. At the end of the exercise, there is a short quiz. The questions are based on observations you will have made in the laboratory and on syllabus information. This quiz is entirely optional; you will grade yourselves.

3. Handle the specimens gently; the tissue tears easily. There are some wooden probes available; gently use them if necessary.
4. For best results, follow the flow of blood when looking at the heart: RA, RV, PA, LA, LV, Aorta. The aorta has coronary ostia and arch vessels! The right and left ventricles have very different morphology and different-looking inlet valves. Note: The right and left ventricles in a newborn have roughly the same wall thickness (during intrauterine development, most of the blood bypasses the lungs and moves through the ductus to the aorta).

There are three groups of "unknown" hearts around the classroom. These are somewhat more complicated and the specimens are not all labelled (although a booklet with information is present at each table). Please feel free to look at these.

5. Pathology residents and attendings, pediatric cardiologists, and cardiothoracic surgeons will be around the classroom to answer questions and talk with you about interesting or baffling hearts.

B. STUDY QUESTIONS FOR CONGENITAL HEART DEFECTS

**** HANDLE THE HEARTS GENTLY ****

1. VSD; ASD; PDA

Identify the location and appearance of the above defects. Visualize the resulting hemodynamic alterations and thus some of the potential consequences of each defect. What are the other possible complications? Under what circumstances might the above defects actually be helpful?

2. Endocardial Cushion Defect (common AV canal)

Look down into the right atrium and through the right A-V valve. Notice that you can see (or probe) into the right ventricle and the left ventricle from the right atrium. This is possible because the lower portion of the atrial septum and a significant portion of the ventricular septum are missing. Note that the tissue representing the atrioventricular valve is not divided into tricuspid and mitral valves but is more a circle of valve tissue which "crosses over" the ventricular septum so that the right A-V valve components are continuous with the left A-V valve components over the septum. Some of the ECD hearts will have a "band" around and constricting the pulmonary artery: for what purpose?

3. PS and AS

Identify these defects and notice the corresponding hypertrophy of the associated ventricle. If corrective surgery could not be performed immediately, what helpful procedure could be done for pulmonic stenosis? How would severe aortic stenosis affect coronary blood flow?

4. Coarctation of the Aorta

Most (or possibly all) of the examples of coarctations will be of the "preductal" type. Identify the narrowed aortic arch segment. Is the ductus patent? Is the AV normal? Can you identify LVH? What are the possible effects/complications of aortic coarctations? What would be the most extreme "version" (far end of the spectrum) of an underdeveloped aortic arch?

5. Tetralogy of Fallot

Identify the four "features" of Tetralogy of Fallot. Which one is a physiologic response to abnormal anatomical structures? Notice where the VSD is in Tetralogy of Fallot, as opposed to the location of the usual VSD. What palliative procedure would improve blood flow to the lungs, if "corrective" surgery (repair of VSD, relief of pulmonic stenosis) can not be readily accomplished? Complications of Tetralogy of Fallot?

6. Transposition of the Great Vessels (TGV)

Follow the flow of blood in the example of TGV to identify the origin of the aorta from the right ventricle and the origin of the pulmonary artery from the left ventricle. What shunts between right and left sides of the circulation would help ameliorate this severe defect; which one(s) is(are) present in your specimen?

NOTE: There also exists a so-called "corrected" TGV in which the great vessels are indeed transposed (aorta is anterior, pulmonary artery is posterior) but the anteriorly placed aorta arises from a ventricle which sits on the left side and receives pulmonary venous return but morphologically resembles a right ventricle. The pulmonary artery arises from a ventricle which sits on the right side and receives blood from the right atrium (systemic venous return) but morphologically resembles a left ventricle (inversion of the ventricles). The flow of blood is thus normal. However, the left-sided AV valve is a tricuspid valve and the left-sided ventricle has the muscle mass and arrangement of a morphologic right ventricle. These structures (tricuspid valve and right ventricle), which must serve as a high-pressure left ventricle with AV valve, tend to decompensate over a period of time. Tricuspid insufficiency and ventricular failure may result.

7. Hypoplastic Left Heart Syndrome

Look at the external surface of the heart and great vessels. Identify the course of the anterior descending branch of the left coronary artery and the posterior septal coronary artery branch: these vessels will delineate the area of the left ventricle. Notice the almost inapparent hypoplastic ascending aorta and the relatively large aortic arch, (patent) ductus and descending aorta. Identify the mitral valve stenosis/atresia, aortic valvular stenosis/atresia [you may not be able to do this latter maneuver, for some of the very hypoplastic aortas have not been opened (too small--please don't attempt to open them)]. Most of the specimens will not have an opened left ventricle because some are, for practical purposes, non-existent. Are there any shunts present?

SIMPLE ANSWERS TO CONGENITAL HEART DISEASE STUDY QUESTIONS

1. VSD, ASD, PDA

All of these are left to right shunts. One potential and important complication of all left to right shunts is pulmonary hypertension. Also, enlargement/hypertrophy occurs in the portions of the heart/great vessels which are subjected to an increased volume/pressure load. Thus with a VSD, enlargement/thickening of the RV, PA, LA and LV would occur.

Another hemodynamic result could be congestive heart failure. Another potential complication, as in all congenital heart defects, is endocarditis.

2. ECD

Any left to right shunt with the potential for excessive flow/pressure load on the pulmonary arteries might benefit from pulmonary artery banding which protects the pulmonary arteries from the excessive load. Most ECD's are left to right shunts.

3. PS and AS

PS: A shunt from an aortic arch branch to a pulmonary artery would increase blood flow to the lung, a helpful maneuver

AS: Severe aortic stenosis may so diminish the mean diastolic pressure (during which time most of the coronary blood flow occurs) that less than optimal perfusion of coronary arteries may occur.

4. Coarctation of the Aorta

25% to 50% of patients with coarctation of the aorta will have a bicuspid AV. LVH will be present if the patient has survived long enough and/or if the coarct is "post-ductal." Effects/complications of coarctations are:

Pre-ductal: LV failure

Post-ductal: Decreased development of legs and disparity of B/P readings between upper and lower extremities

Rupture of aorta proximal to coarct.

Increased incidence of cerebral artery aneurysms with possibility of hemorrhage

"Endocarditis"

LV failure

5. Four features of Tetralogy of Fallot:

PS

VSD

Overriding aorta

RVH: "physiologic" response to PS and VSD

The VSD in Tetralogy of Fallot sits in the outflow tract of the RV anterior and superior to the usual VSD (beneath the septal leaflet of the TV). As with any situation involving decreased blood to the lungs, a shunt from the aorta or subclavian artery to a pulmonary artery will help.

Complications:

Polycythemia, with increased incidence of cerebral artery thrombosis

Endocarditis

Brain abscess

6. TGV

Any shunts (ASD, VSD, or patent ductus) which would increase the mixing of arterial and venous blood would be helpful.

7. Hypoplastic left heart syndrome

Some of the hearts will have a still patent ductus or an ASD. Occasionally, a very small VSD is present; in this case, usually the LV is a little larger.

CONGENITAL HEART DISEASE LABORATORY
QUIZ QUESTIONS

A TYPE: One best response type

Select the one best answer or completion

_____1. A patient with Tetralogy of Fallot would be expected to:

- (A) develop pulmonary hypertension eventually
- (B) be benefitted by a patent ductus arteriosus
- (C) be without cyanosis
- (D) have a large pulmonary artery which "overrides" the left ventricle
- (E) demonstrate coarctation of the aorta as one of the four features

_____2. Congenital heart defects which result in left to right shunting include:

- (A) pulmonary stenosis, aortic stenosis, and Tetralogy of Fallot
- (B) transposition of the great vessels, coarctation of the aorta, and hypoplastic left heart syndrome
- (C) patent ductus arteriosus, atrial septal defect, and ventricular septal defect
- (D) Tetralogy of Fallot, coarctation of the aorta, and atrial septal defect

B TYPE Matching type

For each numbered item, select the one heading most closely associated with it. A lettered heading may be used as an answer once, more than once, or not at all.

- (A) Stenotic or hypoplastic segment of aorta is present
- (B) Abnormal aortic valve is or may be present
- (C) Pulmonic stenosis is an integral part of the defect
- (D) Both A & B are true
- (E) Both B & C are true

_____3. Hypoplastic left heart syndrome

_____4. Coarctation of the aorta

QUIZ ANSWERS

1. B
2. C
3. D
4. D

SEMINAR-TUTORIAL CASE #4-A

“Sudden back pain”

This 80 y.o. white female was found on the floor of her kitchen conscious, alert but confused. She complained of pain that "ran up her neck" and that she "didn't feel good". She complained of a severe occipital headache at the E.R. of the local hospital and was noted to have a drooping of the left side of the face, as well as some left-sided motor weakness. She also complained of severe back pain. Her blood pressure was just palpable; the hematocrit was 20.9%. She received two units of blood, with an increase in hematocrit to 43.4%. At this time she was transferred to the MUH for further evaluation.

Past Medical History: Significant for Meniere disease, removal of an ovarian cyst, cholecystectomy for cholelithiasis, pancreatitis, and questionable temporal arteritis.

Current Medications: Carafate, Buspar 10 mg po qd, Prozac 20 mg po qhs, and Deltasone 10 mg po qam.

Physical Examination: At admission the patient was in no acute distress, was moderately obese and well developed. PERRL. Her mental status was found to be intact without alteration of orientation. All cranial nerves were intact bilaterally. She had no palpable cervical lymphadenopathy. Her neck was without evidence of bruit and her breasts were symmetrical without mass or nodules. Her chest was clear to auscultation bilaterally. Her abdomen was soft, nontender and nondistended with bowel sounds and no evidence of mass or bruit. Blood pressure at the time of admission was 126/90 in both upper extremities. The patient's rectal examination revealed normal tone with heme negative stool. Musculoskeletal revealed lower lumbar tenderness of the spine. Neurologically she was alert and oriented times three with good equal, symmetrical bilateral reflexes, moving all extremities equally and with no disturbance of motor or sensory function.

Hospital Course: Upon arrival at Medical University Hospital, the patient underwent a CT scan to rule out evidence of dissection of her aorta. She received IV hydration and was noted to be in a profound metabolic acidosis with evidence of renal insufficiency. Her initial CT scan showed no evidence of aortic dissection. General Surgery service was consulted for evaluation of a possible gastrointestinal bleed, though the patient was hemodynamically stable. No evidence for such was found. The Cardiology service was consulted with recommendations of a transesophageal ECHO to better evaluate the patient's thoracic aorta. This was performed, showing a markedly dilated ascending aorta and descending aorta with a possible flap in the aorta suggestive of dissection. However, a magnetic imaging resonance was recommended for better visualization of this anatomical lesion.

Through the first 24 hours of hospitalization, the patient suffered an acute deterioration in her renal function, and a worsening of her respiratory status with hypoxia and hyperventilation suggesting a possible ventilation perfusion mismatch and pulmonary embolus. She underwent emergent VQ scanning which showed no evidence of a pulmonary embolus. Hemodynamically the patient remained stable without evidence of further decrease in hematocrit or decrease in her blood pressure. Cardiology recommended beta blockade with continuous infusion, Brevi block for control of blood pressure, as well as nitrates and this clinical regimen was followed. Further evaluation by Cardiology felt that the patient was volume overloaded and recommended vigorous diuresis and digitalization. These recommendations were followed, as well as the performance of a magnetic imaging resonance

scan which was reported as no dissection and without evidence of an intimal flap. After evaluation of all available data, it was decided that the patient was indeed volume overloaded, with her acute renal insufficiency accounting for metabolic acidosis and no evidence of gastrointestinal bleeding, neurologic dysfunction or aortic dissection. She was transferred to the Cardiology Service for treatment of her congestive heart failure and further diuresis. On transfer the afternoon of her third hospital day, she was noted to be in good spirits, alert and talkative with transporters until her arrival in the CCU at which point she manifested seizure-like activity and lost consciousness. The patient's cardiac rhythm became bradycardic without blood pressure or pulse, and she became apneic. She was orally intubated and full ACLS protocol instituted though no response was ever achieved. Code was continued for approximately 33 minutes without success. Needle aspiration of the left chest revealed straw-colored effusion without evidence of blood. The patient was pronounced dead and permission for postmortem examination was obtained from the patient's family.

Gross Findings (condensed and selected)

At autopsy, the pericardial sac was distended with 1000 cc of clotted blood. There was a 3.9 cm horizontal linear through-and-through tear of the ascending aorta located 2.5 cm above the aortic valve. The entire length of the thoracic aorta was markedly dilated. The aorta was opened to reveal an intimal tear which was 5 cm. in length and led to the area of rupture noted externally. There was a dissection within the wall of the aorta down to the ostia of the coronary arteries. There was a suggested second dissection within the aortic wall of the descending thoracic aorta. There was focally severe atherosclerosis of the entire length of the aorta extending to the iliac arteries. A mural thrombus overlaid an area of severe atherosclerosis just proximal to the bifurcation of the aorta.

The heart weighed 410 gms and demonstrated hypertrophy and dilatation of the left ventricle (1.6 cm thick). The aortic valve contained calcified nodules on the cusp surfaces, but was mobile; there was annular calcification of the mitral valve. Coronary and renal arteries were not significantly atherosclerotic.

The lungs weighed 1110 gms together. Congestion but no frank edema was noted.

The kidneys weighed 220 gms and 240 gms. There was a 1.5 cm cyst filled with clear fluid on the surface of the right kidney. The capsular surfaces were fairly smooth; there was mild edema of the renal parenchyma but good demarcation of cortex and medulla, without specific lesions.

The brain weighed 1220 gms and was normally formed. No evidence of infarction, hemorrhage, contusion or edema was noted.

Study Questions for Students

Case #4-A

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. Can you reconcile this patient's course with the pathological findings at autopsy, i.e., jaw pain, back pain, syncopal episode and transient neurologic deficits, etc.?
2. What are some of the underlying conditions associated with dissecting aneurysms of the aorta? Which of these might have been present in this patient? How extensive can the dissection be? What is the cephalic extent of the pericardial sac, i.e., where does it attach to the aorta?
3. What are the possible fates of a dissection of the aorta? Surgical repair possible?
4. Look at the images of the aorta (ST4A-1 through ST4A-9). What abnormalities can you document microscopically? Describe intimal and medial changes.

SEMINAR-TUTORIAL CASE 4-B

“Xanthelasmas, tendon xanthoma”

A 44 year old garage mechanic has his triglyceride and cholesterol values tested in a reliable laboratory as part of a routine check up. The following values were obtained: cholesterol 380 mg/dl and triglycerides 178 mg/dl. Repeat studies 1 week later revealed almost identical results. His weight has been stable, about 5 pounds heavier than ideal body weight, and he is essentially free of complaints. He drinks about 4 ounces of alcohol daily. His past history is unremarkable and his family history revealed that several of his siblings on the paternal side have had myocardial infarcts in their fifty's.

Physical examination is unremarkable except for the thickening of his Achilles tendons and the presence of xanthelasmas in both upper eye lids (ST4B-1).

His routine lab work (CBC, comprehensive metabolic profile) is within normal limits with the exception of his lipid levels.

Study Questions for Students Case #4-B

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. Which other information pertinent to this case would you obtain from the patient based on lipid levels. Which hypotheses of diagnosis would you entertain in this patient?
2. Which is the most probable diagnosis? Why?
3. If the triglyceride levels of this patient were 500 mg/dl would your differential diagnosis be different?
4. Would you expect to have different physical findings if the lipid levels were those reported in 3? Why? Would you expect a different family history? Why?
5. Which laboratory data would you request to adequately characterize the type of lipid disorder and establish a definitive diagnosis?
6. At what levels of cholesterol would you start dietary therapy in this patient?
7. Which specific recommendations would you give this patient? What is his prognosis and possible complications?

SEMINAR-TUTORIAL CASE #4-C

“Substernal pain”

A patient, a 47 year old male executive, was driving to work when he experienced an initial “heaviness” in his anterior chest region. This progressed to a distinct moderately severe substernal pain but without radiation. He decided to drive directly to the emergency room and was seen by a physician within 10 minutes of arrival. It was estimated that 50 minutes had elapsed between his chest discomfort and examination. He was noted to be agitated; facial pallor and marked facial and trunk sweating were also noted. His pulse was irregular, B.P. 130/70 and auscultation of the lungs was unremarkable. An EKG at this time was interpreted as within reference range.

Social history suggested a hyperactive lifestyle with excessive diet, alcohol and smoking. He was admitted to the coronary holding unit.

The following cardiac markers were obtained 60 minutes after the initial event:

Time	cTnl	Total CK	mCK-MB	Myoglobin	%LD ₁ :LD ₂
Admission (Base)	< 2 ng/mL	160 U/L	3.2 ng/mL	65 ng/mL	24:33
2 Hours	< 2 ng/mL	180 U/L	3.8 ng/mL	150 ng/mL	25:36
6 Hours	4 ng/mL	250 U/L	12.9 ng/mL	580 ng/mL	26:36
24 Hours	60 ng/mL	400 U/L	56 ng/mL	70 ng/mL	36:28
72 Hours	15 ng/mL	175 U/L	2.5 ng/mL	40 ng/mL	30:30

Study Questions for Students Case #4-C

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. What is the diagnosis and why?
2. Are there non-cardiac related causes of mCK-MB increase?
3. Are there other causes of the reversal of the LD₁ to LD₂ ratio?
4. When does mCK-MB reach peak concentration?
5. Discuss the clinical use of the Relative Index (RI). Calculate the RI for admission and 24 hrs.
6. Does the LD₁/LD₂ flip always occur? If it does, how long will it persist?
7. What is the significance of a persistent mCK-MB in a patient post myocardial infarction?
8. Is the total CK of prognostic value?
9. Discuss the significance of the rise and fall of cTnl from the onset of symptoms related to an AMI.

MICROSCOPIC SLIDE ASSIGNMENT

SLIDE 16: This section shows an interlacing network of bands of fibrin, often enclosing pools of red blood cells and leukocytes. This is a **thrombus**. Some sections show an attached segment of arterial wall. The fixation of such a structure to a vessel wall is another characteristic of thrombus.

SLIDE 17: A section of anorectal tissue, beneath which are prominent dilated venous spaces filled with blood. In many instances these intravascular masses of blood show extending into their periphery spindle cells or fibroblasts. This process is referred to as **organization of a thrombus** and indicates that it has been present for at least several days.

SLIDE 28: **Aorta** revealing moderately severe to advanced **atherosclerosis**. The intima is generally thickened by hyalinized fibrous tissue and myointimal cells. There are focal areas of even greater thickening due to deposits of amorphous material including lipid debris and occasionally slit-like clefts where cholesterol has been deposited. Also, there may be scattered nuclear fragments, new capillaries, focal hemorrhage and early calcification.

SLIDE 29: This is an example of **coronary atherosclerosis**. Sections of the coronary artery reveal up to 80% diminution of the lumen of the vessel by an irregularly thickened intima which shows a layer of hyalinized fibrous tissue enclosing macrophages which contain lipid debris and show numerous clear clefts representing spaces where cholesterol has been deposited. There is destruction of the internal elastic lamina in one area and in this same area there is partial loss of the underlying media, secondary to the atherosclerotic process. The remaining lumen contains blood clot, possibly thrombus.

SLIDE 68: (VA 30-79) Kidney showing **arterio- and arteriolosclerosis**. These are essentially end stage or nonfunctioning kidneys. The primary disease process is not conclusively known but it may well be vascular. The interlobar and intralobular arteries are uniformly thickened by fibrous and hyalinized fibrous tissue as well as some showing an increase in ground substance. The arterioles show thickened walls which are almost totally hyalinized. In addition the renal parenchymal (primarily cortex) is markedly diminished. Many glomeruli are partially to totally scarred. The tubules are largely atrophic with focal areas of dilatation and filled with inspissated proteinaceous material, some of which is calcified. The interstitial tissue reveals increased fibrosis and scattered inflammatory cells.

SEMINAR-TUTORIAL CASE #5

“Dyspnea”

This 69 year old white male died of pulmonary disease on December 9, 2002. He began smoking cigarettes at age 19 and smoked two packs a day of cigarettes up until the year prior to his death. A chronic cough was present productive of several tablespoons of phlegm each day. This began 30 years ago and became progressively worse. He complained of severe dyspnea on mild exertion but claimed that if he moved very slowly he could get around fairly well. He complained also that his feet were swelling more lately. He was hospitalized with a complaint of increasing dyspnea. Chest CT had been performed two weeks prior to that which showed an enlarged space at the apex of the right lung containing an air fluid level. He had been treated with Septra and Penicillin. Prior to this he had been on steroids and 2-4 liters of oxygen by nasal cannula at home. Pulmonary function tests several months prior to hospitalization revealed a vital capacity of 2.5 liters (normal 4.5), total lung capacity 6.5 (expected 6), CO diffusing capacity 60%, FEV₁ 0.8 liters (expected 4). PO₂ on room air was 50, pCO₂ 50, and pH 7.35. White count was 8,000, 60% neutrophils. Oral temperature = 100.4, BP 148/95. P 72, R 26, Hb 16, Hct 50.

On physical exam, this was a caucasian male appearing older than his stated age in moderate respiratory distress. Positive findings on physical exam included 2+ arteriosclerotic eyeground changes, enlarged chest, and hyperresonance to percussion, with distant breath sounds. Diaphragms were low with poor excursion. Heart sounds were distant, but an accentuated P2 was noted. Neck veins were distended in the upright position. Liver was mildly enlarged. Mild sacral edema was found.

On the second hospital day, ultrasound revealed a questionable thrombus in the left femoral vein. PO₂ continued to be low, even on 60% oxygen. CO₂ continued to be elevated. Considering his declining status, a DNR was signed by his wife that disallowed use of a ventilator or CPR. On the fourth hospital day, cardiac enzymes were noted to be elevated suggesting a possible MI. Sporadic episodes of hemoptysis occurred. Oxygen saturation decreased on 100% oxygen and cardiac ejection fraction fell from 40% to 20%. On the 8th hospital day, the patient died and an autopsy was authorized.

At autopsy, the heart weighed 420 grams. Severe calcific atherosclerosis narrowed the left coronary and left anterior descending coronary arteries by 75%, and the circumflex and right coronaries by 50%. The left ventricular wall measured 1.5 cm. in thickness, and the right 1.0 cm. Evidence of old and recent left ventricular infarction was noted. The right lung weighed 500 grams and the left 480. Thin-walled balloon-like air-filled cystic structures protruded from the pleura of the upper lobes, and focal loss of pulmonary substance in the upper lobes was noted. Airways contained mucus plugs. This was mixed with blood in the central bronchi on the right.

Study Questions for Students

Case #5

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. Does this patient meet the criteria for a clinical diagnosis of COPD? Review images ST5-1 through ST5-4.
2. Does he meet the criteria for a diagnosis of chronic bronchitis?
3. Why were his diaphragms said to be low with little motion?
4. What were the enlarged thin-walled balloon-like protrusions from the pleura found at autopsy?
5. Why was his CO₂ elevated?

MICROSCOPIC SLIDE ASSIGNMENT

SLIDE 6: Section of lung of a girl who developed rheumatic fever at age 14 with subsequent mitral stenosis and death at age 18. There is extensive collapse of alveolar spaces and there is less blood in the vascular spaces than one would expect. However, the other features are those which one might see with **chronic passive congestion**; namely, large accumulations of pigmented macrophages or so-called heart failure cells within many of the alveolar spaces. The pigment at times appears to be brown to black due to a dense accumulation of the brown pigment of **hemosiderin**. In addition to this, the alveolar walls are appreciably thickened. Some of this thickening may be due to collapse of the alveolar spaces but, at least in part, it is due to fibrosis and a real thickening of these structures.

SLIDE 7: Sections of lung show intense and extensive filling of all vascular channels with erythrocytes. This is a picture of **acute congestion** as seen in the case of acute or rapid failure of the heart which in this case resulted from a thrombus in the right coronary artery. Also note the black pigment present in and around peribronchial lymphatics, representing anthracotic pigment.

SLIDE 14: Sections of lung (A67-15) from a patient who died as the result of cardiac arrest. Consequently, there was a backing up or congestion or filling of all venous channels, particularly in the pulmonary system as seen in this slide. In addition, the pooling of blood increases the venous pressure. This increased venous pressure, together with hypoxia which damages the endothelial lining, permits the outflow or diapedesis of red blood cells into the alveolar spaces, thus producing **intra-alveolar hemorrhage**.

SLIDE 26: **Bronchial asthma**. Sections of lung with large bronchi. The lining epithelial cells show pronounced secretory activity. The basement membrane is thickened and hyalinized and the smooth muscle wall appears to be hypertrophied. The bronchial lumen contains large amounts of mucus, a moderate number of macrophages and eosinophilic leukocytes and similar cells plus lymphocytes are seen in the wall of the bronchus.

SLIDE 60: Sections of lung from an **oat cell carcinoma** (S78-17330). Sections of lung showing portions of bronchial wall and masses of neoplastic cells with extensive areas of necrosis. Neoplastic cells occur in bands and sheets and are largely undifferentiated. Although not as small as many so-called oat cell carcinomas, these cells are characteristic of the **small cell anaplastic carcinoma**. Some individuals divide this group into small and intermediate type and many of these probably are intermediate in size. The typical oat cell carcinoma may simulate malignant lymphoma or neuroblastoma on morphologic grounds.

SEMINAR-TUTORIAL CASE #6-A

Neuropathology

A 29 year old Caucasian female originally from New York came into the ophthalmology clinic complaining of double vision. On exam, she exhibited problems with extra-ocular muscle movements and also had visual field defects. Further questioning revealed a history of fatigue, lack of energy, weight loss and vague muscle/joint aches and pains. Physical exam demonstrated that her balance with her eyes closed was not good and that she was hyperreflexic with bilateral upgoing toes and an intention tremor.

As part of her lab work, CSF and blood were obtained. The protein electrophoresis is shown in image ST6A-1. An MRI was ordered of brain and spinal cord (ST6A-2).

Study Questions for Students Case #6-A

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. Compare CSF and serum lanes on the protein electrophoresis (ST6A-1). The CSF protein electrophoresis shows what abnormality? Is this finding specific?
2. Where are the lesions on the MRI (ST6A-2)?
3. Where are the lesions on the coronal autopsy section of brain (ST6A-3)?
4. Describe the histologic features in the surgical H&E section (ST6A4-5), the autopsy H&E section (ST6A6-7), and the corresponding myelin (ST6A-8) and silver (ST6A-9) stains.
5. What is the diagnosis in these cases?

SEMINAR-TUTORIAL CASE #6-B

Neuropathology

(note: no new microscopic slides assigned)

A 55-year-old black male was found by his wife, unconscious on kitchen floor.

PMH (from wife) – hypertension (treated off and on during the last decade), peripheral vascular disease, and diabetes which has not been well controlled.

Social History – 1 pack per day for 40 years smoking history, several beers per week

A CT of the head was performed (ST6B-1). The patient never regained consciousness and died. Permission was given for autopsy

Study Questions for Students Case #6-B

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. What is the orientation of the CT scan (Image ST6B-1)? Where is the lesion on the CT scan?
2. What is the orientation of the gross slice of brain (Image ST6B-2)? Where is the lesion and where did it most likely begin? What is the most common cause of hemorrhage in this area of the brain? What are other possibilities? Where would you expect other lesions to most likely be found?
3. Describe the histologic H&E findings (Image ST6B-3).
4. Describe the abnormality on the silver stain (Image ST6B-4).
5. What are this patient's risk factors for brain hemorrhage?

SEMINAR-TUTORIAL CASE #7A

“Vaginal bleeding”

This 73 y.o. G₇P₈ (1 set twins) white female was referred to the MUSC following an episode of heavy vaginal bleeding. She had been post-menopausal for 23 years.

Past Medical History: The patient had an appendectomy in 1949. She also had a back injury 9 years ago, treated by a chiropractor successfully. The chiropractor recommended that she see a M.D., but she did not. The patient had never had a PAP smear or a mammogram. Menarche was at age 14, with monthly cycles until 23 years ago. She had 7 normal spontaneous vaginal deliveries, one of which was a twin delivery. There were no known chronic medical illnesses.

Family History: The patient's mother had had some kind of skin cancer.

Social History: The patient is married. She denies use of alcohol or tobacco.

Clinical Course: Biopsies were obtained immediately (outpatient basis) of the endometrium, endocervix, and cervix, with the same diagnosis rendered on each site, represented by images ST7A-2 and ST7A-3 of the cervix.

The patient was admitted one week later to the MUH for a radical hysterectomy, bilateral salpingo-oophorectomy and retroperitoneal pelvic and periaortic lymphadenectomy. The physical exam was within normal limits except for pelvic findings of a cervix which was enlarged by a bulky tumor without obvious vaginal involvement. Rectal exam was negative. An IVP was normal.

At surgery, a 7cm. freely mobile cervix with a normal-sized uterus was found. The ovaries were atrophic. There was one suspicious left iliac node which was positive for tumor on frozen section. Estimated blood loss was 1500 cc., with evidence of a "slight" post-operative coagulopathy. The post-operative hemoglobin was 7.7, hematocrit 22.7 (preoperative 12.0, 35.7 respectively). She received 2 units of packed RBC's and 2 units of fresh frozen plasma, with correction of the coagulopathy, hemoglobin and hematocrit to normal values. In the recovery room, there were lateral EKG changes consistent with ischemia. Telemetry and cardiac enzymes did not document a myocardial infarction. A urinary tract infection was treated with Macrochantin and the patient was discharged on post-operative day #9, to return 6 weeks later for radium therapy.

The pathologic examination of the surgical specimen indicated that tumor extended to one vaginal margin (ST7A-4) and involved one left internal iliac node and one right internal iliac node (IST7A-5). Within the endocervix-cervix, tumor extended through 20 mm. of a 22 mm. cervical wall. The endometrium was atrophic and the fallopian tubes and ovaries were described a histologically unremarkable.

Study Questions for Students Case #7A

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. From the clinical assessment, what is the most likely diagnosis for this patient? Stage (clinical)? See ST7A-1, gross image
2. Examine Images ST7A-2 and ST7A-3 (cervical biopsies). Enumerate the abnormalities in cells and growth patterns in the slide of cervix . Identify the depth of invasion in the full section of the cervix (Image ST7-4). Recognize the tumor in the section of lymph node (Image ST7A-5). What does this finding imply as to prognosis? How do you classify this tumor?
3. What is the natural history of this tumor? What is the best, low-cost method for identifying the process?

SEMINAR TUTORIAL CASE #7B

“Breast mass”

A 45 year old female presents to her gynecologist because she feels a “small lump” in her breast. She can not remember if the lump changes during the month, but she does state that it has been present for about 6 months. She has never had a mammogram because she thought that she was too young.

Past Medical History: Unremarkable. She has no children.

Social History: She admits to smoking and drinking “recreationally”. She only smokes when she drinks, and she drinks about 3 -4 drinks a week. No history of drug use.

Family History: Her mother is 73 and has had two benign breast masses and a hysterectomy for fibroids. Her father has high blood pressure. Her sister and brother have high blood pressure and high cholesterol.

Physical Examination: The patient is 5 feet and 7 inches tall, and she weighs 134 pounds. A breast examination reveals a 1-2 inch in greatest dimension, firm, mobile mass in the right upper outer quadrant. The remainder of the examination is normal. A mammogram is performed (ST7B-1). An ultrasound-guided core biopsy is performed followed by a right mastectomy and lymph node dissection 2 weeks later.

The gross mastectomy specimen is shown in image ST7B-2. The mass within the breast is tan-yellow, 2.3 x 2.0 x 1.8 cm. The mass has an irregular margin and appears to infiltrate into the surrounding breast and adipose tissue. Upon sectioning, the mass is firm and “gritty”. Microscopic examination of both the core biopsy and mastectomy specimen are depicted in images ST7B-3 and ST7B-4. Sectioning throughout the breast reveals the mass to approach within 1.2 cm of the deep margin. The skin is not involved. Lymph node dissection is negative for 15 out of 15 nodes.

STUDY QUESTIONS FOR STUDENTS

Case #7B

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. What is the patient’s diagnosis?
2. Name some different types of breast cancer.
3. What is a fibroadenoma?
4. What are some risk factors for breast cancer?

MICROSCOPIC SLIDE ASSIGNMENT

SLIDE 5: Portion of fibrofatty breast tissue. Throughout the section much of the adipose tissue reveals a slightly smudgy appearance with replacement by histiocytes having a relatively clear or coarsely granular cytoplasm. In some sections, giant cells may be present as well as areas of scarring. A few lobules of adjacent breast tissue show a scattering of inflammatory cells consisting of lymphocytes and eosinophils. This is an example of **traumatic fat necrosis**.

SLIDE 18: This is a section of lymph node and adjacent fibrofatty tissue. They are largely replaced by a malignant neoplasm of epithelial origin which tends to reproduce gland-like structures. Particularly near the periphery there are numerous vascular structures. Some of these are blood vessels and others are lymphatics. Many of these contain plugs of these cancer or neoplastic cells and these represent **tumor emboli to lymph node**.

SLIDE 21: This section of breast tissue shows fibrofatty tissue infiltrated by individual cells, distorted glands and cord-like columns of cells. The infiltrative characteristic is particularly well demonstrated where one finds neoplastic cells surrounded on all sides by lobules of adipose tissue and showing little or no supporting fibrous stroma. The bulk of this neoplasm, however, shows the features of a **carcinoma** in that there is excessive production of fibrous and collagenous tissue. Grossly, this would be represented as a stony hard neoplastic mass.

SLIDE 22: This is a section of myometrium which demonstrates a well demarcated mass composed of intermingled or interlacing bundles of benign smooth muscle cells with a small amount of supporting fibrous stroma. This is a benign neoplasm of the uterus, properly called **leiomyoma**, also referred to as fibromyoma or fibroid.

SLIDE 23: This is a section of uterus having an atrophic endometrial surface and significant changes within the myometrium. This consists of partial replacement by sheets of spindle and fusiform cells tending to form bundles which intertwine with each other and showing significant nuclear variation and atypicality. Likewise, there is a lack of encapsulation of this mass and this is characteristic of a **leiomyosarcoma** of the uterus.

SEMINAR-TUTORIAL CASE #8-A

“Neck mass”

Present Illness: This 59 y.o. white male with a long history of asthma/COPD began having "anginal" pain 4 months prior to admission. He underwent cardiac catheterization which demonstrated a 60% stenosis of the LAD coronary artery as well as mild cardiomegaly. A stress thallium test revealed stress-induced ischemia involving the apex and the anterior, septal, and inferior walls of the left ventricle. He was placed on medical management (nitroglycerin patches) for coronary artery disease. He was also found to have diabetes mellitus, hypertension, hypercalcemia and a thyroid nodule. The patient denied episodes of nephrolithiasis, costovertebral angle tenderness or symptoms of pancreatitis.

Neck ultrasound studies indicated a right thyroid adenoma with cystic changes. A small area of calcification and a cyst was noted in the left lobe of the thyroid. A thyroid/parathyroid scan suggested a possible left parathyroid adenoma. X-rays of the extremities did not demonstrate the bone changes of hyperparathyroidism.

The patient was admitted for neck exploration.

Family History: Positive for colon cancer, diabetes mellitus and hypertension.

Past Medical History and Review of Systems: As above. No anginal episodes had occurred since cardiac medications began. No recent episodes of asthma or shortness of breath had been noted. The patient was allergic to penicillin (skin rash). No use of tobacco, but social use of alcohol was reported. A 2000 calorie ADA diet was being followed. Exercise was a one mile walk daily.

Medications:

Theodur	Nitropatch
Diabeta	Ventolin inhaler

Physical Examination: Pulse 60, B.P. 152/86, Respirations 18. General appearance was that of a well developed, well nourished male appearing younger than his age. Examination of the skin, head, eyes, ears, nose, oral cavity and tonsils was normal. There was no lymphadenopathy. There was minimal enlargement of the right hemithyroid. There were good breath sounds bilaterally, without wheezes or rales. There was a regular cardiac rate and rhythm with a II/VI systolic ejection murmur along the left sternal border. No jugular venous distention was appreciated and the peripheral pulses were intact. The abdomen was soft, non-distended, non-tender with normal bowel sounds and no masses. Evaluation of the G.U. system (including the prostate) and rectum revealed no abnormalities. Evaluation of the musculoskeletal and neurological parameters yielded normal findings.

Labs: Hgb 15.9, Hct 46.4, WBC 10,000 with a normal differential, 205,000 platelets. Na 144, Cl 112, K 5.2, CO₂ 27, BUN 23, Creatinine 1.3, Glucose 87. Mg 2.3, Phosphorus 2.9, Ca 12.6. PT 11.3 (11.1-12.5), APTT 26.4 (24.4-36.5). Cortisol 15 (10-18). Urine catecholamines/VMA = normal; urine metanephrine - 1.41 (0-1.0). Urinalysis: Yellow, clear; 7.0, 1.012, protein, glucose, ketones, bile negative

EKG: Sinus bradycardia

Chest X-ray: Slightly increased pulmonary vascularity compatible with mild heart failure. Heart size still slightly increased (compared to chest x-ray 4 months previously).

Hospital Course: On the following day, exploration of the neck was undertaken with the following findings: A lymph node adjacent to the isthmus of the thyroid was almost totally replaced by thyroid tissue (Images ST8A-1 and ST8A-2, frozen section). A very small parathyroid gland, thought to be the right superior parathyroid, was then biopsied, with the frozen section documenting normal parathyroid tissue. A further search for another right parathyroid yielded only a small nodule which on frozen section was essentially identical to the first specimen. The right lobe of the thyroid was then resected. This tissue was carefully sectioned with the frozen section diagnoses (and final diagnoses) being: (1) Papillary thyroid carcinoma (follicular variant) within the superior pole; (2) Multinodular goiter; (3) Fetal adenoma (Images ST8A-3 and ST8A-4). Exploration of the left neck yielded two large parathyroid glands which were similar on frozen section and are represented by Images ST8A-5 and ST8A-6. At this point, the decision was made to remove the left lobe of the thyroid in order to complete the thyroidectomy and to cease searching for another parathyroid gland on the right side.

The postoperative course was relatively uneventful, with a low grade fever resolved in several days with negative blood urine and sputum cultures and negative chest films. Serial CPK and LDH enzymes were within normal limits postoperatively. Calcium levels were carefully followed: one dose of IV calcium was required 48 hours postoperatively. The patient was discharged 5 days postoperatively on Os-Cal and Cytomel, to be followed carefully on an outpatient basis.

Study Questions for Students Case #8-A

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. List some of the causes of hypercalcemia. Primary hyperparathyroidism suggests what lesions of the parathyroid glands? What is an explanation for the difficulty of finding all the parathyroid glands?
2. What are the two most common types of thyroid carcinoma? Main differential points between the two?
3. Examine Images ST8A-1 and ST8A-2. What is the implication of finding a lymph node which is apparently replaced by thyroid tissue? Note the bland nature of this thyroid tissue. Examine Images ST8A-3 and ST8A-4 of the carcinoma within the right superior thyroid lobe. Are there histologic features that you can recognize as indicating malignancy?
4. Examine Images ST8A-5 and ST8A-6. Are there features suggesting parathyroid adenoma vs. hyperplasia?

SEMINAR-TUTORIAL CASE #8-B

“Weight loss, nervousness and sweaty”

A 40-year old woman was seen by her general internist for an annual physical examination. One year ago she gave an unremarkable history, had a normal physical examination, and laboratory tests including a chemistry profile and thyroid profile were all within normal limits.

The clinical history reveals that the patient had 9 to 10 pounds of weight loss over 2 months while continuing to maintain an excellent appetite. She has noticed easy fatigability and has spontaneous episodes of nervousness in the absence of stress. She sweats easily and becomes quite uncomfortable during hot days or in warm rooms. She has frequent bowel movements, and diarrhea on a weekly basis; she has missed her last two menstrual periods and expresses decreased sexual interests. She has noticed a rapid pulse on numerous occasions. During the past months she has noticed prominence of her eyes with occasional double vision. Approximately two weeks prior to this visit, she developed a "fullness" in her throat with mild difficulty in swallowing.

Physical examination revealed extremely thin middle-aged female. Her eyes were bulging and there was an easily demonstrated diffuse mass in the anterior lower neck. She had a fine tremor of the fingers, the skin was hot and damp, and there was focal hair loss of the scalp. She had a rapid, bounding peripheral pulse. She was nervous, and began crying at the end of her physical examination. Neuromuscular examination showed inability to lift her arms over her head and inability to rise from a squatting position. Rectal examination was negative including a Guaiac negative stool examination. Pelvic examination was unremarkable. Chest X-ray was unremarkable, and EKG showed sinus tachycardia.

Laboratory Studies were as follows:

Serum Electrolytes - within normal limits

The following chemistries were abnormal:

		<u>Reference Values</u>
Total protein	5.4 g/dL	6.3 - 8.2 g/dL
Serum albumin	3.4 g/dL	3.9 - 5.0 g/dL
Cholesterol	75 mg/dL	< 200 mg/dL
Thyroid studies:		
Thyroxine (T ₄)	18 ug/dL	4.5 - 12 ug/dL
Free Thyroxine (FT ₄)	2.8 ng/dL	0.7-1.9 ng/dL
Thyroid Stimulating Hormone (TSH)	< 0.06 mU/L	0.4-6.0 mU/L

See Images ST8B-1 through 4, diagram and gross depictions of the entity.

Study Questions for Students Case #8-B

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. What is your diagnosis based upon the clinical findings and laboratory data (Image ST8B-1)?
2. Why was it important to provide an extensive history and physical examination in this case (Images ST8B-2 through 4)?
3. List diseases which could mimic the findings given in the history and physical examination.
4. Assume the patient had clinical symptoms of hyperthyroidism with undetectable TSH; however, the free T₄ and total T₄ were within reference intervals. What additional testing would you perform on this patient?
5. Assume that the patient had no clinical symptoms and the screening laboratory study gave the following result:

T₄ Thyroxine - 12 ug/dL

What three additional tests should be performed? Explain your rationale for the additional testing. What results would you expect from the testing?

SEMINAR-TUTORIAL CASE #8-C

“Dry and thick skin and puffy eyes”

The patient was a 60 year old female and had noticed gradual hair loss, constipation, and fatigue for almost twenty years. Prior to menopause she noticed heavy bleeding during her periods (menorrhagia). For approximately 10 years, she has had muscle stiffness, cramps, and aches and pains in her joints. At times, her speech is slightly slurred and she has had recent bouts of imbalance (ataxia). She finds it difficult to climb a flight of stairs and sometimes has chest pain following prolonged exercise. A relative recently remarked that her face was "puffy", especially around her eyes.

Last week, she decided, for the first time, to donate blood; she was rejected as a blood donor due to severe anemia and was advised to seek medical attention from her family doctor.

She presented to her family doctor with symptoms of "fatigue and weakness." The medical is as given above. Physical examination revealed a middle-aged female who seemed lethargic and had slow speech. She had a slow pulse rate (approximately 40/minute); the ECG showed low voltage. Her skin was dry, scaly, cold and thickened, especially below the ankles. She had a delayed relaxation phase of her ankle jerk. Her face was puffy, with thick lips and coarse features (see Images ST8C-1 and 2).

Laboratory studies were as follows:

1. CBC - severe normocytic anemia (Hct - 24%)
2. Serum electrolytes - Sodium decreased: 130 mM/L
3. The following chemistries were abnormal:

		<u>Reference Values</u>
Cholesterol	240 mg/dL	< 200 mg/dL
Triglycerides	505 mg/dL	# 150 mg/dL
CK	410 U/L	< 135 U/L

4. Thyroid Studies

Free Thyroxine (FT ₄)	0.3 ng/dL	0.7 – 1.9 ng/dL
TSH	50 mU/L	0.4 – 6 mU/L

Study Questions for Students Case #8-C

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. What is your diagnosis based upon the clinical findings and laboratory data?
2. Why was it important to provide an extensive history and physical examination in this case (Image ST8C-1 and 2)?
3. List diseases which could mimic the findings given in the history and physical examination.
4. Assume that your patient reluctantly admitted to chronic galactorrhea three years after the presentation to clinician. A visual examination showed visual field defects. Patient recently complained of headaches and double vision.

What diagnosis would be necessary to rule out? What laboratory tests should be ordered?

5. How can you reconcile the findings of a recent onset disease (question #4) together with a chronic disease process?
6. Assume that this patient's primary disease process was secondary to an autoimmune condition. What additional endocrine testing might be appropriate to rule out associated disease processes (Image ST8C-3, Hashimoto thyroiditis, gross)?

SEMINAR-TUTORIAL CASE #8-D

“Central obesity and hirsutism”

A 35 year old female is seen in general medicine with a 10 month history of slowly increasing central obesity, facial hirsutism and acne. She complains of muscle weakness confined to her arms and thighs. Her menstrual cycle is irregular and in comparison with two years ago is considerably less in blood flow.

Examination confirms the weight gain and pigmented striae are noted on the abdomen. There are ecchymoses on the back, while dependent ankle edema is also observed. Blood pressure is 190/110 mm Hg. Patient smokes 2 packs a day x 20 years.

Laboratory Data:

Blood (Fasting)	K	- 3.5 mEq/L
	Na	- 142 mEq/L
	Bicarbonate	- 34 mEq/L
	Chloride	- 92 mEq/L
	Glucose	- 140 mg/dL
	Creatinine	- 1.4 mg/dL

Plasma Cortisol	6 a.m. - 56 ug/dL
	4 p.m. - 64 ug/dL

Urine (Fresh)	pH 7.8
	Protein - +
	Glucose - ++
	Urinary free cortisol - 290 ug/24 hours

Specialty Tests:

Dexamethasone Suppression at 8 mg dose = 90% Suppression of serum cortisol concentration.

MRI Head Scan: 8mm microadenoma of pituitary

MRI Abdominal Scan: Adrenals – bilateral hyperplasia

Images ST8D-1 through 4 = gross depictions

Image ST8D-5 for comparison of normal and hyperplasia

Study Questions for Students

Case #8-D

These questions should help you understand some aspects of this case. These will be discussed in your seminar-tutorial group.

1. If there is sufficient data, can a diagnosis be made? Can we measure ACTH concentration?
2. What are the other possibilities?
3. Is it necessary to perform urinary free cortisol?
4. Is a GTT necessary in view of the abnormal fasting glucose?
5. Are there immediate metabolic dangers in this patient?