Asthma - Vit D Hype & “Likker” livers

1 PICTURE IS WORTH A THOUSAND WORDS
• UNDER STAND WHAT YOU CAN
• FLUSH WHAT YOU CANT!
• We uploaded these first six slides on asthma before.

• If you missed them ENJOY THEM THIS TIME AROUND!
Asthma

Bart Simpson
Diseases caused by a disturbed immune system

Allergy

Normal bronchiole

Bronchiole in asthma

Bronchiole in asthma

Mast cells in asthma
Normal Lung

Pulmonary Oedema
Inflammation: Fibrin Mesh and Cellular Infiltrate
Why asthma makes it hard to breathe

Air enters the respiratory system from the nose and mouth and travels through the bronchial tubes.

In an asthmatic person, the muscles of the bronchial tubes tighten and thicken, and the air passages become inflamed and mucus-filled, making it difficult for air to move.

In a non-asthmatic person, the muscles around the bronchial tubes are relaxed and the tissue thin, allowing for easy airflow.

Inflamed bronchial tube of an asthmatic

Normal bronchial tube
Asthma

- Antigens
- Plasma leak and edema
- Goblet cell discharge
- Epithelial shedding
- Sensory nerve
- Efferent nerve
- T lymphocyte
- Neutrophil
- Eosinophil
- Macrophage
Airway narrowing in an asthma attack
Normal Kidney
In cross section, this normal adult kidney demonstrates the lighter outer cortex and darker medulla with central pelvis.
This slide and the next show the pelvis of the normal kidney. The two slides following demonstrates what a stone in the pelvis looks like!

Try very high doses of Vit D as advised in the links put up by Resarcher, and see what your kineys will look like just before you are planted!
Staghorn calculus or stone
The passage of a calculus (stone) through the urinary tract is diagrammed here. Calculi form when there is increased excretion of solutes such as calcium and when urine alkalinity, acidity, stasis, and/or concentration are favorable. The most common varieties of calculi are:

- **Type of Stone Frequency** Calcium oxalate (or phosphate) 75% Magnesium ammonium phosphate (struvite, or "triple phosphate") 12% Uric acid 6% Cystine 1% Other 6%
• Stones containing calcium are far more frequent than other types, and about half the time occur when there is hypercalciuria. Only about 10% of the time do they appear as a consequence of hypercalcemia. The struvite stones are also known as "infection" stones because bacteria such as Proteus that split urea to ammonia favor their formation. Uric acid stones may be seen in association with gout, but often are not, and may just reflect increased precipitation of urates in an acid urine. Rare cystine stones also form in acid urine.

• Urinary tract calculi are usually unilateral and about 1 to 3 mm in size. Their passage is marked by intense abdominal or back or flank pain. This pain can be paroxysmal, known as renal or ureteral "colic". Hematuria may also be present. Larger stones that cannot pass may produce hydronephrosis or hydroureter.
Urolithiasis (Renal Calculi, Stones)

• Stones may form at any level in the urinary tract, but most arise in the kidney
• Urolithiasis is a frequent clinical problem, affecting 5 to 10% of Americans in their lifetime
• Males are affected more often than females
• Peak age at onset is between 20 and 30 years.
• Familial and hereditary predisposition to stone formation has long been known
• Many of the inborn errors of metabolism, such as gout, cystinuria, and primary hyperoxaluria, provide good examples of hereditary disease characterized by excessive production and excretion of stone-forming substances.
Cause and Pathogenesis

- There are four main types of calculi:
  - 75% are calcium containing: composed mostly of calcium oxalate, or calcium oxalate mixed with calcium phosphate.
  - 15% are “Triple stones” or struvite stones, composed of magnesium ammonium phosphate.
  - 6% are uric acid stones
  - 1-2% contain cystine
- An organic matrix of mucoprotein, making up 1 to 5% of the stone by weight, is present in all calculi.
- Although there are many causes for the initiation and propagation of stones, the most important determinant is an increased urinary concentration of the stones’ constituents, such that it exceeds their solubility in urine (supersaturation).
- A low urine volume in some metabolically normal patients may also favor supersaturation.
<table>
<thead>
<tr>
<th>Table 21–13. PREVALENCE OF VARIOUS TYPES OF RENAL STONES</th>
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<tbody>
<tr>
<td>Percentage of All Stones</td>
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<tr>
<td>Calcium Oxalate (Phosphate)</td>
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<tr>
<td>Idiopathic hypercalciuria (50%)</td>
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<tr>
<td>Hypercalciuria and hypercalcemia (10%)</td>
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<tr>
<td>Hyperoxaluria (5%)</td>
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<tr>
<td>Enteric (4.5%)</td>
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<tr>
<td>Primary (0.5%)</td>
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<tr>
<td>Hyperuricosuria (20%)</td>
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<tr>
<td>Hypocitraturia</td>
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<tr>
<td>No known metabolic abnormality (15%–20%)</td>
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<tr>
<td>Struvite (Magnesium Ammonium Phosphate)</td>
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<tr>
<td>Uric Acid</td>
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<tr>
<td>Associated with hyperuricemia</td>
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<tr>
<td>Associated with hyperuricosuria</td>
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<tr>
<td>Idiopathic (50% of uric stones)</td>
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<tr>
<td>Cystine</td>
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<tr>
<td>Others or Unknown</td>
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<tr>
<td>75</td>
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<td>10–15</td>
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<td>6</td>
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<td>1–2</td>
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Urolithiasis (Renal Calculi, Stones)

- **Calcium Oxalate stones**
  - Hypercalciuria
  - Hypercalcemia
  - Hyperuricosuria
  - Hyperoxalauria
  - Hypocitraturia
• Calcium oxalate stones are associated
  • With both hypercalcemia and hypercalciuria (5% of patients)
    – due to Hyperparathyroidism, diffuse bone disease, sarcoidosis, and other hypercalcemic states.
  • Hypercalciuria without hypercalcemia (~ 55%)
    – Absorptive hypercalciuria - hyperabsorption of calcium from the intestine
    – Renal hypercalciuria - an intrinsic impairment in renal tubular reabsorption of calcium
    – Idiopathic fasting hypercalciuria with normal parathyroid function.
  • ~ 20% are associated with increased uric acid secretion (hyperuricosuric calcium nephrolithiasis), with or without hypercalciuria.
    – The mechanism of stone formation in this setting involves “nucleation” of calcium oxalate by uric acid crystals in the collecting ducts.
  • ~ 5% associated with hyperoxaluria, either hereditary (primary oxaluria) or, more commonly, acquired by intestinal overabsorption in patients with enteric diseases.
    – The latter, so-called “enteric hyperoxaluria,” also occurs in vegetarians, because much of their diet is rich in oxalates.
  • Hypocitraturia associated with acidosis and chronic diarrhea of unknown cause may produce calcium stones.
  • In a variable proportion of patients with calcium stones no cause can be found (idiopathic calcium stone disease).
Magnesium ammonium phosphate stones:

- Are formed largely following infections by urea-splitting bacteria (e.g., proteus and some staphylococci), which convert urea to ammonia.
- The resultant alkaline urine causes the precipitation of magnesium ammonium phosphate salts.
- These form some of the largest stones, as the amounts of urea excreted normally are huge.
- **Staghorn calculi** are almost always associated with infection.
• Large stone impacted in the renal pelvis
There was a large renal calculus (stone) that obstructed the calyces of the lower pole of this kidney, leading to a focal hydronephrosis (dilation of the collecting system). The stasis from the obstruction and dilation led to infection. The infection with inflammation is characterized by the pale yellowish-tan areas next to the dilated calyces with hyperemic mucosal surfaces. The upper pole is normal and shows good corticomedullary demarcations.
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This kidney shows much more advanced hydronephrosis. Note that there is only a thin rim of remaining renal cortex. Such a kidney is non-functional and a source for ongoing infection. The problem may originate from the ureteral orifice up to the pelvis. In this case, a large "staghorn" calculus was present that filled up the pelvis and calyceal system. In bilateral cases, the problem originates in the bladder trigone or urethra (or the prostate around the urethra) or may be due to a large neoplasm impinging on both ureters.
• So you want to abuse Vit D and mess up your kidneys and end up on dialysis with kiDneys as in the next slides?

• GO RIGHT AHEAD!

• DO NOT COME BACK AND SAY YOU WERE NOT WARNED ON BU!
ACQUIRED (DIALYSIS-ASSOCIATED) CYSTIC DISEASE

• The kidneys from patients with end-stage renal disease who have undergone prolonged dialysis sometimes exhibit numerous cortical and medullary cysts.

• The cysts measure 0.5 to 2 cm in diameter, contain clear fluid, are lined by either hyperplastic or flattened tubular epithelium, and often contain calcium oxalate crystals, which probably form as a result of obstruction of tubules by interstitial fibrosis or by oxalate crystals.

• Most are asymptomatic, but sometimes the cysts bleed, causing hematuria.

• The most ominous complication is the development of renal cell carcinoma in the walls of these cysts, occurring in 7% of dialyzed patients observed for 10 years.
These kidneys are about normal in size but have a few scattered cysts, none of which is over 2 cm in size. This is cystic change associated with chronic renal dialysis.

Patient with renal failure who undergo dialysis for years may develop multiple cysts in their kidneys. Such cysts are more numerous than the common simple renal cysts, but usually less numerous than cysts with DPKD, and the size of the kidneys is usually not markedly increased.
Approximately 35% of patients on chronic dialysis develop Acquired Cystic Disease in their native kidneys. Renal cell carcinoma develops in approximately 6% of these patients.
This is one of the first power points I ever made for teaching Pathology.

I love it very much. It is mainly about a markedly enlarged prostate, but note that big stone yellowish-brown calculus formed in the bladder.

Would you like one like that in your kidneys?

Well abuse Vitamin D.
• The next two shows the state of the brains of a few posters on BU!
• Nice pictures of cerebral atrophy in a patient with Alzheimer disease.
This is cerebral atrophy in a patient with Alzheimer disease. The gyri are narrowed and the intervening sulci widened, particularly pronounced toward the frontal lobe region.
Brain of an 82 y.o. male (Left) vs 36 y.o. male (Right)
Physiologic atrophy due to age-related diminished blood supply
Neurofibrillary Tangles: Paired Helical Filaments

* MAPS - microtubule-associated protein

Hyperphosphorylated tau ptn, ubiquitin, MAPS*, Amyloid beta ptn
Displace Encircle Nucleus
There are some posters on BU who might not have a stroke, but I am willing to bet that their brains evince a picture of liquefactive necrosis as illustrated, as they cerebrate as though there are large gaps in their brains!

- NO LOGIC
- NO COHERENCE
- NO REASONING
Grossly, the cerebral infarction at the upper left here demonstrates liquefactive necrosis. Eventually, the removal of the dead tissue leaves behind a cavity.
• As this infarct in the brain is organizing and being resolved, the liquefactive necrosis leads to resolution with cystic spaces.
This is liquefactive necrosis in the brain in a patient who suffered a "stroke" with focal loss of blood supply to a portion of cerebrum. This type of infarction is marked by loss of neurons and neuroglial cells and the formation of a clear space at the center left.
• At high magnification, liquefactive necrosis of the brain demonstrates many macrophages at the right which are cleaning up the necrotic cellular debris. The job description of a macrophage includes janitorial services such as this, particularly when there is lipid.
• For those who say and THINK THAT THEY ARE HOLDING THEIR LIKKERS!

• BEHOLD WHAT YOUR LIVER LOOKS LIKE AS WE SPEAK!

• BEHOLD THE DAMAGE DONE BY HIGHLY PROCESSED CANE JUICE! (and I don’t mean swank!)
This liver is slightly enlarged and has a pale yellow appearance, seen both on the capsule and cut surface. This uniform change is consistent with fatty change.
The cut surface of the liver reveals the hepatic adenoma. Note how well circumscribed it is. The remaining liver is a pale yellow brown because of fatty change from chronic alcoholism.
This is fatty change in the liver. There are large fat vacuoles (v) in the hepatocytes. The cytoplasmic contents and nuclei of hepatocytes are pushed to the periphery of the cell by the fat within the cytoplasm.
A high magnification of liver with fatty change. Varying size vacuoles (v) are present within the cytoplasm of the hepatocytes pushing the original contents of the cytoplasm as well as the nucleus to the peripheral part of the cell.
Fatty Liver
This is the histologic appearance of hepatic fatty change. The lipid accumulates in the hepatocytes as vacuoles. These vacuoles have a clear appearance with H&E staining. The most common cause of fatty change in developed nations is alcoholism. In developing nations, kwashiorkor in children is another cause. Diabetes mellitus, obesity, and severe gastrointestinal malabsorption are additional causes.
Here are seen the lipid vacuoles within hepatocytes. The lipid accumulates when lipoprotein transport is disrupted and/or when fatty acids accumulate. Alcohol, the most common cause, is a hepatotoxin that interferes with mitochondrial and microsomal function in hepatocytes, leading to an accumulation of lipid.
Mallory Bodies
Intermediary Filaments
Alcoholic Hepatitis
INCLUSIONS Mallory's hyaline is seen here, but there are also neutrophils, necrosis of hepatocytes, collagen deposition, and fatty change. These findings are typical for acute alcoholic hepatitis. Such inflammation can occur in a person with a history of alcoholism who goes on a drinking "binge" and consumes large quantities of alcohol over a short time.
**Alcoholic Liver**: Hyaline Inclusions (left) and Prekeratin Tangles (on EM, on the right)
Liver, alcoholism, fatty change
This is an example of alcoholic steatosis, which is fatty change of the liver due to acute or chronic consumption of large amounts of alcohol. The band of large white cells seen in the center of the field is composed of hepatocytes which have become filled with lipid. This is called macrovesicular fatty change. Normal sinusoids and cords of normal hepatocytes are seen in the bottom right and the upper left portions of the screen. Sometimes lipogranulomas occur with fatty change. However, none are seen here. Notice that inflammatory cells are not seen within the field of view. Therefore, this is not alcoholic hepatitis.
Intracellular accumulations of a variety of materials can occur in response to cellular injury. Here is fatty metamorphosis (fatty change) of the liver in which deranged lipoprotein transport from injury (most often alcoholism) leads to accumulation of lipid in the cytoplasm of hepatocytes.
The liver injury with chronic alcoholism leads to fibrosis and regeneration of the hepatocytes in nodules. This firm, nodular appearance of the liver as seen here is called **cirrhosis**.
• I WILL BE BACK!   LOL