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|  | **Amyloidosis** | **Iron Deficiency Anemia** | **Plummer-Vinson Syndrome****= “Patterson-Kelly Synd”** |
| **Definition** | - Deposition of amyloid (extracellular proteinaceous material; can have several sources but all have similar molecular structure)- Represents a wide range of conditions- Effects depend on organs involved (mild if only skin involved, death when kidney or heart are involved)- Assoc w/ multiple myeloma or infections | - Most common cause anemia in US- Associated w/ - Excess blood loss (GI uncer, menstrual, delivery) - Inc demand for RBC (pregnancy) - Dec iron intake (kids, poor diet) - Dec iron absorption ( GI prob.) | - Rare syndrome- Composed of - Iron deficiency anemia - Glossitis - Dysphagia - Important since considered a premalignant condition for oral and esophageal SCCa |
| **Clinical**  | - **Organ limited** - Rare in oral soft tissues - Amyloid nodule, asx submucosal deposit - Not assoc w/ systemic sx- **Systemic** - Primary or myeloma associated - Older adults >65 yrs - Male predilection - Initial sx non-specific (fatigue, wt loss)  - Eventually amyloid deposits: macroglossia, dry mouth, carpal tunnel syndrome, hepatomegaly - Skin lesions: waxy papules & plaques, smooth surface (eyelid area, retroauricular, neck, lips) - Secondary - Due to chronic inflammatory process (osteomyelitis, TB, sarcoidosis) - Affects liver, kidney, spleen, adrenals - Hemodialysis-associated - Accumulation of normal protein (beta2-microgloulin) in plasma - Deposits in bones and joins - Carpal tunnel synd, cervical spine pain - Tongue deposits - Heredofamilial  - aka “**familial Mediterranean fever”** - Uncommon, most AD/AR form  - Polyneuropathy, cardiomyopathy, arrhythmias, CHF, renal failure | - Fatigue, palpitations, lightheadedness, lack of energy (all b/c dec O2 delivery)- Oral:  - angular cheilitis - Glossitis: diffuse or patchy atrophy w/ burning sensation 🡪 “bald tongue” (smooth red tongue) - generalized oral mucosal atrophy- Predisposition to oral candidiasis? (mucosa appears too pale or too red due to candidiasis) | - Age 30-50 yrs- Affects northern European or Scandinavian Women- Iron deficiency anemia- Oral: - Glossitis - Angular cheilitis - Dysphasia and odynophagia  - Difficulty or pain on swallowing - Esophageal web (bands of tissue in esophagus)- Koilonychia - Alteration in nail growth pattern, spoon shaped nail (bends up), brittle |
| **Histo** | - Renal biopsy (80% + in 1o amyloidosis)- Gingival and salivary gland biopsy- Extracellular deposit of eosinophilic (pink) material- Appears red when stained w/ Congo Red- Apple-green birefringence when seen under polarized light |  | - EP atrophy, chronic inflam- Atypia or dysplasia may be seen in advanced cases |
| **Dx/Lab** | - Medical work-up to determine type of amyloidosis- Serum electrophoresis: monoclonal gammopathy to r/o multiple myeloma | - CBC w/ RBC indices (Hgb, Hct, MCV, MCH)- Dec # of RBC- Hypochromic microcytic RBC- r/o hypothyroidism, depression, or other anemias | - same as iron def anemia |
| **Tx/Prog** | - No Tx available for most types- If 2o, Tx the underlying cause (eg. Infection) - Renal transplant helps in dialysis associated- Drug trials (Colchicine, Prednisone, Melphalan)- Death due to cardiac failure, arrhythmia, renal failure within a few yrs of Dx | - Dietary iron supplementation (oral ferrous sulfate), RBC return to normal in 1-2 mos- if malabsorption: parenteral iron- Tx underlying cause if applicable | - Dietary iron supplements- may be Esophageal dilatation - 5-50% prevalence of upper aerodigestive tract malignancy - Follow- up to screen for ORAL and ESOPHAGEAL SCC |

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|  | **Pernicious anemia** | **Hyperparathyroidism** | **Hypoparathyroidism** |
| **Definition** | - Uncommon - Megaloblastic anemia caused by poor absorption of cobalamin (Vit B12)- B12 (extrinsic factor) necessary for nucleic acid syn, effects GI, hematopoietic cells w/ rapid turnover- B12 complex can only be absorbed in the intestine if it is bound to Intrinsic factor (produced by parietal cells of stomach)- In most cases 2o to autoimmune destruction of parietal cells (lack of intrinsic factor) - Others: GI bypass operation | - Excess production of PTH produced by parathyroid glands- PTH controls level of calcium in extracellular tissues- When serum calcium dec, PTH is produced- PTH acts on- **Kidney**: inc phosphate excretion, Ca reabsorption, stimulates Vit D production which inc Ca absorption in gut- **Osteoclasts**: activated to resorb bone, liberating Ca- **Primary Hyperparathyroidism**- Uncontrolled production of PTH- 80-90% parathyroid adenoma - 10-15% parathyroid hyperplasia - <2% parathyroid carcinoma - **Secondary hyperparathyroidism** - Excess PTH producton due to low levels of serum Ca  - Chronic renal disease (active vit D is not produced, less Ca absorbed from intestine) | - Reduced production of PTH- Secondary to - Inadvertent removal of parathyroid glands during thyroid surgery- Autoimmune destruction of parathyroid glands- Assoc. w/ DiGeorge Syndrome, Endocrine-candidiasis syndrome |
| **Clinical**  | - Elderly pts of Northern European heritage- Fatigue, weakness, shortness of breath, headaches, feeling faint- Numbness or tingling of extremities- Burning sensation in tongue, lips, buccal mucosa - Papillary atrophy of tongue 50-60% | - age > 60 yrs, female (2-4x)- classic Sx: stones, bones, groans- Stones - renal calculi due to elevated calcium - metastatic calcifications (blood vessel wall, subcutaneous soft tissue, sclera, dura, around joints)- bones (radiographic ft) - resorption of phalanges of index and middle finger - generalized loss of lamina dura around teeth - dec in trabecular density = **“ground glass” appearance** - brown tumor of bone (mandible, clavicle, ribs, pelvis) b/c hemorrhagic 🡪 central giant cell granulomas 🡪 osteoclast - osteitis fibrosa cystic (most severe, degenraion and fibrosis of brown tumors) - if secondary HPT, renal osteodystrophy may occur - striking enlargement of the jaws (uniformly) 🡪 evidence: teeth spacing - ground glass radiographic pattern 🡺 almost looks like Paggets but osteopenia- Abdominal groans: duodenal ulcers- Changes in mental: lethargy, weakness, confusion, dementia | - Chvostek’s sign (twitching of upper lip when facial nerve is tapped below zygomatic process) indicates a degree of tetany- During odontogenesis can lead to hypoplastic enamel (pitting) or failure of tooth eruption - Persistent oral candidiasis may be onset of endocrine-candidiasis syndrome |
| **Histo** | - EP atrophy, may be confused w/ dysplasia | - Brown tumor is identical to CGCG - Vascular granulation tissue proliferation w/ multiple giant cells (osteoclasts)- Renal osteodystrophy: in pts w/ ESRD - Proliferation of woven bone bony spicules, some giant cells and CT |  |
| **Dx/Lab** | - Macrocytic anemia- Reduced serum cobalamin | - Brown tumor (radiographic ft) - Unilocular or multilocular RL, well demarcated borders - Solitary or multiple - Long standing lesions may produce expansion | - Dec PTH (radioimmunoassay)- Dec serum calcium (hypocalcemia)- Elevated serum phosphate- Normal renal fnct |
| **Tx/Prog** | - Monthly IM injection of B12- Rapid response (within 5 days)- 1-2% risk of gastric malignancy | - **Primary** - Remove cause (surgical removal of tumor/hyperplastic tissue)- **Secondary**- Not managed aggressively unless Sx of renal caculi or renal osteodystrophy- Vit D metabolite, restriction of dietary phosphate- Parathyroidectomy - Renal transplantation | - Oral Vit D precursor (ergocalciferol or vit D2)- Dietary supplements of calcium - Most patients can lead normal life |

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|  | **Addison’s Disease (Hypoadrenocorticism)** | **Hypophosphatasia** | **Crohn’s Disease** **(Regional Ileitis)** | **Pyostomatitis vegetans** |
| **Definition** | - Insufficient production of corticosteroid hormones produced in the adrenal cortex- **Primary** - Adrenal cortex gland malfnct- Autoimmune destruction: most common- Infections (TB, Deep fungal- Cryptococcus in AIDS pt)- rarely: metastatic tumors, amyloidosis, sarcoidosis, hemochromatosis- **secondary**- pituitary (or hypothalamus) malfnct leading to dec levels of ACTH | - Rare metabolic bone disease- Inherited AR- Variable expression: the younger age of onset, the more severe expression of disease- Involved factors :  - reduced levels of bone/liver/kidney alkaline phosphatases (Enz for bone production) - bone abnormalities, similar to rickets- **Dental importance** - premature tooth loss b/c lack of cementum  - Large pulp chambers and alveolar bone loss | - Inflammatory condition primarily affecting distal small intestine and proximal colon (can be seen anywhere GI tract)- Unknown cause – immunologically medicated?- Oral implications – oral lesions can be initial representation (30%) | - Rare condition- Represents oral manifestations of inflammat Bowel Disease or Crohn’s disease- Unknown pathogenesis |
| **Clinical**  | - 90% of glandular tissue must be destroyed before Sxs - Fatigue, irritability, depression, weakness, hypotension (🡪 syncope)- Generalized “bronzing” or hyperpigmentation of skin—usually sun exposed areas (due to inc ACTH which stimulates melanocytes)- GI upset, diarrhea, weight loss, anorexia, nausea- Oral manifestations - Diffuse or patchy melanotic pigmentation of oral mucosa - May be the initial presentation of disease - Distinguish from racial pigmentation by history of recent onset | - **Perinatal** - Most severe manifestations - Dx made at birth, death in few hrs due to respiratory failure - Marked hypocalcifcation of skeleton- **Infantile** - Dx at 6 mo due to failure to grow - Skeletal malformations (shortened bowed limbs, rib & skull abnormalities) - nephrocalcinosis, nephrolithias - can have premature exfoliation of teeth- **Childhood** - Early sign is premature loss of 1o teeth, may be the only teeth affected - Large pulp chambers and alveolar bone loss - Premature fusion of cranial fontanels 🡪 inc intracranial pressure and brain damage - **Adult** - Mild presentation - Premature loss of 1o or perm dentition - Stress fratures in feet - Inc # of fracture assc w/ minor trauma | - Usually dx in adolescents- underline problem is inflammation 🡪 granulomas- GI Sx:  - Cramping, pain, nausea, diarrhea, sometimes fever - Wt loss, malnutrition- Oral lesions - Diffuse or nodular swelling in oral mucosa (similar to angioedema clinically) - Cobblestone appearance of oral mucosa - **Deep granulomatous ulcerations** - Linear ulcer along vestibule - Aphthous-like ulcerations | - B/L mucosa, soft palate, ventral tongue- “snail track” ulcerations (may not be truly ulcers): yellow, elevated, linear, serpentine pustules set on an erythematous base- Sxs depend on extent of lesion, some pustules may rupture and ulcerate- Oral lesion appear at same time as bowel sxs or may be initial presentation of disease |
| **Histo** |  | - absence or reduction in amt of cementum (prevents PDL fibers from attaching to tooth) | - Non-necrotizing granuloma in CT- Special stains to r/o infectious process - deep fungal, 3o syphilis, mycobateria (TB) | - Acantholysis, edema, eosinophilic abscess in EP- CT mixed inflam infiltrate - Perivascular inflam |
| **Lab** | - Rapid ACTH stimulation test, plasma ACTH levels- Primary = high ACTH- Secondary = low ACTH | - Dec of serum alkaline phosphatase (may become normal as pt ages)- Inc of phosphoethanolamine in urine and blood |  |  |
| **Tx/Prog** | - Corticosteroid replacement therapy- Physiologic dose = 5-7.5mg day of Prednisone (stress-dose steroids) for hypotension- May need to adjust doses in stressful events (major oral surgery) b/c risk of hypertension - W/ current Tx pts can live normal life span | - Disorder cannot be corrected- Orthopedic surgery/rehabilitation- Dentures (alveolar bone hypoplasia)- Genetic counseling- Prognosis is poor for perinatal and infantile, adult type is compatible w/ normal life | - Initial therapy: Sulfasalazine- Moderate-severe: Prednisone- Surgery if disease cannot be controlled medically- B12 supplement if no ileum- Iron & folate supplements b/o malabsorption | - Oral lesions resolve when bowel disease is managed w/ Sulfasalazine or Prednisone- Oral lesions may recur if medication is discontinued |