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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 |