

USMLE #3

~~Water Balance, Electrolytes,~~ Acid-Base Disorders

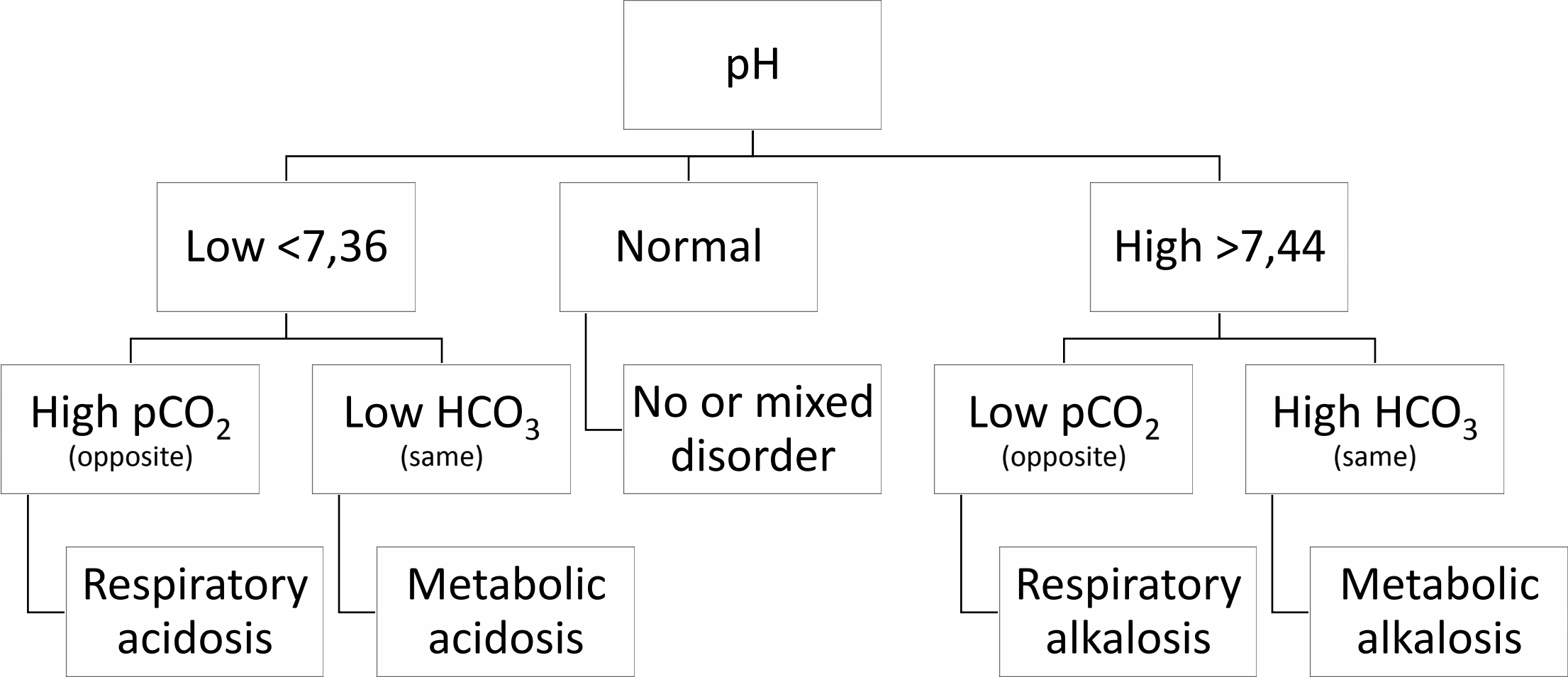
Acid-base homeostasis

- Henderson-Hasselbach formula
- Normal lab values
 - pH = 7,36 - 7,44
 - HCO_3^- = 24 mEq/L (22-30)
 - pCO_2 = 40 mmHg (36-40)
 - AG = 12 mEq/L (10-14)
 - Osmolar gap = <10
- Primary disorders
- Compensatory mechanisms

$$pH = 6,1 + \log \frac{[HCO_3^-]}{\alpha \cdot pCO_2}$$

Approach to acid-base disorders

1. What is the blood pH?
 - Acidemia, alkalemia, normal (=no disturbance/mixed)
2. Type of primary disturbance? Look first at CO_2 , then HCO_3
3. Is there appropriate compensation?
4. Anion gap?
5. Osmolar gap?



Compensation

- Metabolic Acidosis
 - $\downarrow 10 \text{ HCO}_3 = \downarrow 10 \text{ pCO}_2$
- Metabolic Alkalosis
 - $\uparrow 10 \text{ HCO}_3 = \uparrow 5-7 \text{ pCO}_2$
- Respiratory Acidosis
 - Acute: $\uparrow 10 \text{ pCO}_2 = \uparrow 1 \text{ HCO}_3$
 - Chronic: $\uparrow 10 \text{ pCO}_2 = \uparrow 3 \text{ HCO}_3$
- Respiratory Alkalosis
 - Acute: $\downarrow 10 \text{ pCO}_2 = \downarrow 2 \text{ HCO}_3$
 - Chronic: $\downarrow 10 \text{ pCO}_2 = \downarrow 5 \text{ HCO}_3$

If actual pCO_2 change is:

Higher = coexistent respiratory acidosis

Lower = coexistent respiratory alkalosis

If actual HCO_3 is:

Higher = coexistent metabolic alkalosis

Lower = coexistent metabolic acidosis

Anion gap

- Is anion gap elevated? $AG = Na - (HCO_3 + Cl)$
- increase in AG > decrease in HCO_3 = coexistent metabolic alkalosis
- increase in AG < decrease in HCO_3 = coexistent non-AG met. acidosis

ΔAG	ΔHCO_3	Type
0 (+- 2)	> ΔAG	Non-AG acidosis
>2	= ΔAG	AG acidosis
>2	> ΔAG	Combined Non-AG and AG acidosis

Related clinical cases

„An 8-year-old boy presents to the emergency department with a 2-hour history of vomiting after eating dinner at a seafood buffet. Arterial blood gas analysis reveals a pH of 7.50, an bicarbonate level of 34 mEq/L, and partial carbon dioxide pressure of 40 mm Hg. Which of the following best describes the acid-base disturbance occurring in this patient?

- (A) Metabolic acidosis
- (B) Metabolic acidosis/respiratory acidosis
- (C) Metabolic acidosis/respiratory alkalosis
- (D) Metabolic acidosis/respiratory compensation
- (E) Metabolic alkalosis
- (F) Metabolic alkalosis/respiratory compensation“¹

- „**The correct answer is E.** Vomiting typically induces a metabolic alkalosis due to a loss of hydrogen ions from the stomach, leading to an increase in pH. This leaves an increased bicarbonate concentration (generally >24 mEq/L) in the bloodstream. In this case, the partial carbon dioxide pressure is still normal; thus, no respiratory compensation has occurred, and the patient has uncompensated metabolic alkalosis.
- **Answer A is incorrect.** This patient is presenting with a metabolic alkalosis (pH >7.4), not an acidosis.
- **Answer B is incorrect.** This patient has an alkalosis, as evidenced by the pH. The partial carbon dioxide pressure is normal, indicating that there is no respiratory acidosis. Sometimes patients will present with more than one condition causing acid-base imbalance. These are known as complicated or mixed conditions, but this is not true of the patient in the above vignette.
- **Answer C is incorrect.** There is no metabolic acidosis, because the bicarbonate concentration is actually increased. There has been no respiratory change, either, because the partial carbon dioxide pressure is normal.
- **Answer D is incorrect.** This patient does not have an acidosis.
- **Answer F is incorrect.** The patient does have metabolic alkalosis, but because partial carbon dioxide pressure is normal, there has been no respiratory compensation. In respiratory compensation, the partial carbon dioxide pressure would be increased to create more free H⁺ in the bloodstream. This could be accomplished by hypoventilation.“¹

„Respiratory acidosis is a major complication in morphine overdoses. Which of the following laboratory data correspond to a pure respiratory acidosis?

CHOICE	pH	pCO ₂ (mmHg)	HCO ₃ ⁻ (mEq/L)	Na ⁺ (mEq/L)	Cl ⁻ (mEq/L)
A	7.2	42	15	140	89
B	7.2	42	15	140	114
C	7.2	68	15	140	104
D	7.2	68	25	140	104
E	7.4	68	12	140	89
F	7.6	42	20	140	104
G	7.6	68	18	140	104 ^{“1}

- „**The correct answer is D.** Hypoventilation causes an inability on the part of the lungs to excrete the CO₂ the body produces, leading to retention of CO₂. This causes a drop in pH and a compensatory retention of bicarbonate. These acid-base abnormalities are consistent with respiratory acidosis. Hypoventilation (from a variety of etiologies) is a primary cause of respiratory acidosis.
- **Answer A is incorrect.** An increase in anions would be consistent with anion-gap metabolic acidosis. Metabolic acidosis is indicated by the presence of low pH with low plasma bicarbonate and low carbon dioxide and an increased anion gap, measured by $([Na^+] - [Cl^-] - [HCO_3^-])$, which is normally 10–16 mEq/L. The main causes are lactic acidosis, diabetic ketoacidosis, and renal failure.
- **Answer B is incorrect.** Non-anion-gap metabolic acidosis is the presence of low pH with low plasma bicarbonate without an elevated anion gap. The cause is generally gastrointestinal losses of bicarbonate (i.e., diarrhea, biliary drains, emesis, nasogastric tube losses). Another important and common cause of a metabolic non-anion-gap acidosis is the presence of an ileal conduit or bladder reconstruction from colonic tissue. The gastrointestinal tissue absorbs Cl⁻ from the urine in exchange for bicarbonate. Other causes include renal tubular acidosis, or hypochloremia.
- **Answer C is incorrect.** The pH in this answer is low, which corresponds to an acidosis. The P_cCO₂ is high, which is consistent with a respiratory acidosis, however the HCO₃⁻ is low, which is consistent with a metabolic acidosis. Thus this patient has a mixed respiratory and metabolic acidosis.
- **Answer E is incorrect.** The pH in this instance is normal, while there is an increased anion gap. An anion gap usually indicates that the patient has an acidosis. Since the pH of the blood is normal and not lowered, it indicates that this is a mixed acid-base disorder, in which a metabolic or respiratory alkalosis is counteracting a metabolic anion-gap acidosis.
- **Answer F is incorrect.** Respiratory alkalosis can be caused only by an increase in ventilation leading to excessive loss of carbon dioxide, which is balanced by an increased excretion of bicarbonate. Hence, a high pH, a low CO₂, and a low bicarbonate indicate respiratory alkalosis. This is caused by hyperventilation.
- **Answer G is incorrect.** Metabolic alkalosis would present with a high pH, a high bicarbonate, and (with respiratory compensation) a high CO₂. The causes of metabolic alkalosis include vomiting, diuretic therapy, and chloride restriction. The compensation is hypoventilation.“¹

„A 19-year-old woman with a severe gastrointestinal infection presents to the emergency department with a 5-day history of vomiting and diarrhea. Serum chemistry tests show:

Na⁺: 138 mEq/L

K⁺: 3.0 mEq/L

Cl⁻: 88 mEq/L

HCO₃⁻: 21 mEq/L

BUN: 10 mg/dL

Creatinine: 0.8 mg/dL

Glucose: 101 mg/dL

Arterial blood gas analyses shows a pH of 7.38, partial arterial carbon dioxide pressure of 37 mm Hg, partial arterial oxygen pressure of 82 mm Hg, and an oxygen saturation of 96% on room air. Which of the following statements is most accurate regarding this patient's acid-base status?

- (A) She has a metabolic acidosis
- (B) She has a mixed metabolic alkalosis and metabolic acidosis
- (C) She has a mixed respiratory alkalosis and respiratory acidosis
- (D) She has no acid-base disturbances
- (E) She has a respiratory alkalosis¹

- **„The correct answer is B.** While this patient’s pH, bicarbonate, and carbon dioxide levels are all very close to normal, it is always important to look more closely before concluding that there is no disorder. Vomiting is a common cause of a metabolic alkalosis, while diarrhea is a common cause of non-anion-gap metabolic acidosis. The patient has had gastrointestinal symptoms that have led to acute dehydration, which indicates that these symptoms are probably quite severe. It is also important to look at the serum chemistry. One would expect a hypokalemic hypochloremic metabolic alkalosis from vomiting, but only the electrolyte deficiencies are present. The equalized pH suggests that the patient is losing an equal amount of acid through vomiting as she is base through diarrhea. Therefore, it is more likely that she has a mixed acid-base disorder than no electrolyte imbalances at all.
- **Answer A is incorrect.** Non-anion-gap metabolic acidosis is the presence of a low pH with a low plasma bicarbonate level and without an elevated anion gap. It is characterized by a compensatory retention of the other main body anions, which results in hyperchloremia. The cause is generally diarrhea and renal tubular acidosis.
- **Answer C is incorrect.** While a mixed respiratory disorder could lead to this electrolyte profile, the patient has no respiratory pathology. Therefore, it is more likely that her acid-base status is being determined by a metabolic process.
- **Answer D is incorrect.** Although this patient’s pH, bicarbonate, and carbon dioxide levels are close to normal, the gastrointestinal symptoms (vomiting, diarrhea) suggest that she has a mixed acid-base disorder than no electrolyte imbalances at all.
- **Answer E is incorrect.** Respiratory alkalosis can be caused only by an increase in ventilation leading to excessive loss of carbon dioxide, which is balanced by an increased excretion of bicarbonate. Hence, a high pH and low carbon dioxide and bicarbonate levels indicate respiratory alkalosis.“¹

Questions from other topics

May odds be ever in your favor

Question #1

„A 42-year-old woman with a history of pernicious anemia comes to the physician complaining of increased anxiety, heart palpitations, heat intolerance, unexplained weight loss, and multiple daily bowel movements. She has not had a period in 4 months. On physical examination, the patient is found to have a goiter, a thyroid bruit, and mild exophthalmos. Laboratory studies show elevated triiodothyronine and free thyroxine levels, and an undetectable thyroid-stimulating hormone. Which of the following is the most likely etiology of this patient’s disease?

- (A) Autoimmune stimulation of thyroid-stimulating hormone receptors
- (B) Idiopathic replacement of thyroid tissue with fibrous tissue
- (C) Thyroid adenoma
- (D) Thyroid hormone-producing ovarian teratoma
- (E) Viral infection leading to destruction of thyroid tissue“¹

- **„The correct answer is A.** This patient presents as a classic case of Graves’ disease. In Graves’ disease, thyroid-stimulating IgG antibodies bind to TSH receptors and lead to thyroid hormone production. This causes glandular hyperplasia and enlargement characteristic of the goiter associated with Graves’ disease. Graves’ disease is the most common cause of thyrotoxicosis. Patients with this condition may have other autoimmune diseases, such as pernicious anemia or type 1 diabetes mellitus, and frequently present with anxiety, irritability, tremor, heat intolerance with sweaty skin, tachycardia and cardiac palpitations, weight loss, increased appetite, fine hair, diarrhea, and amenorrhea or oligomenorrhea. Signs include diffuse goiter, proptosis, periorbital edema, and thickened skin on the lower extremities. Laboratory values reveal increased thyroid hormone levels and decreased TSH levels.
- **Answer B is incorrect.** Idiopathic replacement of thyroid and surrounding tissue with fibrous tissue is seen in Riedel’s thyroiditis; patients may present with dysphagia, stridor, dyspnea, and hypothyroidism, although more than 50% of patients are euthyroid. The disease can mimic thyroid carcinoma, which is high on the list of differential diagnoses for a patient with Riedel’s thyroiditis.
- **Answer C is incorrect.** Most thyroid adenomas present as solitary nodules and are usually nonfunctional.
- **Answer D is incorrect.** Thyroid hormone producing ovarian teratomas are known as struma ovarii, a tumor consisting of thyroid tissue. These tumors can cause hyperthyroidism, but given the patient’s history of autoimmune disease, Graves’ disease is the better answer choice.
- **Answer E is incorrect.** Viral infections such as mumps or coxsackievirus can lead to destruction of thyroid tissue and granulomatous inflammation, as seen in subacute granulomatous thyroiditis. Patients typically present with flu-like symptoms and thyroid tenderness and pain. The disease is typically self-limited and can include a transient hyperthyroid state.“¹

High-yield associations

- **Graves' disease**
 - MCC of hyperthyroidism
 - Autoimmune = women
 - Exophthalmos (proptosis)
 - Pretibial myxedema
 - Low TSH, high T3,T4

Question #2

„A 23-year-old man comes to the physician because of intermittent severe headaches, anxiety, and heart palpitations. While he has no significant medical history, his uncle had similar symptoms. When probed for a deeper family history, he says that his mother and two cousins have had their thyroids removed. Which of the following conditions most likely accounts for the clinical scenario?

- (A) Acromegaly
- (B) ACTH-secreting pituitary adenoma
- (C) Hyperparathyroidism
- (D) Nonfunctioning pituitary adenoma
- (E) Pheochromocytoma¹

- „**The correct answer is E.** The headache, anxiety, and palpitations suggest an excess of catecholamines stimulating the sympathetic nervous system. A pheochromocytoma may be suspected, and since there appears to be familial involvement, the related multiple endocrine neoplasia (MEN) syndromes should also be considered. MEN type II (used to be called type 2a) consists of medullary thyroid carcinoma (MTC), pheochromocytoma, and tumors of the parathyroid. MEN type III (used to be type 2b) usually includes MTC, pheochromocytoma, and neuromas instead of parathyroid tumors. It is therefore likely that this patient's relatives had their thyroids removed due to MTC. One could further differentiate the two types by looking for neuromas on the lips, tongue, or eyelids or in the gastrointestinal tract causing constipation/diarrhea, or for hyperparathyroidism manifesting in bradycardia, hypotonia, fatigue, and bone pain.
- **Answer A is incorrect.** Acromegaly can lead to headaches; however, it does not commonly cause palpitations and is not associated with multiple endocrine neoplasia. Clinical signs of acromegaly include coarse facies, enlarged tongue, and increased size of hands and feet.
- **Answer B is incorrect.** An ACTH-secreting pituitary adenoma, which defines Cushing's disease, would cause hypercortisolemia secondary to ACTH stimulation from the anterior pituitary, with elevated serum ACTH levels. Clinical findings would include characteristic moon facies, striae, obesity, hypertension, weakness, and hirsutism.
- **Answer C is incorrect.** Up to 80% of patients with hyperparathyroidism are asymptomatic at diagnosis, and their disease is caught by routine blood tests. Some have nonspecific symptoms such as fatigue, mild depression, and anorexia. If severe, metastatic calcification and osteoclastic bone lesions can occur.
- **Answer D is incorrect.** A nonfunctioning pituitary adenoma could suppress ACTH in the serum and would generally be accompanied by hypocortisolemia. Clinical findings would include weight loss, hypotension, fatigue, nausea, abdominal pain, and muscle cramps.“¹

High-yield associations

- **Pheochromocytoma**

- MC tumor of adrenal medulla in **adults** (kids?)
- Urinary VMA, metanephrines
- Surgery: alpha and beta antagonists
 - first alpha, only then beta !!!

- 5P: pain, pressure, perspiration, palpitations, pallor
- 10%: malignant, bilateral, extra-adrenal, calcify, kids
- Neurofibromatosis I
- MEN 2A, 2B

Question #3

„A 16-year-old boy with sickle cell disease has complained of a weak right leg for the past 10 days. He is unable to put much weight on it. On physical examination, the area over the right tibia is found to be swollen and erythematous. The organism responsible for this patient’s infection most likely has which of the following features that makes it particularly pathogenic?

- (A) Capsule
- (B) Flagella
- (C) Lack of cell wall
- (D) Mycolic acids
- (E) Pili¹

- „**The correct answer is A.** Since sickle cell disease leads to autosplenectomy, a condition in which fibrosis results from repeated infarcts of the spleen due to adherence of sickled RBCs. The spleen is unable to perform its normal functions, such as sequestering capsulated organisms. Since the spleen is the major defender against these organisms, patients without splenic function are susceptible to infection by encapsulated organisms such as *Salmonella typhi*. The symptoms suggest that the boy has osteomyelitis of the tibia, and the most important determinant of virulence in sickle cell patients with osteomyelitis is the presence of a capsule. *S. aureus* is the most common cause of osteomyelitis in all groups, but *Salmonella* osteomyelitis has a particular association with sickle cell disease, and it is this association that is often tested on the Step 1 USMLE.
- **Answer B is incorrect.** The flagellum of *Salmonella* is indeed a virulence factor that acts as an antigen that can be varied (antigenic variation or switching). However, it is not the presence of the flagellum that makes *Salmonella* more pathogenic in sickle cell patients.
- **Answer C is incorrect.** *Mycoplasma* species are bacteria that lack a cell wall and that most often cause pneumonia (*M. pneumoniae*) or nongonococcal urethritis (also *Ureaplasma urealyticum*).
- **Answer D is incorrect.** Mycolic acids are found in the outer cell membrane of mycobacteria. Mycobacteria can cause osteomyelitis, but autosplenectomy does not particularly put sickle cell patients at a higher risk.
- **Answer E is incorrect.** Pili are structures on some bacteria that aid in adhesion to host cells.“¹

High-yield associations

- **Sickle cell disease**
 - β chain – glu->val
 - Resistance to malaria
- Autosplenectomy (Howell-Jolly)
- Vaso-occlusive crisis (e.g. dactylitis)
- Acute chest syndrome
- Aplastic crisis (parvo B19)
- Encapsulated bacteria
- African-American
- Hemolytic crisis (G6PD deficiency)
- *Salmonella* osteomyelitis

Q1 A 68-year-old, well-developed, well-nourished black man presents to the emergency department complaining of shortness of breath. He denies chest pain. He has no significant past medical history and takes no medications. A chest x-ray film shows clear lung fields, mild cardiomegaly, and a widened thoracic aorta with linear calcifications. An MRI of the chest shows aortic dilatation in the thorax, extending proximally, with atrophy of the muscularis and wrinkling of the intimal surface. What is the most likely etiology of this condition?

- (A) Atherosclerosis
- (B) Hypertension
- (C) Marfan syndrome
- (D) Syphilis infection
- (E) Takayasu arteritis

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The correct answer is D. Although rare now because of advances in treatment, syphilitic aortitis and aneurysm are still seen, especially in underserved populations. This complication generally occurs 10 to 40 years after initial infection. The vasa vasorum of the aorta undergoes obliterative endarteritis, leading to atrophy of the muscularis and elastic tissues of the aorta and dilatation. Linear calcifications are often seen in the ascending aorta by x-ray. The intimal wrinkling or „tree barking“ is also a common feature. Syphilitic aneurysm can be associated with respiratory distress, cough, congestive heart failure, and rarely, rupture.

Atherosclerosis (**choice A**) is the most common cause of aortic aneurysms. These are most often located in the abdominal aorta, distal to the renal arteries. Intimal wrinkling and linear calcifications are not seen.

Hypertension (**choice B**) is usually responsible for dissecting aneurysms located within 10 cm of the aortic valve. Patients present with sudden chest pain that is usually severe and tearing in nature. The chronic hypertension causes a cystic medial necrosis, allowing the separation of vessel layers.

Marfan syndrome, an autosomal dominant connective tissue disorder (**choice C**), is also associated with dissecting aneurysms, usually of the ascending aorta. The patients are often very tall with arachnodactyly and ligamentous laxity. Their life span is generally shortened. This patient's description and age are not consistent with this diagnosis.

Takayasu arteritis (**choice E**) is a syndrome characterized by ocular disturbances and weak pulses in the arms. It occurs frequently in young females. It is considered a giant cell arteritis and does not cause aneurysms.

You've survived! Thank you.

References

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