**CASE 1**
A 39 year old male is seen in the ER for a 3 month history of abdominal pain, fatigue and neuropsychiatric symptoms. On abdominal exam, there is mild hepatomegaly. Neurological exam reveals cogwheel rigidity, bradykinesia but no tremor. Furthermore, the patient is found to be ataxic. Laboratory studies show elevated liver enzymes. Which of the following cannot be found in the late stages of this disease?
A. Kayser Fleischer Rings  
B. Angular Chelitis  
C. Type II Renal Tubular Acidosis  
D. Hypoparathyroidism  
E. Nephrocalcinosis  
F. Dialated Cardiomyopathy

**CASE 2**
A 41 year old female presents to the clinic with a 6 month history of increasing fatigue and dyspnea. Physical exam reveals normal vitals and a resting $O_2$ saturation of 96%. Her lungs are clear with no crackles or wheezes. A loud P2 and a II/VI soft systolic murmur is noted at the left sternal boarder. Her JVP shows a prominent V-wave. Chest X-ray is suggestive of right ventricular hypertrophy and enlarged pulmonary arteries. Which of the following is the next best step in establishing the diagnosis?
A. Bronchoscopy  
B. Cardiac stress test  
C. Echocardiogram  
D. Alpha-1 antitrypsin levels  
E. Cardiac angiogram

**CASE 3**
A 70 year old gentleman was intubated in the ER due to pulmonary edema. Bedside echo showed an ejection fraction of 45% and severe mitral regurgitation. Despite aggressive diuresis with furosemide, the patient continues to be on mechanical ventilation due to the pulmonary edema. The patient’s current blood pressure is 109/78. What is the next best step in this patient’s management?
A. Start another loop diuretic  
B. Start a beta blocker  
C. Start digoxin or milrinone  
D. Start IV ACE inhibitor  
E. Prepare for a mitral valve replacement surgery

**CASE 4**
A 30 year old male is being evaluated for hypertension. His blood pressure is 180/105. He complains of polyuria and mild muscle weakness. He is currently on no medications. On physical examination, the patient has a sustained apex and S4 is heard. There are no signs of congestive heart failure and no edema is found. All pulses are equal and normal. Laboratory investigations reveal
Sodium: 148 mmol/L  
Potassium: 2.5 mmol/L  
Chloride: 112 mmol/L  
Bicarb: 28 mmol/L

Which of the following is the best diagnostic test for this condition?
A. Chest CT  
B. 24 hour urine for cortisol  
C. Renal angiogram  
D. Serum aldosterone and renin activity ratio  
E. Urinary metanephrine levels
CASE 1: ANSWER B
The patient likely has Wilson’s disease, an autosomal recessive genetic disorder of copper overload. Excess copper deposits in various tissues of the body predominantly the brain and the liver. Under physiologic circumstances, copper serves the function of a cofactor for a number of enzymes. Following absorption in the GI tract, copper is transferred to the liver via the portal circulation, with the help of enzyme ATP7A. Liver cells take it up and further release it in the circulation packaged with ceruloplasmin, albumin and macroglobulins. Excess copper is excreted in bile by the liver. Both secretion into the bloodstream and excretion into the bile are under the control of enzyme ATP7B. In Wilson’s disease, both these fuctions of ATP7B are impaired and excess copper accumulates in the liver.¹

The excessive free copper precipitates throughout the body, particularly in the brain, eyes and the kidneys. In the brain, majority of the deposition occurs in the basal ganglia giving rise to the Parkinsonism. Angular chelitis cannot be found in Wilson’s disease. In the kidney, type II renal tubular acidosis, a disorder of bicarbonate handling develops further leading to nephrocalcinosis. Copper deposition in the descemet’s membrane (at the scleral and corneal interface) leads to the pathognomonic Kayser-Fleischer rings, seen in the eyes. Parathyroid gland damage by the copper also can lead to hypoparathyroidism. Rarely, copper deposition in the heart can lead to dilated cardiomyopathy.¹

CASE 2: ANSWER B
The patient likely has primary pulmonary hypertension. A broad approach to pulmonary hypertension includes primary/idiopathic and secondary (associated with other illnesses). Some of the secondary causes include left sided heart disease (atrial, ventricular or mitral stenosis), pulmonary pathology (interstitial lung disease, chronic obstructive pulmonary disease), systemic illnesses (scleroderma, systemic lupus erythmatosis, congenital shunts between the systemic and pulmonary circulation).²

Echocardiogram is a reliable non-invasive first step to establish the diagnosis. Once the pulmonary hypertension is confirmed, secondary causes can be ruled out (unlikely to be found in this patient as there are no clinical or radiographic evidence of pulmonary or cardiac disease). Following an echo study, patients often undergo right heart catheterization (considered the gold standard) with measurement of pulmonary vascular resistance, in response to various pulmonary vasodialators.³

Bronchoscopy is usually not a first step investigation for dyspnea following chest X-ray. A stress test is usually indicated if suspicion of ischemic heart disease is high. In this patient, it may show nonspecific decline in exercise tolerance. Alpha-1 antitrypsin levels would be considered if a young non-smoker develops an obstructive lung disease. If chronic obstructive lung disease was suspected, one might find clinical and radiographic evidence (O₂ desaturation and/or signs of hyperinflation).

CASE 3: ANSWER D
This patient is suffering from severe mitral regurgitation (MR) resulting in severe pulmonary edema requiring mechanical ventilation. The heart pumps blood to the path of least resistance during systole. In this patient, the left ventricular flow is determined by the amount of resistance in the aorta (afterload) and the amount of resistance to flow across the malfunctioning mitral valve. As the resistance to retrograde flow across the leaky mitral valve decreases, a larger portion of the left ventricular ejection fraction flows into the left atrium, rather than into the aorta. To increase antegrade flow through the aortic valve, afterload reduction therapy is needed, allowing more blood to enter the systemic circulation. Vasodialators, such as ACE inhibitors and hydralazine, are frequently used.⁴

Adding another loop diuretic will likely not be beneficial in stabilizing the patient hemodynamically. Beta blockers do not have a significant vasodialatory effect (when compared with ACE inhibitors), and will not be useful in afterload reduction. Contractility is usually preserved in MR, so an inotropic agent like digoxin or milrinone would not be beneficial. The patient will likely benefit from a valve replacement, but needs more stability before surgery.

CASE 4: ANSWER D
The patient has severe diastolic hypertension with unprovoked hypokalemia. In the setting of a normal physical exam and no history of diuretic use, inappropriate aldosterone overproduction is a prime consideration in hypertension with hypokalemia. Aldosterone hypersecretion leads to increased sodium uptake (leading to hypertension) in exchange for potassium at the distal convoluted tubule, progressively depleting potassium from the body. Elevated aldosterone levels and low plasma renin activity suggest the diagnosis of primary hyperaldosteronism. A ratio higher than 30 suggests aldosterone oversecretion. However, lack of aldosterone suppression (via a 2-L saline load over 4 hours) is necessary for definitive diagnosis of primary hyperaldosteronism. CT scan of the adrenal glands is then ordered to distinguish bilateral adrenal hyperplasia from an adrenal secreting tumour.⁵

CT scan of the chest is ordered if there is a high suspicion of coarctation. 24 hour urine for cortisol is suggested
in suspected Cushings syndrome. Urinary metanephrines is a screening test for pheochromocytoma. Renal angiography is used to diagnose renal artery stenosis. However, in the given scenario, none of these diagnoses are as likely as hyperaldosteronism.

A broader differential along with an age based approach should be considered in the setting of suspected secondary hypertension. Some of the etiologies, aside from those mentioned, include pheochromocytoma, renal parenchymal disease, obstructive sleep apnea, hypercalcemia, hyper/hypo-thyroidism. A thorough history and physical examination should guide the choice of tests ordered.⁶

REFERENCES