Saint Alphonsus
A Member of Trinity Health

WORK-UP OF POLYCYTHEMIA (ERYTHROCYTOSIS)

Definition (Adults)

Men: Hemoglobin >16.5 g/dL OR hematocrit >49%
Women: Hemoglobin >16.0 g/dL OR hematocrit >48%
Always repeat CBC before initiating a workup to confirm persistence.

Step 1: Confirm It's Real (Rule Out Relative Polycythemia)

Relative (spurious) polycythemia = hemoconcentration
Ask about:

- Dehydration
- Diuretics
- Vomiting/diarrhea
- Alcohol excess
- Acute illness

*If Hgb/Hct normalize after volume repletion > no further workup.

Step 2: Initial History & Examination (High Yield)

Key History

- Smoking or vaping (including marijuana)
- Chronic lung disease or OSA symptoms (snoring, daytime sleepiness)
- Cardiac disease or cyanosis
- Testosterone or anabolic steroid use
- Prior thrombotic events
- Pruritus after warm showers
- Headache, dizziness, visual changes
- Family history of polycythemia or thrombosis
- High-altitude residence or recent travel

Physical Exam

- BMI, blood pressure
- Pulse oximetry at rest
- Cyanosis or clubbing
- Plethora
- Splenomegaly

Step 3: First-Line Labs (Order These Up Front)

- CBC with differential
- Peripheral smear
- Serum erythropoietin (EPO)
- CMP (renal/liver disease)
- Ferritin (iron deficiency is common in PV)
- Pulse oximetry (or ABG if concern for hypoxia)

Step 4: Is It Primary or Secondary?

A. Suspect Primary Polycythemia (Polycythemia Vera)
Clues:

- Low or suppressed EPO
- Leukocytosis and/or thrombocytosis
- Pruritus, splenomegaly
- No hypoxia

Next step:

- Order JAK2 mutation testing (V617F ± exon 12)
  ~95% of PV patients are JAK2-positive.

B. Suspect Secondary Polycythemia (Usually EPO-driven.)

Common causes:

- Chronic hypoxia (COPD, OSA, obesity hypoventilation)
- Smoking / carbon monoxide exposure
- Testosterone therapy
- Renal disease or tumors
- Cyanotic heart disease
- High altitude

Work-up guided by suspicion:

- Sleep study (if OSA suspected)
- Carboxyhemoglobin level (smokers)
- Renal ultrasound (if EPO elevated or kidney disease suspected)
- Review medications carefully

EPO level is **normal** or **elevated**

Step 5: Management in Primary Care

If Secondary Polycythemia

- Do NOT delay referral
- Avoid empiric phlebotomy unless symptomatic or advised
- Start low-dose aspirin (if no contraindication) after discussion with hematology

When to Refer to Hematology (Clear Triggers)

✓ JAK2-positive
✓ EPO low without clear secondary cause
✓ Persistent Hct >52% (men) or >48% (women)
✓ Splenomegaly or constitutional symptoms
✓ History of thrombosis
✓ Unclear etiology after initial evaluation

Common Primary-Care Pitfalls
X Ordering JAK2 without confirming persistent elevation
X Missing testosterone or OSA as causes
X Assuming smoking alone explains very high hematocrit
X Performing routine phlebotomy without diagnosis
X Forgetting to check EPO

One-Line PCP Summary

Confirm persistence, check EPO, assess hypoxia and testosterone use, and order JAK2 when EPO is low—most cases are secondary, but PV must not be missed.