Red Flags 

For each case in this resource we have tried to identify indicators that should prompt the primary care physician to (1) consider a genetic cause or contribution to a patient's condition and (2) act accordingly. These indicators, presented as "red flags," are clearly not 100% sensitive or specific, but may raise a clinician's awareness of possible genetic influences on the patient. A red flag as we have defined it suggests further action. This action may be testing, intervention, counseling, follow-up, or referral to a medical geneticist.

To facilitate memory, we have organized several general principles that help to identify red flags for particular conditions in the easily remembered mnemonic, **Family GENES**.*

Family history: multiple affected siblings or individuals in multiple generations. Remember that lack of a family history does NOT rule out genetic causes.

G: **group of congenital anomalies.** Common anatomic variations are, well, common; but two or more anomalies are much more likely to indicate the presence of a syndrome with genetic implications.

E: **extreme** or **exceptional presentation of common conditions.** Early onset cardiovascular disease, cancer, or renal failure. Unusually severe reaction to infectious or metabolic stress. Recurrent miscarriage. Bilateral primary cancers in paired organs, multiple primary cancers of different tissues.

N: **neurodevelopmental delay** or **degeneration.** Developmental delay in the pediatric age group carries a very high risk for genetic disorders. Developmental regression in children or early onset dementia in adults should similarly raise suspicion for genetic etiologies.

E: **extreme** or **exceptional pathology.** Unusual tissue histology, such as pheochromoctyoma, acoustic neuroma, medullary thyroid cancer, multiple colon polyps, plexiform

neurofibromas, multiple exostoses, most pediatric malignancies.

S: **surprising laboratory values.** Transferrin saturation of 65%, potassium of 5.5 mmol/L, and sodium of 128 mmol/L in an infant; cholesterol of >500 mg/dL and unconjugated bilirubin of 2.2 mg/dL in an otherwise healthy 25-year-old; phosphate of 2 mg/dL and glucose of 35 mg/dL in a six-month-old child.

* This mnemonic was developed by the Red Flags Working Group of the Genetics in Primary Care (GPC) project (Alison Whelan MD, Chair).

References

Whelan AJ, Ball S, Best L, Best RG, Echiverri SC, Ganschow P, Hopkin RJ, Mayefsky J, Stallworth J (2004) Genetic red flags: clues to thinking genetically in primary care practice. *Prim Care* 31:497-508, viii [Medline]