Strategies for generating differential diagnoses

A number of different strategies can be used to generate a differential diagnosis. Certain strategies work better for different symptoms. After generating a differential, you may decide that you would like to expand upon it. At those times adding a different strategy often reveals more conditions.

Practice this using a number of strategies with a few different complaints. See what you come up with.

Here is a list of strategies with descriptions and examples of how they may be useful.

Name of strategy	What it is good for (examples)	Comments
• Symptom Complexes	• Everything	• A good database is needed.
• Local anatomic approach	• Bad sore throat • Abdominal pain • cough • stridor	• This is a great start but it may be good to step back and expand this approach using a more general strategy as well.

• Systems approach
  • Head to toe + hidden
  • VINDICATE
	• Vomiting
	• Cough
	• Coma
		• Remember, the whole body is connected and inter-related.

• Mechanism approach	• Jaundice • Anemia • Amenorrhea	• Superb method when chosen well.

Symptom Complexes

Whenever you are taking a history from a patient things come into your mind as you hear the details of the story. You put together two or three symptoms or findings and a specific condition pops into your mind. There may be more than one condition that is possible but a specific condition comes to mind, maybe because it is very common, or because the symptoms fit it particularly well. Maybe you just saw someone with this condition. The following are some examples:

Symptom Complex	Diagnosis
fever, vomiting, and diarrhea	Gastroenteritis
fever, and a red, hot, painful elbow	Septic arthritis
Cough, weight loss, and steatorrhea	Cystic fibrosis
Barky cough in an infant	Croup
Cough and wheezing	Asthma
Cough + wheezing in a 3 mo. old in the winter	Bronchiolitis
Chest pain radiating to the left arm	MI
Chest pain worse with movement	musculoskeletal pain

Benefits: It's fast, the common things usually come to mind, and it is how most clinicians think during an interview.

Limitations: You need a good database in your head. If you don't know that you get steatorrhea with cystic fibrosis than CF will not come up on your radar screen. If this method is used alone the differential is often too narrow.

Local Anatomic
In this method you think locally. If the complaint is abdominal pain, ask yourself, "What structures are here? What structures are here that could cause pain"? In this example "look" inside someone's abdomen. What's there? Make sure you start from the outside and go in. Try and be as systematic as possible. The following exemplifies this approach (we are not listing every disease entity):

Differential diagnosis of Abdominal Pain (Anatomic Approach)

Anatomic Structure	Diagnosis
Skin	Herpes zoster (shingles)
Muscle (abdominal wall)	Trauma/infection
Nerve	Zoster/nerve damage 2^{o} surgery
Liver	Hepatitis
Gall bladder	Cholecystitis/stones
Pancreas	Pancreatitis
Spleen	Trauma/enlargement (multiple causes)
Stomach	Ulcer/gastritis
?esophagus	esophagitis/foreign body
Small intestine	gastroenteritis (viral, bacterial, parasitic)/ cow's milk protein intolerance/obstruction/ malrotation/intususseption/IBD
Appendix	Appendicitis
Large intestine	Infection, diverticulitis, obstruction/IBD
GU system	UTI/stones
Female reproductive	ectopic pregnancy/ovarian cyst/ovarian torsion, etc.
Vessels	Aortic dissection/SMA syndrome
Muscles (intra-abdominal)	Abscess
Lymph nodes	Mesenteric adenitis

Benefits: A nice, fairly extensive differential is generated this way. By thinking systematically, about the abdominal anatomy *many* things come to mind. Many more things are likely to come to mind this way as opposed to random thinking or by using the symptom complex approach. Once they are listed you may find one that fits nicely. You may find that you don't know much about some of these conditions but by having the name of the condition it could be looked up.

Limitations: Processes outside the abdomen may also cause abdominal pain, for example, lower lobe pneumonias, addisons disease, and others.

Systems Approach
One method is to think anatomically from head to toe. Try looking at someone and literally go from the top down. To this list I would add: the mnemonic MATCHED (See table on next page).

Systems Approach:

Differential Diagnosis of _____ :

CNS	Psych	Eyes	Ears	Nose
Throat	**Pulmonary**	**Cardiovascular**	**GI**	**GU**
Musculo-Skeletal		**Metabolic**	**Allergic/ Autoimmune**	**Toxins/ Trauma**
Congenital	**Heme**	**Endo**	**Drugs**	

When to think, "Metabolic": Recurrent vomiting, poor feeding, failure to thrive, lethargy, developmental regression, unexplained bouts of dehydration and acidosis, afebrile seizures, unusual body odor or urine odor, young family member with unexplained death, hypoglycemia especially without ketosis, and organomegaly.

When to think, "Genetic" ("Congenital"): Any major dysmorphism, multiple minor dysmorphisms, or involvement of 2 or more organ systems. Remember: Development is a system (mental retardation, developmental delay, autism). Growth is a system (failure to thrive, short stature (esp. in girls), overgrowth, asymmetric growth.

Certain behavioral conditions are common (LD, ADD, and behavior problems). These can also be secondary to "genetic" conditions. When faced with a child with one of these behavioral conditions, when should you think "genetic"? Think "genetic" if you have an atypical clinical course. For example, if the child's ADD or behavior problem is very severe consider other possibilities. If the child does not respond to good therapy (a good family who are doing everything right yet there is no improvement in the behavior, think "genetic". Additionally, if you have any of these behavioral conditions plus any dysmorphisms, think "genetic".

Benefits: Very extensive.
Limitations: Not necessary for all presenting complaints.

Mechanism approach
This is an excellent method for generating a differential diagnosis when the chief complaint has to do with a biochemical, endocrine, or other ***pathway***. You should ask yourself, "How does one normally grow, breakdown bilirubin, make RBC's, menstruate, etc." Then ask, "Where can problems arise?" The answer is usually, "anywhere along this pathway, although certain steps are more likely to give problems."

The following exemplifies this approach:

- **Jaundice**:
  - What makes jaundice?..... Bilirubin.
  - Where does bilirubin come from?..... The breakdown of hemoglobin in red cells. Hb goes to biliverdin which goes to bilirubin (unconjugated).
  - Then what does the body do with the unconjugated bilirubin?.... It is transported to the liver.
  - Once in the liver what happens?..... It is conjugated by two enzymes.
  - Then what happens?..... Conjugated bilirubin is excreted by the liver, through the bile ducts into the duodenum.
  - Then what happens?..... Most of the bilirubin is now excreted in the stool but some of it is unconjugated spontaneously and also by an intestinal enzyme. This unconjugated bilirubin is then reabsorbed (enterohepatic recirculation). Bacteria in the intestine break down the conjugated bilirubin to stercobilin which is very stable and easily excreted.

  - Now ask, "Where can things go wrong?".... Basically everywhere.
  - You should now start filling in specific conditions under each of the above categories. The following exemplifies this approach (this table is not meant to show a complete list of disease entities):

Differential Diagnosis of Jaundice:

Category	Disease entities
Red cell breakdown	• Too many red cells (polycythemia) • Hemolysis • Sepsis
Transport of bilirubin to liver	• Transport protein deficiencies

Conjugation	• Enzyme deficiencies or poor function:
	  • Physiologic
	  • Prematurity
	  • Breast milk jaundice
	  • Gilberts syndrome
	  • Sepsis
	  • Down's syndrome
	  • Many others

Transport to the intestine	• Obstruction or disruption of ducts or portal system:
	  • Hepatitis
	  • Congenital viral infections
	  • Biliary atresia
	  • choledocal cyst

Increased enterohepatic circulation	• Intestinal obstruction • Constipation

- **Anemia** (Too few red cells)
  - Why can there be "too few red cells"?
    1. You don't make enough.
       a) What do you need to make red cells?
          - Iron, B12, folate, hemoglobin, some enzymes, and erythropoetin.
       b) Where are red cells made?
          - In bone marrow.
    2. They break down too fast. What would make them break down too fast?
       a) Something extrinsic to the cell.
       b) Something intrinsic to the cell.
    3. They leak out.

    In other words.... keep it simple. Follow the sequence. Be specific.

Differential Diagnosis of Anemia

Category	Disease entities

Decreased production	• Anything that damages marrow:
	  • Leukemia
	  • Drugs
	  • Radiation
	  • Viruses
	• Iron deficiency
	• B12 deficiency
	• Folate deficiency
	• Renal disease (erythropoetin)
	• Hemoglobin synthesis problems
	  • Thalasemia

Increased breakdown	• Hemolysis:
	  Extrinsic:
	  • Antibody
	  • Mechanical factors:
	  • Hypersplenism
	  • Endocarditis
	  Intrinsic:
	  • Abnormal Hb (sickle cell)
	  • Abnormal membrane (spherocytosis)
	  • Deficient RBC enzymes (G6PD)

Blood loss	• Obvious hemorrhage (gun shot) • Occult GI blood loss • Contained space (femur fracture)