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CAUSES OF ABNORMALITIES REPORTED IN NUCLEAR MEDICINE TESTING

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Nuclear medicine imaging and function testing has provided remarkably sensitive, but frequently nonspecific data in detecting disease processes. For most individual nuclear medicine procedures there is a differential diagnosis for abnormal findings which should be mentioned in reporting the test results to the physician caring for the patient studied. Often a combination of nuclear medicine procedures or a simple correlation with other laboratory and clinical data provides the correct diagnosis. However, in those instances where the abnormality may have more than one explanation, this must be communicated to the referring physician.

The reader should be aware of causes of false-negative as well as false-positive results in order to give readings with the highest degree of specificity and sensitivity, as defined by Lusted (*1*).

The list of differential diagnoses which follows has been employed for clinical and didactic purposes at the Radioisotope Laboratory of the University of Cincinnati Medical Center. It has been updated through frequent review by the entire professional and technical staff. Since this gamut will almost certainly have missed some cause of true- or false-positive or false-negative findings, the author would appreciate communication concerning any omissions, so that the list can be made as accurate and complete as possible.

REFERENCE

1. LUSTED LB: Decision making studies in patient management. *N Engl J Med* 284: 416–424, 1971

I. Schilling Test

A. True Abnormal: Less than 8% of the oral dose of ^{57}Co excreted in urine in 48 hr (without intrinsic factor orally: Stage I).
   1. Other intestinal disease besides pernicious anemia
      a. Gastric
      b. Pancreatic
      c. Small-intestinal diseases including mucosal alterations by drugs, vitamin deficiencies, or parasites
   2. Renal disease with delayed excretion
   3. Antibodies to intrinsic factor

B. Falsely Abnormal: Falsely abnormal results in the presence of normal intrinsic factor and normal intestinal mucosal absorptive ability.
   1. Old age with slow intestinal transit and slightly reduced renal function
   2. Azotemia (BUN > 25 or glomerular filtration rate under 50% normal)
   3. Failure to give a "flushing" dose of vitamin B_{12}
   4. Exogenous B_{12} within 5 days prior to test, causing inhibition of mucosal transport
   5. Improper urine collection

C. Falsely Normal: Falsely normal Schilling test with fecal contamination of urine.

II. Liver Scan: Abnormalities generally show decreased uptake of radiopharmaceutical.

A. True Abnormal
   1. Inflammatory–infectious lesions
      a. Abscess
      b. Hepatitis
      c. Occasionally, subphrenic abscess
      d. Granuloma
   2. Tumor
      a. Primary
      b. Metastatic
      c. Hamartoma
   3. Post-traumatic
      a. Surgical changes
      b. After biopsy
      c. Hematobilia
      d. Hematoma
   4. Vascular
      a. Infarct
      b. Hemangioma
      c. Arteriovenous malformation
      d. Intrahepatic or contiguous aneurysm
      e. "Hot" spots from superior vena cava obstruction, other caval–portal shunts, hamartoma, hemangioma, hepatic veno-occlusive disease
      f. Hepatic vein thrombosis

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5. Cysts, acquired or congenital
6. Fibrosis–cirrhosis
   a. Scleroderma
7. Infiltrative
   a. Glycogen storage
   b. Amyloid
   c. Fat
8. Following therapeutic irradiation
9. Dilated bile ducts (obstruction)
10. Focal nodular hyperplasia

B. Falsely Abnormal
1. Objects overlying liver
   a. Breast shadow or large rolls of fat
   b. Any metallic object including pocket lighters
   c. Barium in intestine
2. Artifacts from diaphragm motion
3. Anatomic variants
   a. Thinning at the dome, left lobe, or caudal right lobe of liver as it crosses the vertebral column
   b. Enlarged fossa for inferior vena cava, porta hepatis, gallbladder
   c. Pressure from normal kidney, diaphragm, colon, or abnormal extrinsic masses and organs
   d. Hepatic veins emerging from the liver
4. "Hot" spot from injection through malpositioned central venous catheter or hypertrophied caudate lobe

C. Falsely Normal
1. Lesion of smaller size than the resolving power of the system
2. Lesion with a large amount of overlying normal tissue

III. Brain Scan (static scan): Abnormalities generally show increased uptake of radiopharmaceutical.

A. True Abnormal
1. Increased area of uptake within the brain
   *†a. Tumor, primary or metastatic
   b. Infection
      1) abscess
      2) granuloma
      3) meningoencephalitis
   c. Vascular
      *1) infarct, thrombotic or embolic
      *2) hemorrhage
      †3) arteriovenous malformation
      †4) aneurysm
      5) contusion
      6) after seizure
   d. Demyelination
      1) multiple sclerosis
      2) progressive multifocal leukencephalopathy
2. Areas of increased uptake in scalp–skull–meningeal region
   a. Vascular, intracerebral
      1) subdural hematoma
   b. Tumor
      1) meningioma, other primary brain tumors
      2) metastases
   c. Scalp lesions
      1) lacerations
      2) abscesses
      3) tumors
      4) herpes zoster
      5) EEG needle trauma
   d. Skull lesions
      1) tumor
      2) postcraniotomy or fracture for at least 2 years
      3) hyperostosis (including hyperostosis frontalis interna)
   e. "Metabolic"
      1) hyperparathyroidism
      2) Paget's disease
      3) fibrous dysplasia
3. Decreased uptake
   a. After surgical resection
   b. Cysts (neoplasm, arachnoid, porencephalic, hygroma)
   c. Brain death
   d. Complete occlusion of one internal carotid artery
   e. Thrombosis of superior sagittal sinus
   f. Metallic plate
   g. Grossly dilated lateral ventricle
   h. Epidural hematoma

B. Falsely Abnormal
1. Anatomic variants
   a. Coronal suture
   b. Middle meningeal veins anterior to the sella
   c. Asymmetry in the lateral sinuses (right usually carries greater activity than the left)
   d. Draining surface veins
   e. Choroid plexus if perchlorate not given
   f. Salivary glands
   g. Large occipital sinus
2. Artifactual attenuation
   a. Metal plate in skull
   b. Hair clips
   c. Fingers of technologist holding head, especially wearing a ring
3. Infiltration of a scalp vein

C. Falsely Normal
1. Lesions of smaller size than the resolving power of the system
2. Lack of sufficient abnormal vasculature permeable to radiopharmaceutical around or within a lesion, as in a low-grade astrocytoma
3. Improper timing of scan relative to administration of radiopharmaceutical
4. Deep lesion (e.g., midline) with attenuation of emitted radioactivity
5. Posterior fossa activity missed because of patient's inability to flex head

IV. Lung Scans: Correlation with chest x-ray required. Abnormalities generally show decreased uptake.

A. True Abnormal: True areas of decreased perfusion
1. Vascular obstruction
   a. Thromboembolism (blood clot)
   b. Vasculitis
   c. Vasoconstricting drugs
   d. Recent bronchography
   e. Radiation-induced changes
   f. Pulmonary veno-occlusive disease
   g. Tumor metastases
2. Altered vascular dynamics
   a. Congestive heart failure
   b. Previous cardiopulmonary surgery
   c. Intracardiac or pulmonary shunts
   d. Pulmonary venous hypertension

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* Decreased early activity in the flow study.
† Increased early activity in the flow study.

e. "Clear lung" syndrome
f. Stenosis, atresia of pulmonary artery
3. Pulmonary parenchymal disease
*a. Pneumonitis
*b. Emphysema
*c. Bronchitis, acute or chronic
*d. Asthma
*e. Bullae, cysts
f. Atelectasis of any cause, endobronchial foreign body
g. Cystic fibrosis
h. Radiation-induced fibrosis
i. Lobectomy, pneumonectomy
4. Tumor, primary or metastatic
5. Physical alteration of lung from extrinsic pressures
a. Kyphoscoliosis
b. Pectus excavatum
c. Enlarged hilar nodes
d. Aneurysm
e. Cardiomegaly
f. Pleural effusion
g. High diaphragm
h. Pleural disease

B. Falsely Abnormal
1. Anatomic artifacts
a. Obesity
b. Large breasts
c. Deformed chest cage
d. Arm–scapula interposition
e. Cardiomegaly
2. Extrinsic artifacts
a. Pacemakers
b. Pendants, etc.
3. Injection artifacts
a. Injection of a radiopharmaceutical in the upright position
b. "Hot" spots from injecting small labeled clots (surrounding lung appears relatively underperfused)

C. Falsely Normal
1. Lesions smaller than the resolving power of the system
2. Anomalous blood supply to lungs (i.e., perfusion is normal but from abnormal source)
3. Nonocclusive mural thrombus of a main pulmonary artery

V. Thyroid Scans

A. True Abnormal
1. Cold nodules or heterogeneity may be caused by:
a. Tumor
1) cancer, primary or secondary
2) adenoma
3) lymphoma
b. Degenerative changes
1) involution
2) cysts
3) calcified lesions
4) hematoma
5) fibrosis as from postradiation change
c. Extrathyroid masses
d. Inflammation
1) thyroiditis, acute or chronic
2) abscess
2. Uptake seen in only one portion of the thyroid or one lobe of a thyroid gland
a. Hyperfunctioning autonomous adenoma, carcinoma (?)
b. Postoperative changes
c. Congenital absence of a lobe of the thyroid gland
d. Localized inflammatory disease (e.g., abscess, Hashimoto's disease)
e. All causes of cold nodules listed above
3. Ectopic areas of iodine uptake due to functioning of thyroid tissue (after excluding concentration by salivary glands, stomach)
a. Substernal thyroid
b. Sublingual thyroid
c. Pyramidal lobe
d. Functioning metastatic carcinoma
e. Struma ovarii

B. Falsely Abnormal with Iodine
1. Overlying soft-tissue masses, metallic objects on the neck
2. Medications

C. Falsely Normal
1. Lesions smaller than resolving power of the system
2. Functioning tissue which is pathologically abnormal embedded within and surrounded by normal tissue

VI. Bone Scans: Abnormalities generally show increased uptake of radiopharmaceutical.

A. True Abnormal
1. Tumor, primary or secondary
2. Fractures and surgical osteotomy
3. "Metabolic"
a. Hyperparathyroidism
b. Paget's disease
c. Osteoporosis
4. Inflammation of bone
a. Osteomyelitis
b. Abscess
c. Sterile osteitis (e.g., osteitis pubis)
d. Granuloma including sarcoid, eosinophilic granuloma
e. Fibrous dysplasia
f. Hyperostosis frontalis interna
g. Renal osteodystrophy
h. Hypertrophic pulmonary osteoarthropathy
5. Arthritis
a. Osteoarthritis
b. Rheumatoid arthritis
c. Gouty arthritis
6. Soft-tissue calcifications
a. Myositis ossificans
b. Soft-tissue osseous metaplasia
c. Soft-tissue tumors with calcification or ectopic bone formation
d. Vascular calcification, especially femoral artery
e. Calcific tendonitis
f. Abscess
g. Infarct, cerebral or myocardial
h. Thrombophlebitis
7. Vascular
a. Surrounding bone infarct
8. Decreased uptake
a. Tumor

* Ventilation study with ^{133}Xe may show prolonged xenon retention in the area of decreased perfusion.

b. Disuse of limb (may also be increased with osteoporosis)
c. Vascular obstruction (e.g., sickle cell disease, aseptic necrosis)

B. Falsely Abnormal
1. Renal artifacts or disease
a. ^{99m}Tc-diphosphonate in bladder
b. Hydroureter–hydronephrosis with ^{99m}Tc-diphosphonate
c. Contamination of clothing or skin with urine
2. Physiologic variants
a. Growing epiphysis and apophysis
b. Cartilage uptake
c. Shoulder uptake corresponding to handedness
d. Multiple sternal ossification centers
e. Breast uptake
f. Changes in spine distance from collimator
3. Recent surgical procedures on bone or soft tissue
4. Free pertechnetate in saliva, stomach, thyroid
5. Biopsy site
6. Colloid formation with liver–spleen uptake

C. Falsely Normal
1. Lesions of smaller size than the resolving power of the system
2. Purely lytic lesions (e.g., some myelomas)
3. Jewelry, prostheses, pacemaker overlying a lesion

VII. Pancreatic Scans: Abnormalities show decreased uptake of radiopharmaceutical.

A. True Abnormal
1. Carcinoma, primary or secondary
2. Obstruction at Vater's ampulla with subsequent degeneration
3. Pancreatitis, acute or chronic
4. Pseudocyst

B. Falsely Abnormal
1. Thinning in the area where the pancreas passes over the spine
2. Pancreas obscured by overlying organs
3. Barium in large bowel

C. Falsely Normal
1. Lesions smaller than the resolving power of the system
2. Attenuation of overlying tissues, including liver, bowel, etc.

VIII. Gallium-67 Scan: Abnormalities show increased uptake of radiopharmaceutical.

A. True Abnormal
1. Any cancer
2. Any abscess, sterile or septic
3. Other inflammatory disease

B. Falsely Abnormal
1. Physiologic uptake in mediastinum, female breast, salivary glands, large intestine

C. Falsely Normal
1. A minority of squamous cell and a higher percent of adenocarcinomas and sarcomas do not concentrate ^{67}Ga
2. Lesions of smaller size than the resolving power of the system

IX. Ectopic Gastric Tissue: Abnormalities concentrate pertechnetate.

A. True Abnormal
1. Meckel's diverticulum
2. Barrett's esophagus
3. Gastrogenic mediastinal cyst
4. Retained gastric antrum after gastrectomy
5. Ectopic gastric mucosa of small intestine with or without cyst formation

B. Falsely Abnormal
1. Carcinoid of the small bowel
2. Intussusception
3. Duplication cyst of ileum
4. Hemangioma
5. Duodenal ulcer
6. Arteriovenous malformation
7. Hydronephrosis
8. Inflammatory bowel disease
9. Ureteral obstruction
10. Angioblastic transformation of intestine
11. Abdominal aneurysm

C. Falsely Negative
1. Functioning gastric mucosa insufficient to yield a visible image