Approach to Chorea

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Disclosures: None

Outline

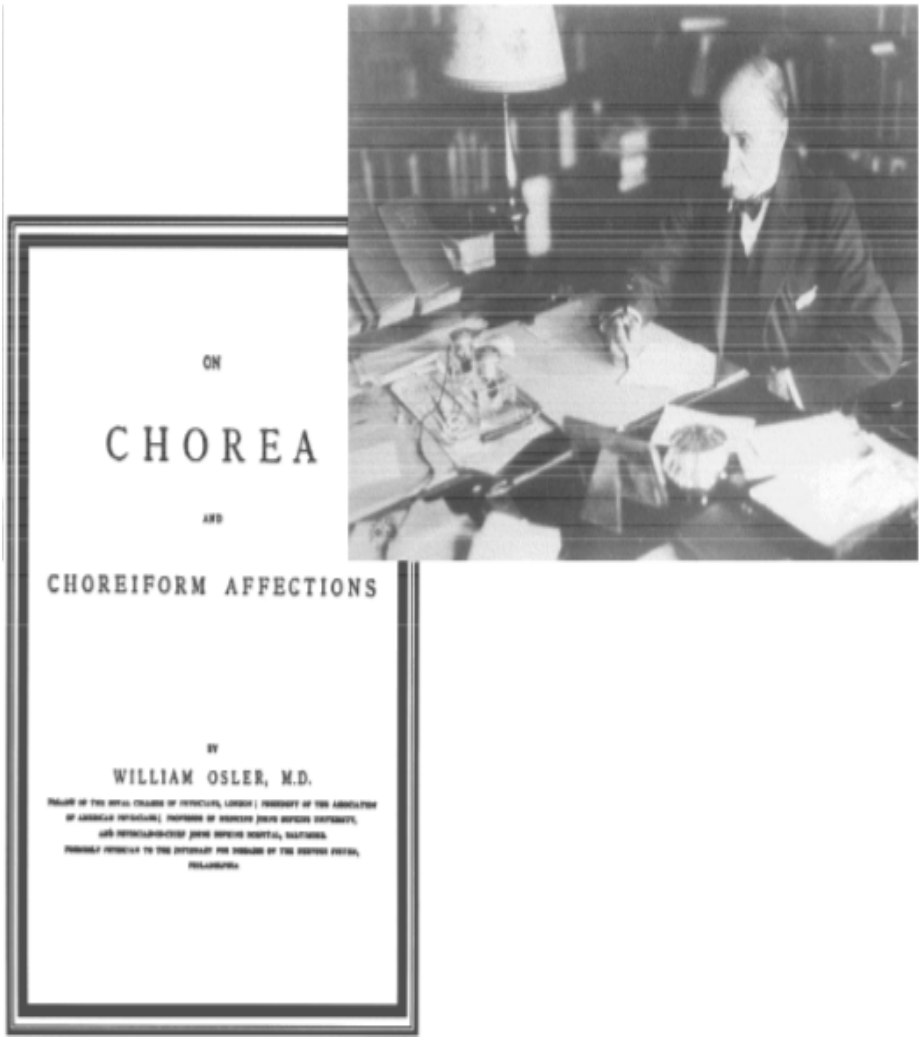
- Chorea definition
- Pathophysiology
- Classification
- Approach to management
- Patient's Videos

In 1894

William Osler wrote:

"In the whole range of medical terminology, there is no such "olla podrida*" as chorea which for centuries served as a nosological pot into which authors have cast indiscriminately"

**olla podrida: mixed stew*



What is Chorea ?

- **Definition**
  - The term chorea is derived from the Greek term for dance “choros”
  - Chorea consists of involuntary, continual, abrupt, rapid, brief, unsustained, irregular movements that flow randomly from one body part to another*

Parakinesia; Patients frequently camouflage some of the movements by incorporating them into semi purposeful activities

- **Motor impersistence;** The inability to maintain voluntary contraction
  - milkmaid grip
  - tongue protrusion

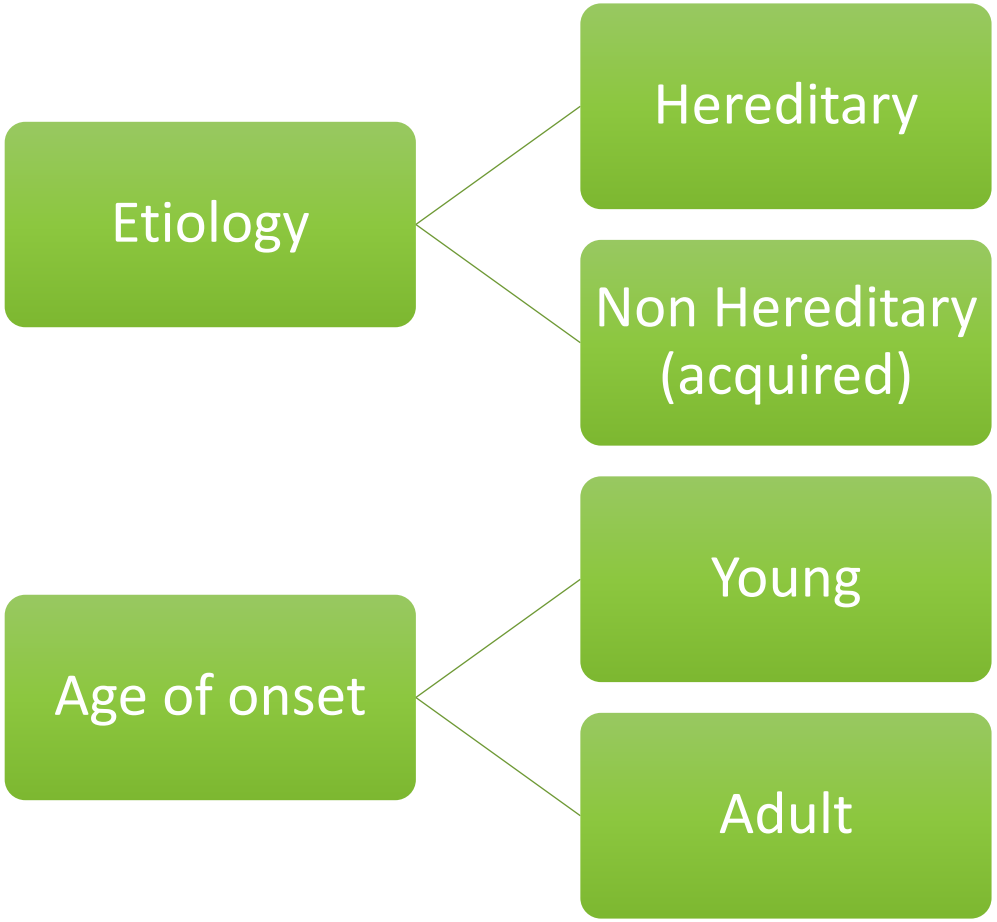
- **Pseudochoreoathetosis;** a movement disorder that is phenomenologically similar to chorea due to loss of proprioception(1)

- **Athetosis;** is a slow, continuous, involuntary writhing movement that prevents maintenance of a stable posture
  - In contrast to chorea, in athetosis the same regions of the body are repeatedly involved (2)

1. Walker, Mov Disorders, Sept 2010

2. Jankovich et al , Parkinson's and movement disorders book

Classification of Chorea



Classification of chorea "Etiology"

- **<u>Hereditary</u>**
  - AD
    - **Huntington's disease**
    - HDL 1, 2,
    - SCA 17
    - DRPLA
    - Neuroferritinopathy
  - AR
    - NBIA, Niemann pick type C
    - Ataxia (FA, AT, AOA)
  - X-linked
    - Neuroacanthocytosis, Lesch-Nyhan , x-linked parkinsonism dystonia
  - Mitochondrial
    - Leighs syndrome

- **<u>Non Hereditary</u>**
  - **Drug induced**
  - Vascular
  - Infectious
  - **Immunological**
  - Endocrine metabolic
  - Miscellaneous

When the family history is negative

- A parent carrying a causative mutation may have died before the disease manifested
- Partial pentrance can be seen
- Phynotypic variation may result in a disease not recognized be the family members
- Psychiatric features may resulted in long term care that the neurological disease was not recognized
- Non paternity
- De novo mutation

Walker, Mov Disorders, Sept 2010

Classification of chorea "Age of onset"

- **Adult onset**
  - Genetic
    - **Huntington's dis**
    - Huntington's phenocopies
    - Benign hereditary chorea
    - Others
  - Acquired:
    - Stroke
    - **Drugs**
    - Metabolic
    - Infectious
    - Autoimmune

- **Young onset**
  - Genetic:
    - Benign hereditary chorea
  - Acquired :
    - **Sydenham's**
    - Basal ganglia stroke\post op ischemic changes
    - psychogenic

Immunological chorea's

- Sydenham’s chorea
  - Chorea gravidarum
  - Contraceptive induced chorea
- Systemic lupus erythematosus
- Antiphospholipid Syndrome
- Para neoplastic
- others

Sydenham's Chorea

- The most common cause of acute chorea in children
- Major feature of acute rheumatic fever
- Complication of group A Beta hemolytic strep. Infection

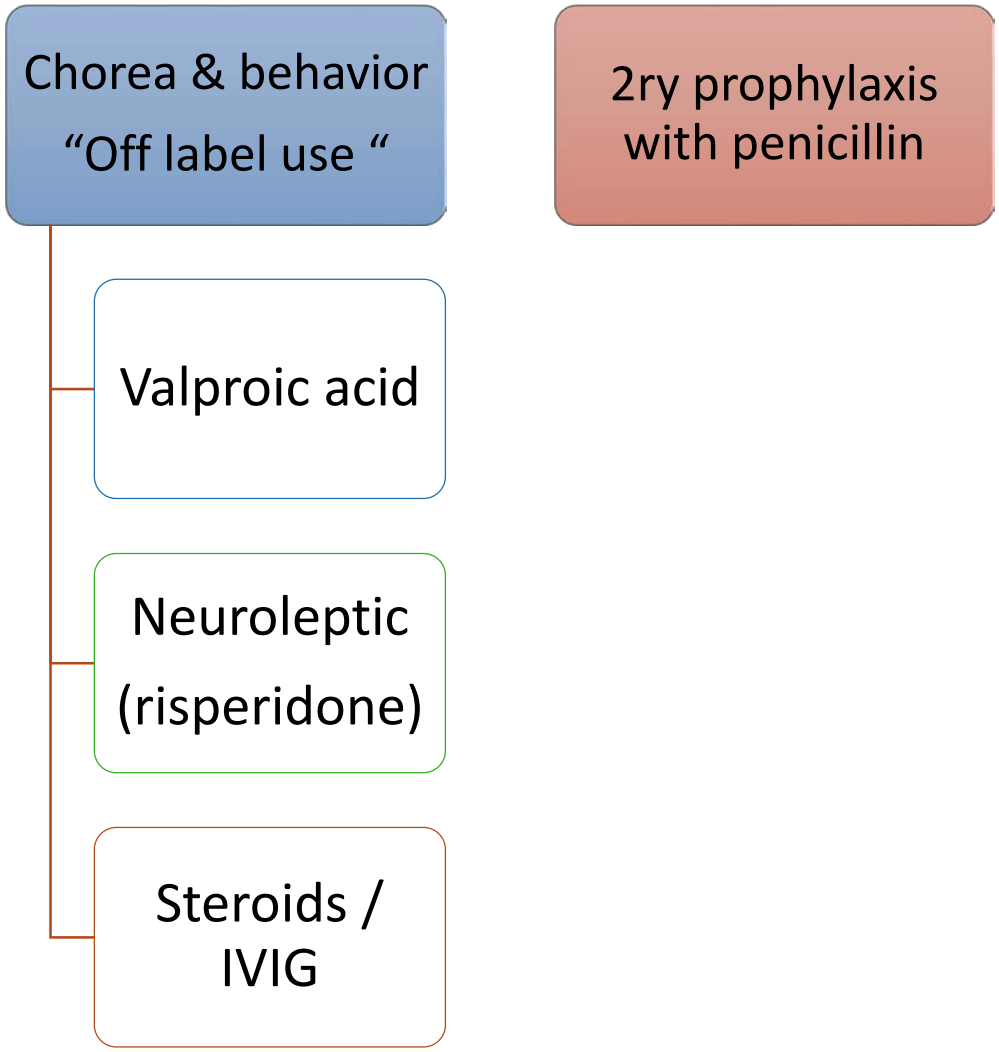
You tube video

Sydenham's Chorea

- Clinically
  - Age of onset : 8 years
  - Female >male
  - 4-8 weeks after infection
  - Hemichorea/ Generalized
  - OCD, ADHD
  - 60-80% have carditis
- How to diagnose ?
  - Evidence of recent Strep infection
  - Cardiac involvement
  - Rule out alternative causes (SLE, APAS)

Cardoso, Park dis & mov disorder, Ch20, Pg. 207:2016

Management of Sydenham's chorea



Cardoso, Park insondis & mov disorder, Ch20, Pg. 207:2016

Notes:

- SC is the most common cause chorea in children
- 25% remain with persistent chorea
- Treatment requires
  - Antichoreic drugs
  - Strep prophylaxis

Cardoso, Park dis & mov disorder, Ch20, Pg. 207:2016

Huntington's disease

- HD is a rare disorder
- Age of onset 30 -50 years
  - Juvenile < 20 years
  - Lateonset > 70 years
- 5:100,000
- CAG expansion in Ch4q
- Anticipation
- Clinically :
  - Cognitive & Behavioral disorders
  - Movement disorder

Sanitint and frank , PD & movement disorder, Ch 19, Pg 197

Penetrance Based on CAG repeat Length

CAG repeat	Probability of disease development
≥ 40	Definite
36 – 39	High risk
27 – 35	Low– no risk
< 26	normal repeat length

Santinti & Frank, PD & Mov Disorders Chapter 16, pg 198

Management of Huntington's disease

- No disease modifying therapy
- Gene silencing therapy
- Chorea
  - Tetrabenazine
  - Neuroleptics
- Behavioral problems
  - Neuroleptics and antidepressants

Therapeutic guidelines in HD
AAN -2012

DOPAMINE-MODIFYING DRUGS

Moderate evidence	If HD chorea requires treatment, clinicians should prescribe tetrabenazine (TBZ) (up to 100 mg/day) (**Level B**). Clinicians should discuss possible adverse effects (AEs) with patients with HD and monitor for their occurrence.
	TBZ likely has very important antichoreic benefits. Clinicians should discuss possible AEs with patients with HD and monitor for their occurrence, particularly parkinsonism and depression/suicidality with TBZ.
Insufficient evidence	Data are insufficient to make recommendations regarding use of clozapine or other neuroleptics for HD chorea treatment (**Level U**).

GLUTAMATERGIC-MODIFYING DRUGS

Moderate evidence	If HD chorea requires treatment, clinicians should prescribe amantadine (300–400 mg/day) or riluzole (200 mg/day) (**Level B**). Clinicians should discuss possible AEs with patients with HD and monitor for their occurrence, particularly elevated liver enzymes with riluzole.
	Riluzole 200 mg/day likely has moderate antichoreic benefits (**Level B**).
Insufficient evidence	The degree of benefit for amantadine is unknown (**Level U**).
Moderate evidence	Whereas riluzole 200 mg/day likely decreases chorea, clinicians should *not* prescribe riluzole 100 mg/day for moderate short-term benefits (**Level B negative**) or for any long-term (3-year) HD antichoreic goals (**Level B negative**). Modest short-term benefits of riluzole 100 mg/day cannot be excluded.

Tetrabenazine:
It should be started at a low dose and increased slowly
Maximal dose is usually 75 mg /day
CYP2D6 genotyping is recommended if the dose more than 50mg/day to identify slow metabolizers

Amantadine:
Experts do not usually use it
The evidence is sparse

Riluzole:
Data available do not support it

VIEWPOINT

Pharmacological Treatment of Chorea in Huntington's Disease–Good Clinical Practice versus Evidence-based Guideline

Ralf Reilmann, MD, PhD*

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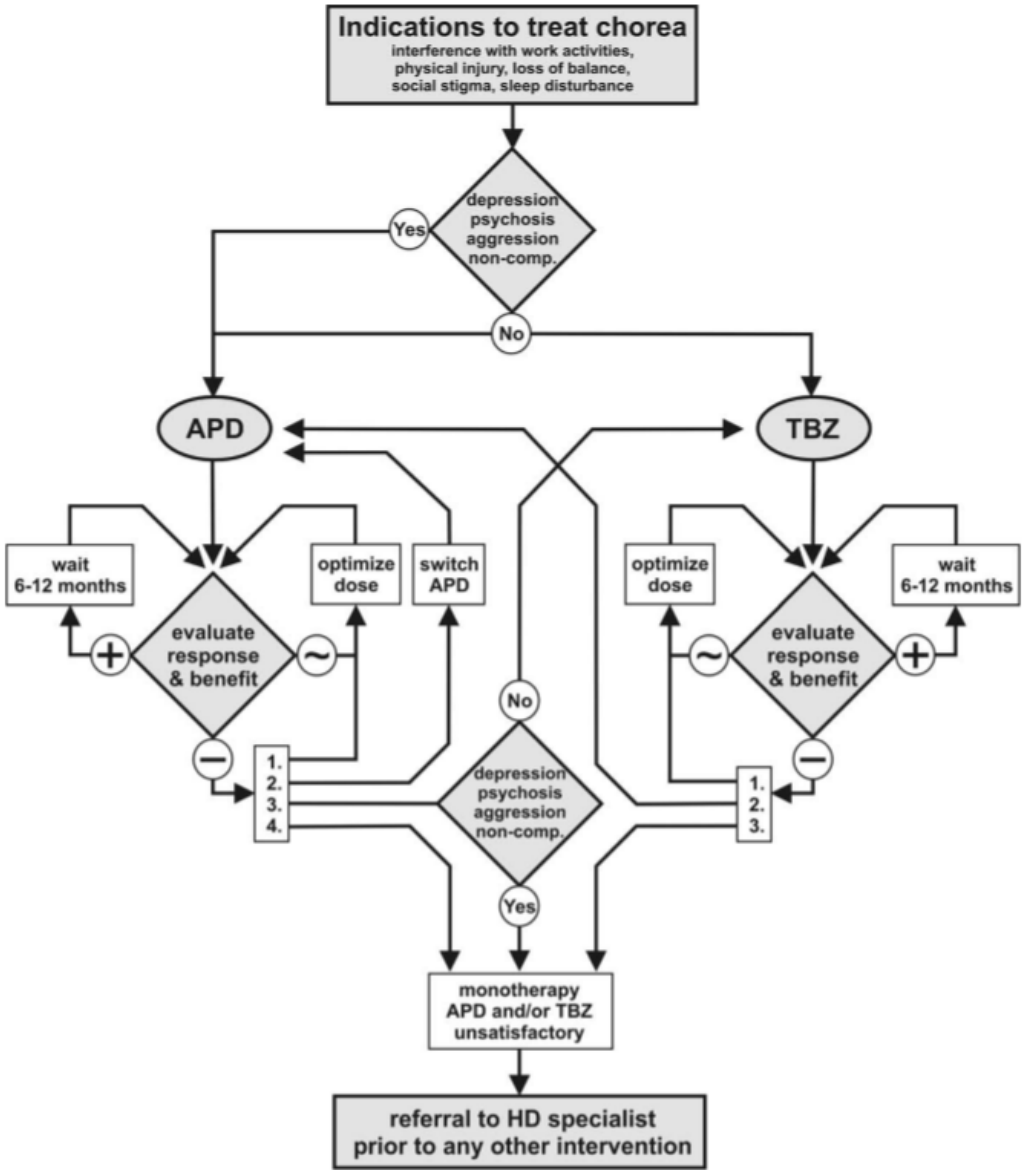
R.Reilmann, MovDisorders, Vol 29, No 8 , 2013



Reilmann, MovDisorders, Vol 29, No 8 , 2013

Dec 2017: Promising Huntington's Therapy "IONIS-HTTRx"

The randomized, double-blind, placebo-controlled trial (NCT02519036) tested the safety and tolerability of several increasing doses of IONIS-HTTRx in Huntington's disease patients

The drug was found to have an acceptable safety and tolerability profile. It also reduced the amounts of the mutant huntingtin protein (mHTT) that causes Huntington's disease in the patients tested

Initiating an open-label extension of the study for participants who completed the Phase 1/2a trial

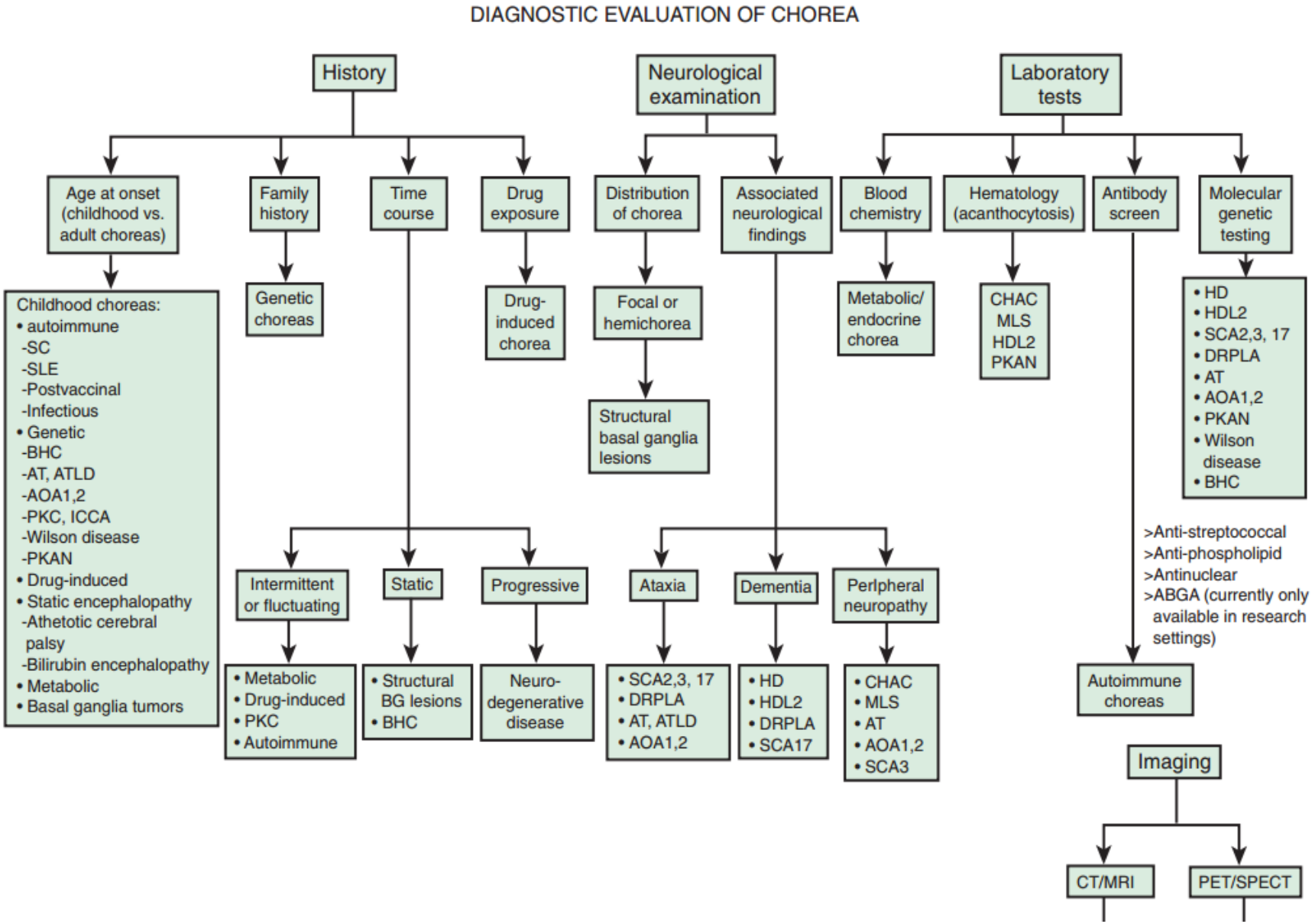
Drug induced Chorea

- **Dopaminergic drugs**

- Neuroleptics (tardive dyskinesia, withdrawal emergent syndrome)

- Stimulants
  - amphetamines, cocaine, oral contraceptives

- Toxins
  Alcohol intoxication and withdrawal, carbon monoxide, manganese, mercury, thallium



Jankoviche et al, Parkinson dis & mov disorder, Ch20,

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Thank you