The Hills are Alive with Diagnoses – If I Just Knew What They Were

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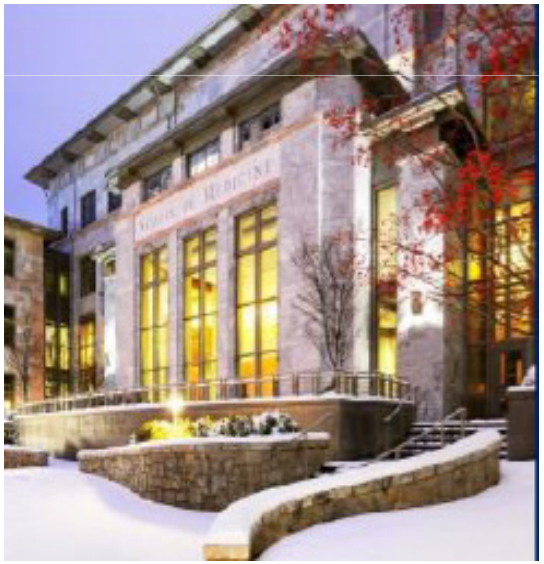
Atlanta, GA

Third International Conference on Rare and Undiagnosed Diseases

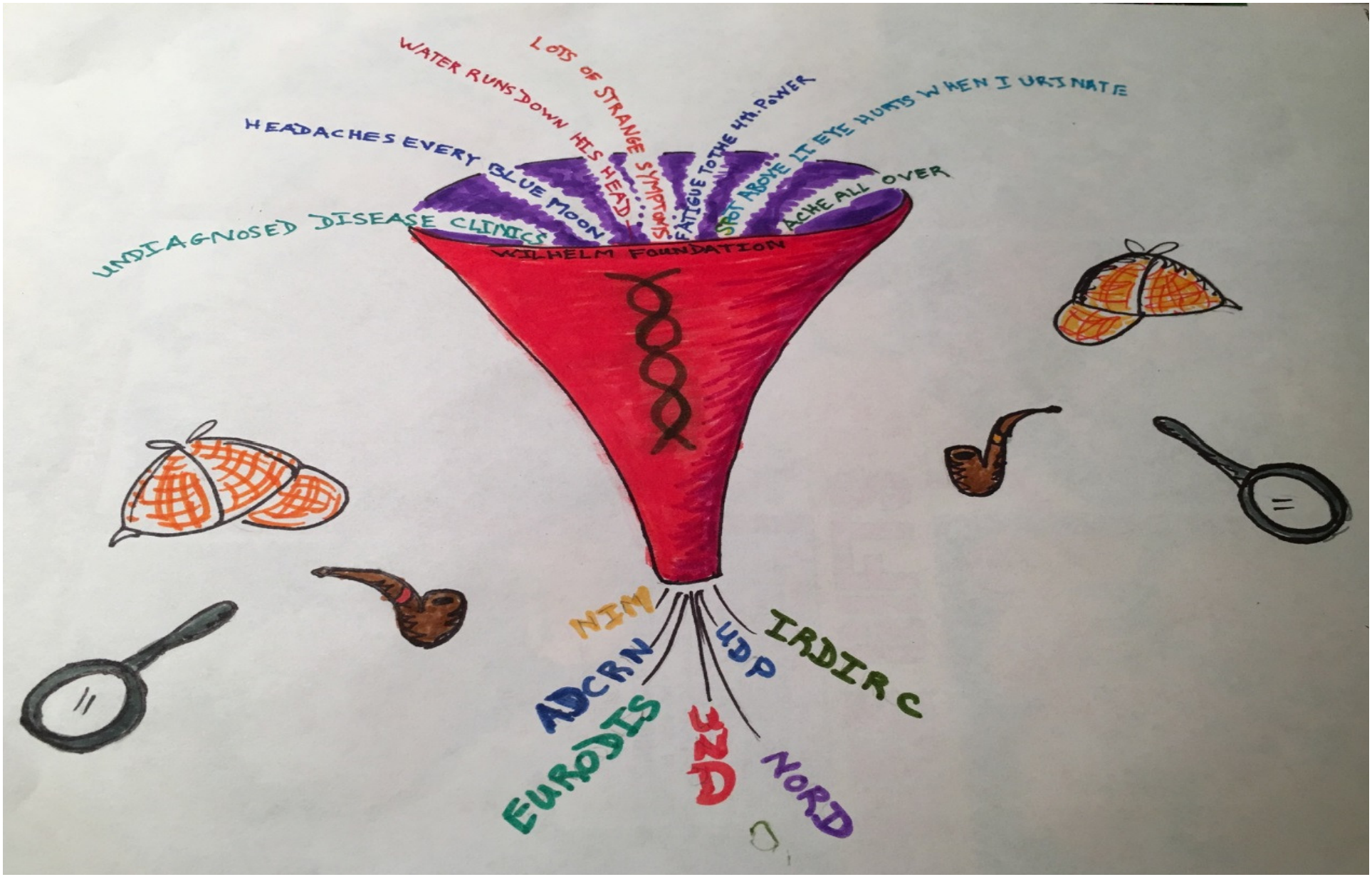
Wien, Austria - 18 February 2016

Emory Special Diagnostic Services

- Open for 30 months as of 1 March 2016
- 196 Patients seen as of 9 Jan 2016
- 8 have Died (undiagnosed neurological illness; testicular cancer (suicide?); acute MI (hepatoma); lung cancer; Renal Cell cancer; MAC; Accidental Drug OD (heroin); Undx GI/Neuro
- Screened 630/Accepted 197 (31%)



James B. Williams Medical Education Building Emory University

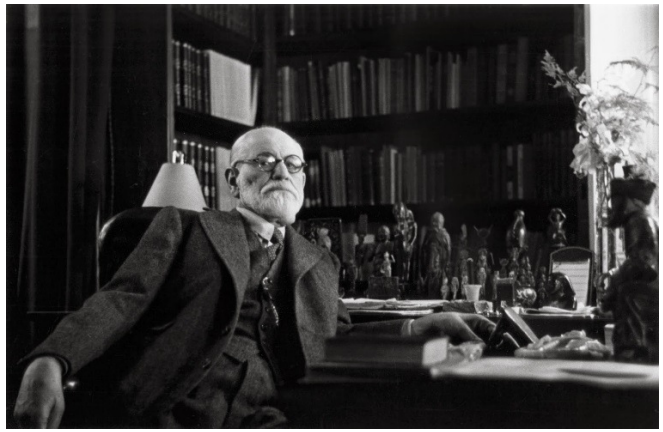

WATER RUNS DOWN HIS HEAD
LOTS OF STRANGE SYMPTOMS
FATIGUE TO THE 4TH. POWER
IT EYE HURTS WHEN I URINATE
HEADACHES EVERY
BLUE MOON
SPOT ABOVE
ACHE ALL OVER
UNDIAGNOSED DISEASE CLINICS
WILHELM FOUNDATION
NIM
ADCRN
EURODIS
UDP
IRDIRC
NORD

Neurological Phenomenon

- Most common phenotype both pediatric & adults NIH program 43% applicants & 53% accepted patients
- Emory - 20/103 accepted patients primary phenotype neurological (19.4%)
- NIH - Most common diagnostic category 15 (38%) (39/160)
- Emory - 17/102 final diagnosis Neurological ICD-9 (16.7%) > Most of any category
- Emory – Neurology consults

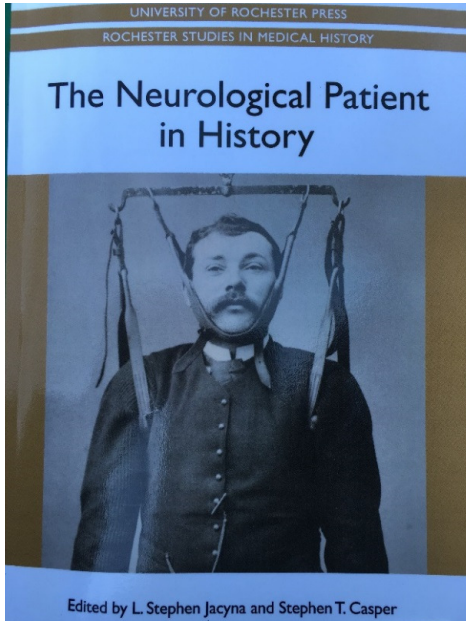
  most in any specialty (50)

S. Freud in office at 19 Berggasse



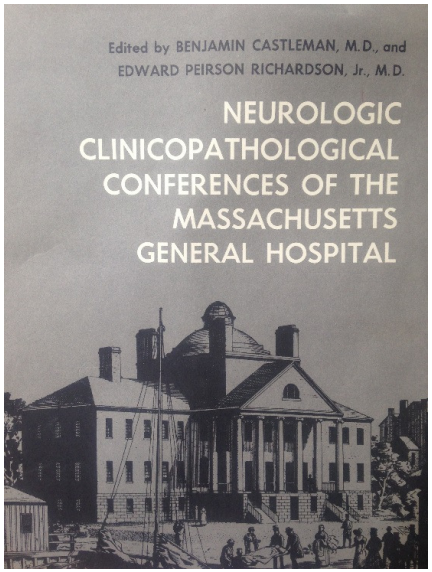
Neurological Patients – Special Status?

- Assertion that more than or differently from other patients reveals something about being human – philosophical status of man
- There clearly are cases where neurological illness appears to touch metaphysics or the monumental
- Neurological patients, compared with other patients, should be seen as the source of qualitatively different insights

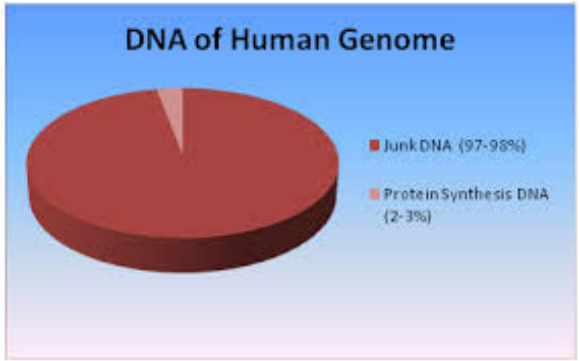


Book Review by Roger Smith: *The Neurological patient in History*, 2012. Ed. By LS Jacyna & ST Casper. In Bull of the History of Medicine, Vol 89(4) Winter 2015, pp.810-812

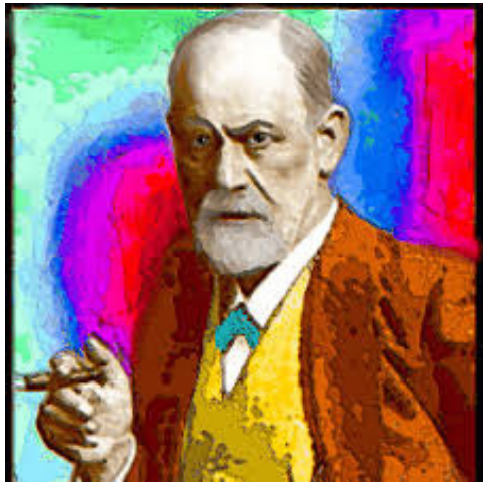
The Neurological Question



- The neurological patient is special? If so, WHY??
- Distance between insanity and neurology is not so much. (Functional vs organic)
- Neurology case conferences were some of the earliest
- Neurology cases amenable to popular literature
- No treatment for many of Neurodegenerative diseases (or genetic Diseases many of which manifest neurologically)
- Centrality of nervous system to conception of selfhood
- Neurobiology Undergraduate programs (NBB)
- Subjective symptoms - no visible signs of disease
- Neurological requires patient participation



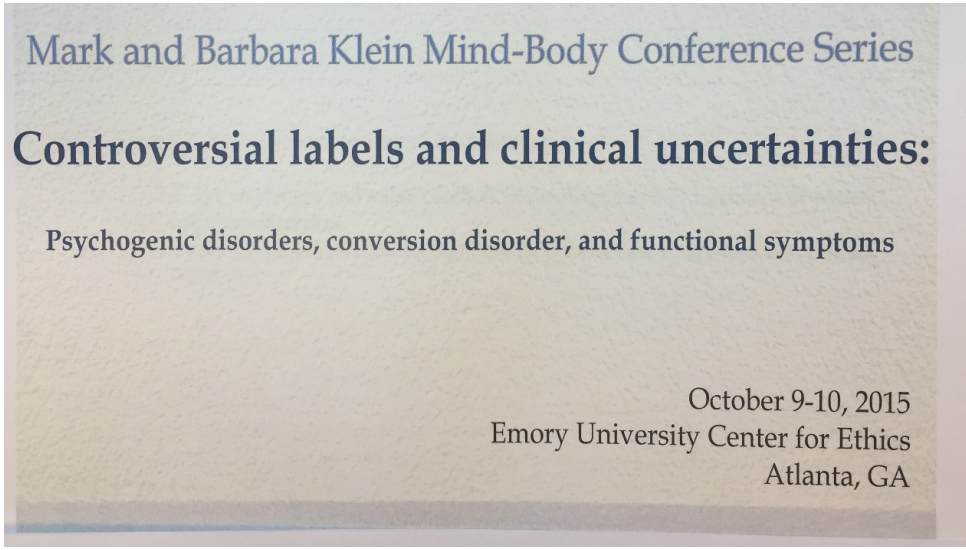
Neuro-Psychiatric Conundrums: What Can Be Done?

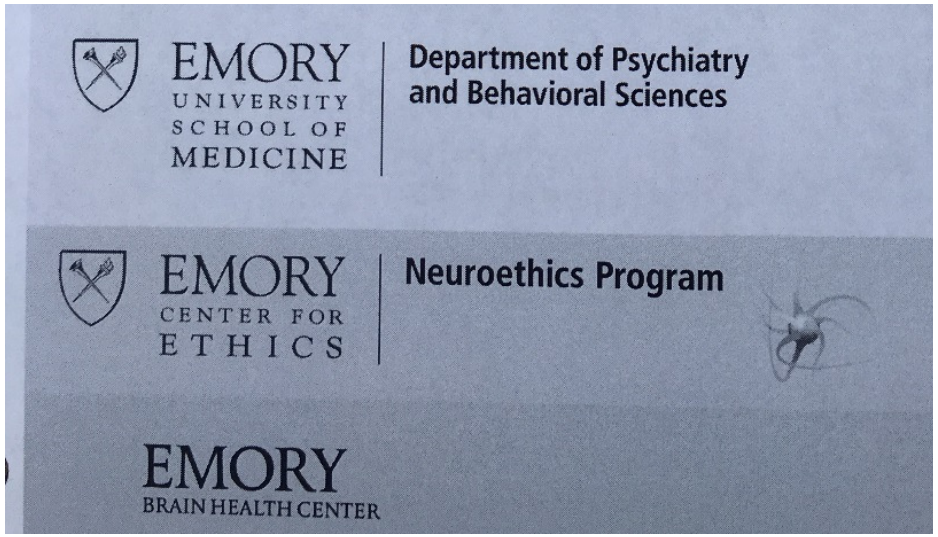


- Interface between neurology and psychiatry is complex (conversion)
- We track Q-LESQ-SF and W&SAS
- Mark & Barbara Klein Mind-Body Conference Series > *Controversial Labels and Clinical Uncertainties: Psychogenic disorders, conversion disorder, and functional symptoms*

Psychosomatic Issues

- Funding for 9 more conferences
- Neurologists & Psychiatrists could work together better
- Why don't psychiatrists do neurological exams?
- Population vulnerable & exquisitely sensitive to sense of abandonment
- Dedicated Clinic for these patients
- Mind-Body dualism evolving





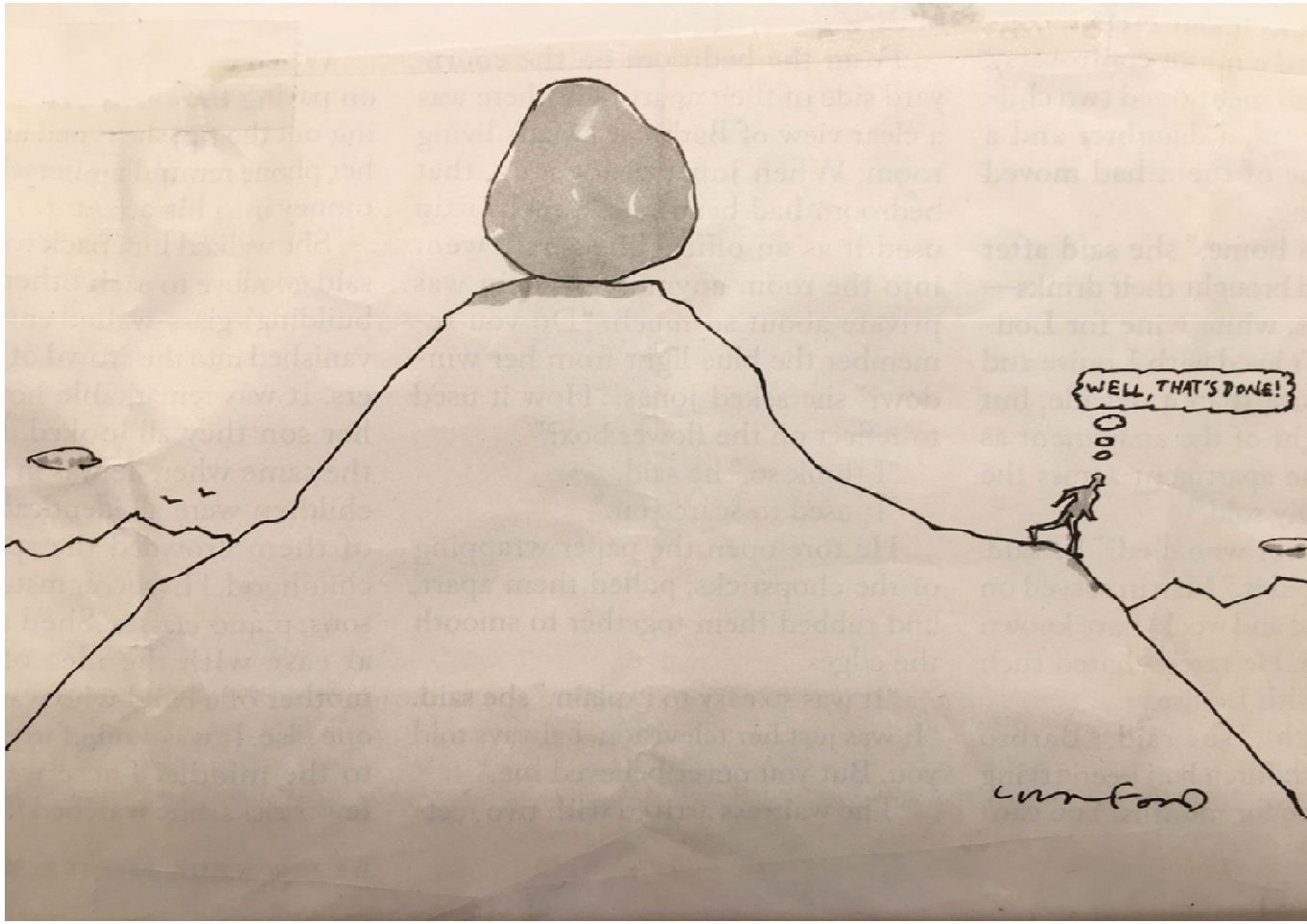
Psychiatric & Neurological Diagnoses

Mental Disorders (n=9)	Nervous System and Sense Organs (n=17)
Depression (3)	Migraines (5)
Conversion disorder	Primary lateral sclerosis (2)
Anxiety (2)	Autonomic gangliopathy
Disordered Eating	Psychogenic Tremors
Sensory Integration Disorder	POTS/Dysautonomia (3)
Mixed Anxiety-Depression	Small Fiber Neuropathy
	Myasthenia Gravis (2)
	Cerebellar Ataxia
Appreciation to NIH, Wilhelm Foundation and University of Vienna	Parkinson's Disease

A Sisyphean Task

- Failure to Make a diagnose remains a common theme

- Success is more sweet when a diagnosis does happen



Today's Agenda

- Review outcomes/statistical data from Emory's Diagnostic Center
- Review ongoing challenge of defining "Correct diagnosis"
- What are the ongoing issues?
- Neurology > The Mind-Body Interface: New thoughts on psychosomatic problems: *Controversial Labels and Clinical Uncertainties*
- One case in the Pipeline: A perfect (?) example of why Diagnostic Centers exist

EMORY CLINIC
Special Diagnostic Services

Defining Diagnosis

- Plural > diagnoses > verb form to diagnose
- Root: distinguish/discern/thoroughly/to learn & to know/perceive
- OED: determination of the nature of a diseased condition; identification of a disease by careful investigation of its history and symptoms; also the formally stated opinion resulting from such investigation. Term entered language around 1625 > *Physicke diagnosticke*.
- More difficult issue: what constitutes a correct diagnosis?

Defining Correct Diagnosis

- NIH: *"Most satisfying definition of diagnosis includes an understanding of disease pathogenesis, linking genetic and clinical findings and informing prognosis and therapy." (Gahl 2011)*
- Etiology. **Etiology. Etiology.**
- Basis upon which the Diagnosis was achieved
- Speculative vs Definitive
- Symptoms do not count as a diagnosis

*Basis for DX at NIH 39/160

Basis 9/30.13 - 9/30/15	n = 115
Autopsy	0
Biochemical / Lab result	19 (26%)* (16.5%)
Clinical Acumen	59 (100%)* (51.3%)
Culture	0
CSF Fluid	1 (0.008%)
Genomics	0 (49%)*
Pathology	22 *(31%) (19.1%)
Radiology	12 (10.4%)
Response to Treatment	2 (1.7%)
Surgery	0

Dx Clinic OUTCOMES

OUTCOME	YEAR 1 - 2014	YEAR 2- 2015	TOTAL
DEFINITIVE DIAGNOSIS	54 (54%)	42 (52.5%)	96 (53.3%)***
SPECULATIVE DIAGNOSIS	16 (16%)	6 (7.5%)	22 (12.2%)
NO UNIFYING DIAGNOSIS	28 (28%)	12 (15%)	40 (22.2%)
W/U IN PROGRESS	0	18 (22.5%)	18 (10%)
OTHER	2 (2%)	2 (0.3%)	4 (0.2%)

***Generous use of accepting diagnosis as correct and worthy. Some cases turned out to be not so complex. We still have plenty of failure.

PHENOTYPE PRESENTING COMPLAINT

PRIMARY PHENOTYPE	n = 103	PRIMARY PHENOTYPE	n =103
Allergy	0	Neurology	20 (19.4%)
Cardiovascular	15 (15.6%)	Oncology	4 (3.9%)
Dermatology	11 (10.7%)	Ophthalmology	0
Endocrine	0	Orthopedics	7 (6.8%)
ENT	4 (3.9%)	Pain	6 (5.8%)
Fibromyalgia/CFS	4 (3.9%)	Psychiatry	4 (3.9%)
GI		Pulmonary	9 (8.7%)
Gynecology	2 (2.0%)	Renal	3 (2.9%)
Hematology		Rheumatology	2 (2.0%)
Infectious Disease	7 (6.8%)		
Immunology	5 (4.9%)		
Metabolic			

Dx ICD-9 Groups n= 102//Speculative & Definitive

ICD-9 Category	Range	# Dx	ICD-9Category	Range	# DX
Infect/Parasitic	001-139	9	GU	580-629	1
Neoplasm	140-239	8	Pregnancy	630-679	0
Endo/Metab/N	240-279	6	Skin	680-709	4
Blood/Blood For	280-289	1	Musculoskeletal	710-739	11
Mental Disorder	290-319	9	Congenital	740-759	3
Nervous System	320-389	17	Newborn	760-779	0
Circulation	340-459	11	Signs/Symptom	780-799	3
Respiratory	460-519	5	Injury/Poison.	800-999	3
Digestive	520-579	11	V & E codes		0

EMORY CLINIC

Special Diagnostic Services

CONSULTS/PROCEDURES

	2014	2015	2 YEAR TOTAL
NEUROLOGY	22	28	50
GI	18	12	30
CARDIOLOGY	14	17	31
MRIs	23	53	76
CV STUDIES	30	15	45
GI STUDIES	15	3	18
CT SCANS	24	17	41

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Special Diagnostic Services

Case: Be Careful For What You Wish

IVING

HEALTH

Drew Crenshaw (center) and his mother Melissa Coon talk with Dr. Heather Gladue (right) during a recent checkup at Emory Special Diagnostic Services. The practice is dedicated to patients with undiagnosed illnesses, like Crenshaw's severe ankle and joint pain. PHOTOS CONTRIBUTED BY JONATHAN PHILLIPS

Clinic tackling the tough one

Hard-to-diagnose cases a specialty at 'House'-like Emory clinic.

By Helena Oliviero
holiviero@ajc.com

Drew Crenshaw had just graduated from high school when he suddenly – and inexplicably – started experiencing severe ankle pain. An x-ray revealed minor stress fractures in both feet. He was wheelchair bound for six months with casts on his feet and his college plans on hold.

But the pain continued long after the casts were removed and spread to all of his joints.

Finally, after countless visits to doctors across the [illegible] of gout affecting multiple joints, a condition often characterized by recurrent attacks of severe inflammatory arthritis. It's rarely seen in people as young as Crenshaw.

Still, the diagnosis was only the first step in helping Crenshaw get better.

He was placed on an aggressive plan to treat the gout and prevent future flare ups.

Before landing at Emory, Crenshaw said at least one doctor suspected gout but he was never properly treated for the condition. His situation was complicated by a rheumatoid arthritis diagnosis that turned out to be a false positive. While taking powerful medications for that condition, his immune system was lowered, causing a fungal infection on his back.

This new Emory clinic seeks to fill the gap in the way health care is delivered, said Dr. Doug Morris, a cardiologist for more than three decades at Emory Healthcare, who helped lead the effort to open the center, believed to be the first of its kind in Georgia. With so many specialists at Emory, it makes sense for patients to be seen and evaluated by a team rather than going from one doctor to the next in search of a diagnosis, he said.

Led by medical director Dr. Clyde Partin, a team of doctors from every specialty analyzes tests and spends hours with a patient to form a complete picture of their condition. The process begins with a phone call to determine what records, among other things, are needed. An initial visit is scheduled, typically within five days. The first visit lasts up to two hours with one of two clinicians.

From there, specialists determine what lab tests and biopsies are needed. Once doctors make a diagnosis, they craft a treatment plan. Over the past year, doctors have diagnosed everything from heart disease and cancer to a rare condition involving an enzyme in meat causing a gastrointestinal disorder.

Not every medical mystery can be solved, but most patients leave with answers, relief and for Crenshaw, the opportunity to embrace life as a young adult.

By the time he left the hospital about a year ago, Crenshaw, now 26, felt much better. He returned home to take community college classes and plans to attend Florida State University this fall.

"I am not at 100 percent," he said during a recent checkup. "But I feel 100 percent better. It's hard to be 22 and have to spend days at a time in bed. It's not what you would imagine your life to be like at 22. I was depressed. Now I am playing basketball and kayaking again. I feel like I have my life back."

Drew Crenshaw hugs nurse Debbie Cohen after completing his checkup at the Emory Clinic off of Clifton Road in Atlanta on March 13. Crenshaw was just out of high school when he started having severe ankle pain. CONTRIBUTED BY JONATHAN PHILLIPS

ABOUT THE CENTER

The Emory Special Diagnostic Services (ESDS) is a practice within the Emory Clinic dedicated to evaluating patients with hard-to-diagnose cases. Like other parts of Emory Healthcare, ESDS accepts most major insurance plans.

1365 Clifton Rd N.E., Building A, First Floor.
404-778-2900.
emoryhealthcare.org/special-diagnostic-services/index.html

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illnesses, like Crenshaw's severe ankle and joint pain. PHOTOS CONTRIBUTED BY JONATHAN PHILLIPS

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Dr. Heather Gladue puts a Band-Aid on an injection site on Drew Crenshaw's ankle during a checkup. Crensaw had been seeing doctors for six years before he found Emory.

Moving In the Direction of Rain

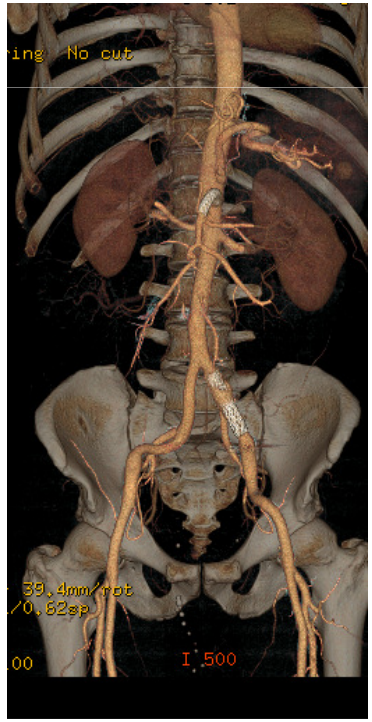
- Patients unhappy because no diagnosis achieved
- Patients unhappy because we declined to accept
- Patients unhappy because they call to make appointment and we ask for records and letter from their doctor
- Patients unhappy because we will not become their primary care doctor
- Patients keep calling with every new symptom

Case: Rare Disease

- 55M from Mexico presents with a history of new onset abdominal pain 2 years ago. Panendocopy was negative.
- CTA showed multiple abdominopelvic aneurysms
- Percutaneous stents placed in iliac & IMA due to dissections .

  Two years later he had recurrent abdominal pain
- Imaging showed a newly occluded

  hepatic artery



Images provided by

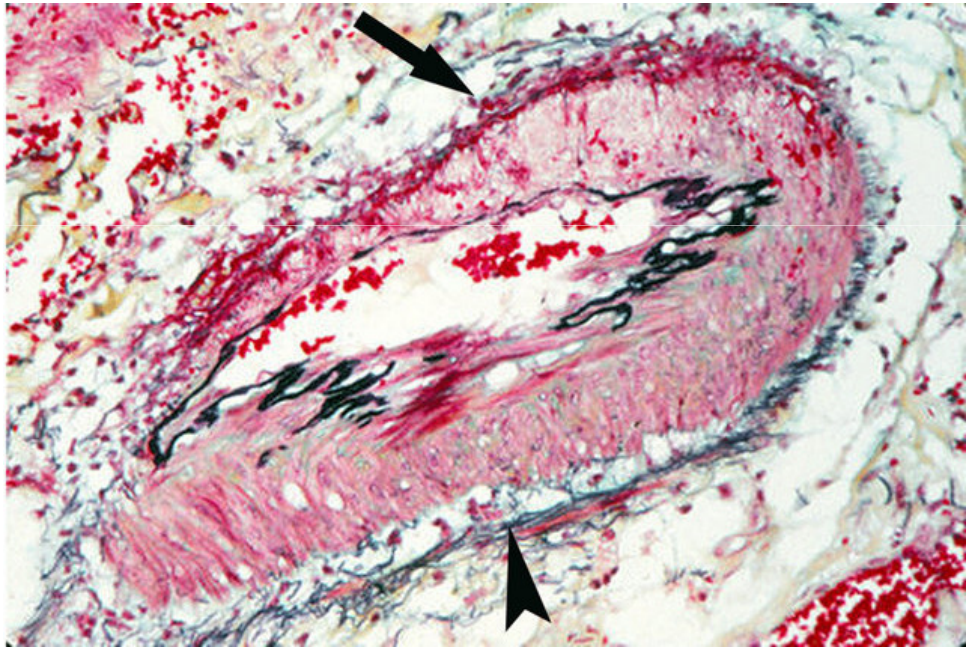
Jon Masor, MD

Emory Lab Data

- WBC 6.5 (normal differential) , HCT 42, MCV 85
- Metabolic Panel – normal, creatinine 0.7
- Lipid Panel LDL 130, HDL 52, Lpa 92 (elevated)
- PSA = 0.98 , ESR = 1, CRP = 1.5. Normal thyroid
- HIV, HBSag, HBSAb, HCV negative
- ANA, ANCA, ENA, C3, C4, RPR, SPEP = negative
- Aortopathy panel negative

Segmental Arterial Mediolysis (2)

- Non-atherosclerotic non-inflammatory arteriopathy
- Etiology: Unknown
- Medial layer arterial wall lysed with subsequent arterial stenosis, dissection, occlusion, and aneurysm formation
- Injurious phase of Segmental Arterial Mediolysis (SAM). *Arrow* shows area of transmural mediolysis *Arrowhead* shows tear separating outer media from the adventitia (1)

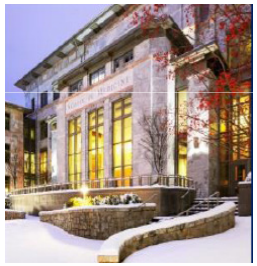


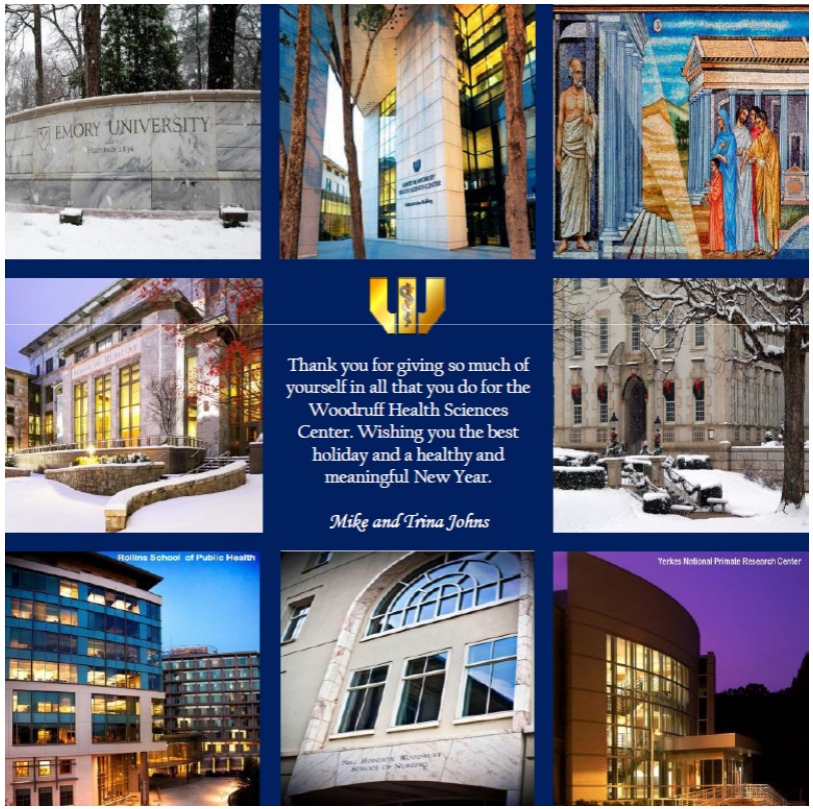
(1) Slavin RE. Segmental Arterial mediolysis: A clinical-pathologic review, its role in fibromuscular dysplasia and description and differential diagnosis of the masquerader-muscular artery cystic necrosis. *World Journal of Cardiovascular Disease*. 2013

(2) Shenouda M, Rija C. Renton S. Segmental Arterial Mediolysis: A Systematic Review of 85 Cases. *Annals Vasc Surgery* 2014

Viennese Medical Heritage

- Theodore Bilroth
- Karl Landsteiner
- Karl Jung
- Victor Eisenmenger




EMORY UNIVERSITY
Thank you for giving so much of yourself in all that you do for the Woodruff Health Sciences Center. Wishing you the best holiday and a healthy and meaningful New Year.
Mike and Trina Johns
Rollins School of Public Health
Yerkes National Primate Research Center