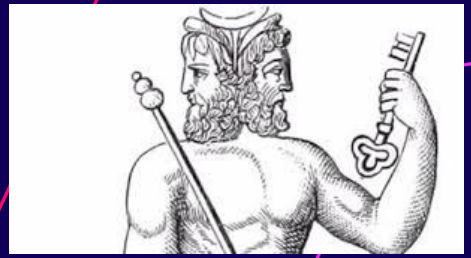
Intermountain Health

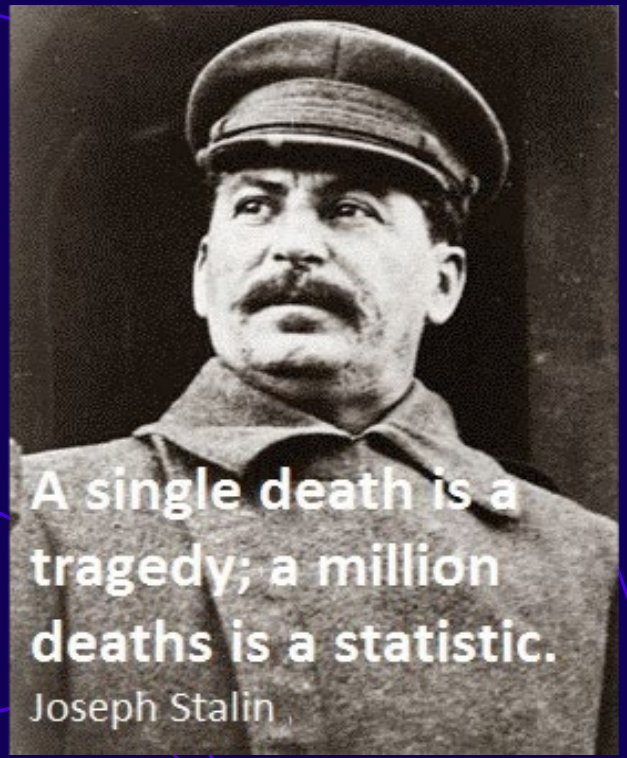
The Oncologist Without the Pathologist Is Blind: The Dual Perspective of a Patient-Physician



Future of Cancer Data Summit
October 18th, 2024

Mark A. Lewis, M.D.
Director, Gastrointestinal Oncology

A surprising source of wisdom



The index patient

- A minister in Belfast develops dysphonia during his sermons
- Progresses to dysphagia
- Develops amnesia, found to have brain metastases
- Dies at age 64 without a firm diagnosis

His older son

42-year-old male

- Lifelong non-smoker
- In usual state of health
- CXR obtained through pre-employment screening

Treatment course

“Lung cancer”

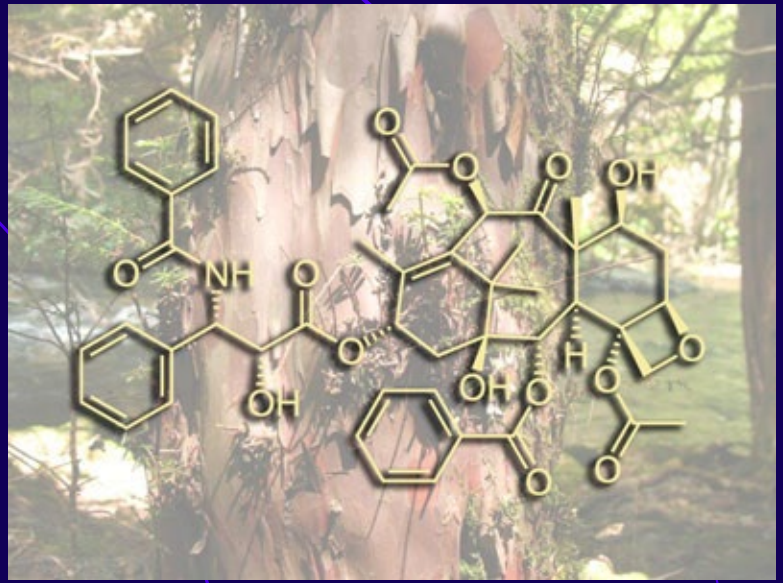
- Pneumonectomy
- Adjuvant radiation therapy to mediastinum

Relapse

- Develops severe back pain while on holiday
- Plain X-rays reveal bone metastases
- Begins cisplatin/etoposide chemotherapy
- Nearly dies after the 1st cycle from infection
- Filgrastim given to counter neutropenia

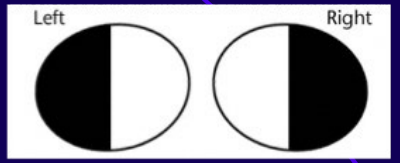
Further history

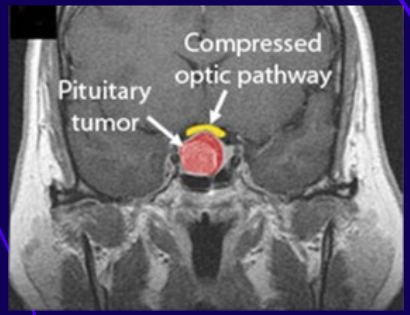
- Disease stabilization after 6 cycles of cisplatin/etoposide
- More metastases develop after a 2-year dormancy
- Transition to a new chemo
- Dies within 8 hours of first paclitaxel exposure



His younger son

- 5 years later, the index patient's younger son developed headaches and visual changes
- MRI reveals a pituitary tumor (macroadenoma)
- Undergoes surgical removal
- Complicated by hemorrhage
- Dies of pituitary apoplexy





His grandson

- 43 years after his grandfather’s death, the grandson develops severe abdominal pain at age 30

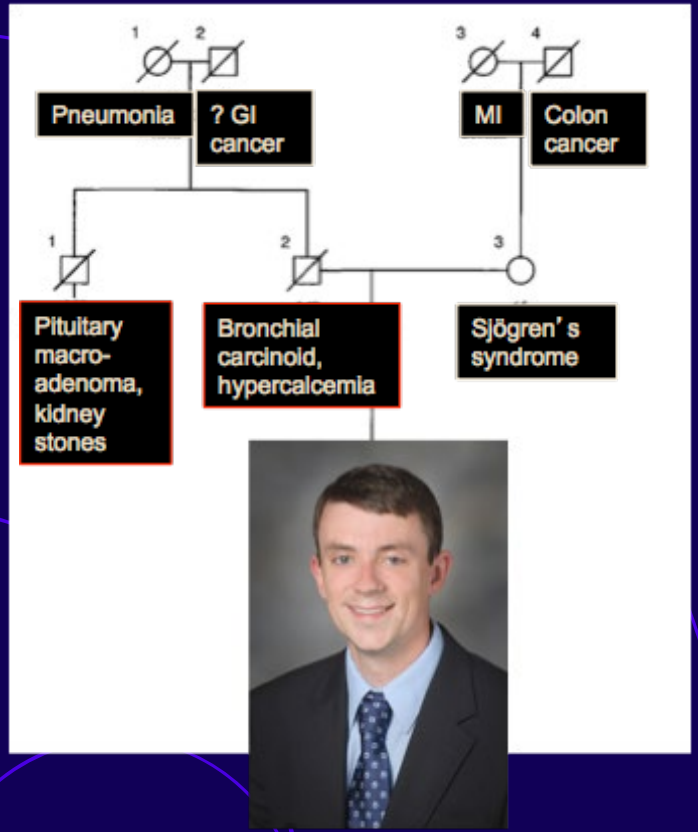
- Calcium = 10.8 mg/dL

The grandson’s history

- 2 years prior to onset of abdominal pain, developed tiny red bumps over the nose

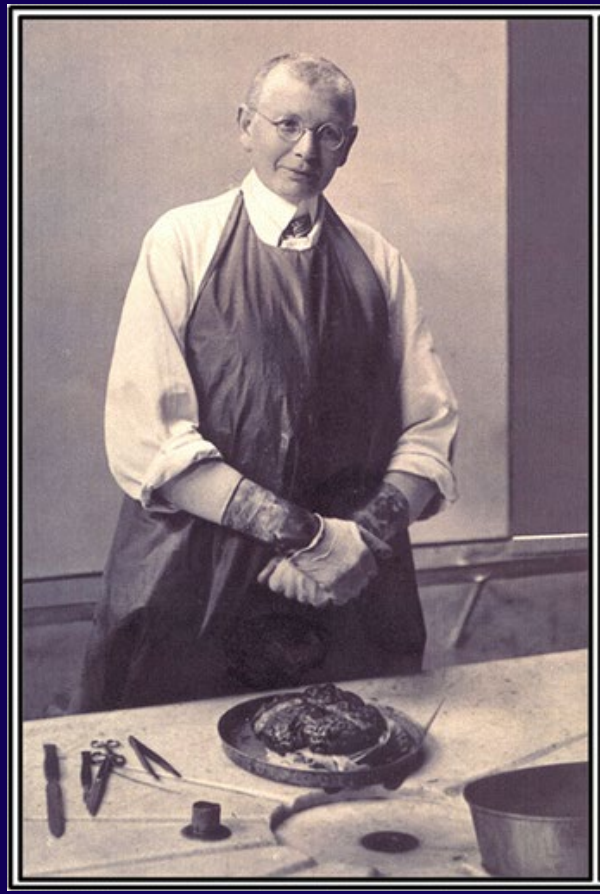
- Diagnosed as angiofibromas
- “Pathognomonic for tuberous sclerosis”

I am the proband



Navigating Familial Cancers: What Pathologists Need to Know to Diagnose MEN1

Join Gladell Paner, MD, FCAP, as he delves into inherited cancer syndromes with surgical pathologist Vania Nosé, MD, FCAP, and oncologist Mark Lewis, MD, who is also a cancer survivor. They focus on multiple endocrine neoplasia type 1 (MEN1), an autosomal dominant disorder affecting the pituitary, parathyroid, and pancreas. Dr. Nosé explores the genetic and clinical aspects of MEN1, while Dr. Lewis shares his personal journey with the condition. Together, they discuss treatment advancements, tumor prognosis, and how personal stories can raise awareness and ease fears about medical procedures.



SITZUNGSBERICHTE

DER

MATHEMATISCH-NATURWISSENSCHAFTLICHEN KLASSE

DER KAISERLICHEN

AKADEMIE DER WISSENSCHAFTEN.

CXIII. BAND. ABTEILUNG III.

JAHRGANG 1904. — HEFT I BIS X.

Über Hypophysenganggeschwülste und Hirncholesteatome

von

Dr. J. Erdheim.

Aus dem Wiener pathologisch-anatomischen Institut. Vorstand Hofrat Prof. Weichselbaum.

(Mit 1 Tafel und 41 Textfiguren.)

(Vorgelegt in der Sitzung am 1. Dezember 1904.)

WIEN, 1904.

AUS DER KAISERLICH-KÖNIGLICHEN HOF- UND STAATSDRUCKEREI

IN KOMMISSION BEI KARL GEROLD'S SOHN,

BUCHHÄNDLER DER KAISERLICHEN AKADEMIE DER WISSENSCHAFTEN.

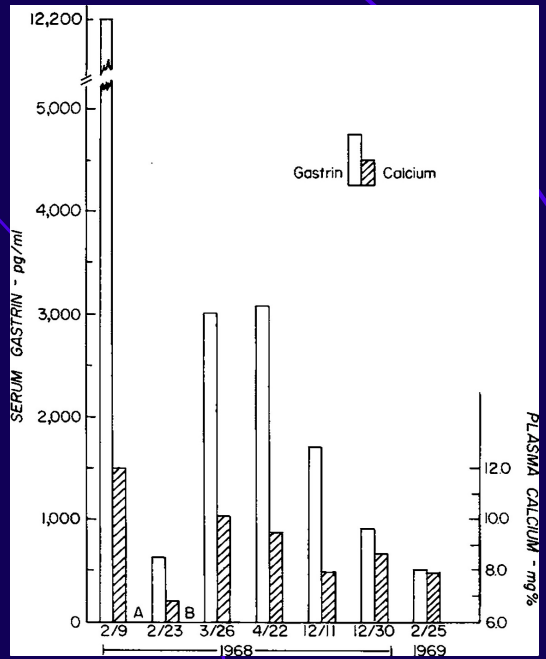
Erdheim J. Zur normalen und pathologischen Histologie der glandula thyreoidea, parathyreoidea und hypophysis. *Beitr Z Pathol Anat* 33: 158-236, 1903,

A thought exercise

Triage

A surprising link

- Primary hyperparathyroidism can lead to elevated gastrin levels in more than 20% of MEN1 patients
- After parathyroidectomy, gastrin tends to normalize
- Seems more linked to the calcium level than the PTH itself
- Gastrin-secreting G cells in the stomach have calcium-sensing receptors (CaRs)



M&M in MEN1

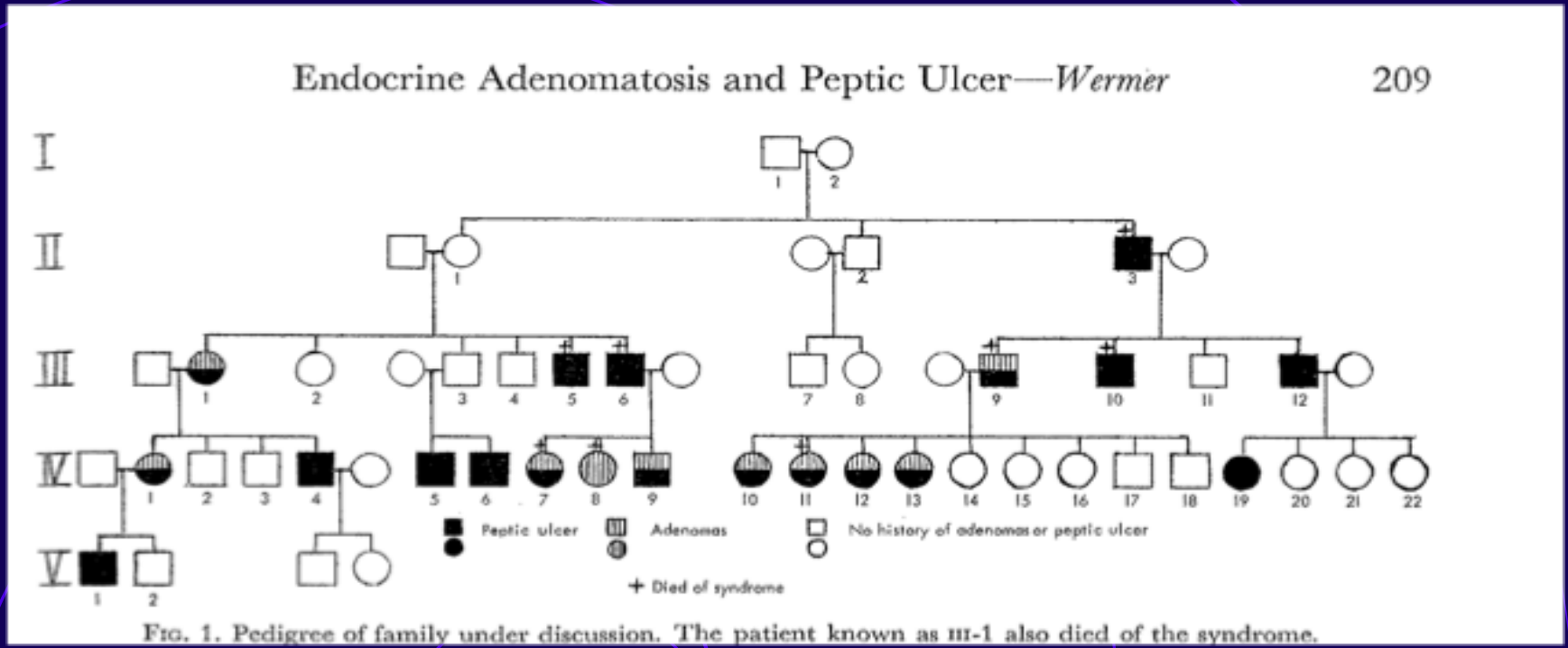


FIG. 1. Pedigree of family under discussion. The patient known as III-1 also died of the syndrome.

Threat assessment

- Historically the main cause of mortality in MEN1 was ulcers
- Since the advent of H2 blockers and PPIs, metastatic pancreatic NETs have become the #1 source of MEN1-related mortality
- The Dutch MEN1 cohort studied MEN1 patients whose PNETs metastasized to the liver and found a 50% life expectancy at 10 years
- But the same research group studied 99 patients with localized PNETs < 2cm in size for up to 16 years and found that most (66%) had stable tumors under that threshold over serial scans (median = 4)

Index EUS

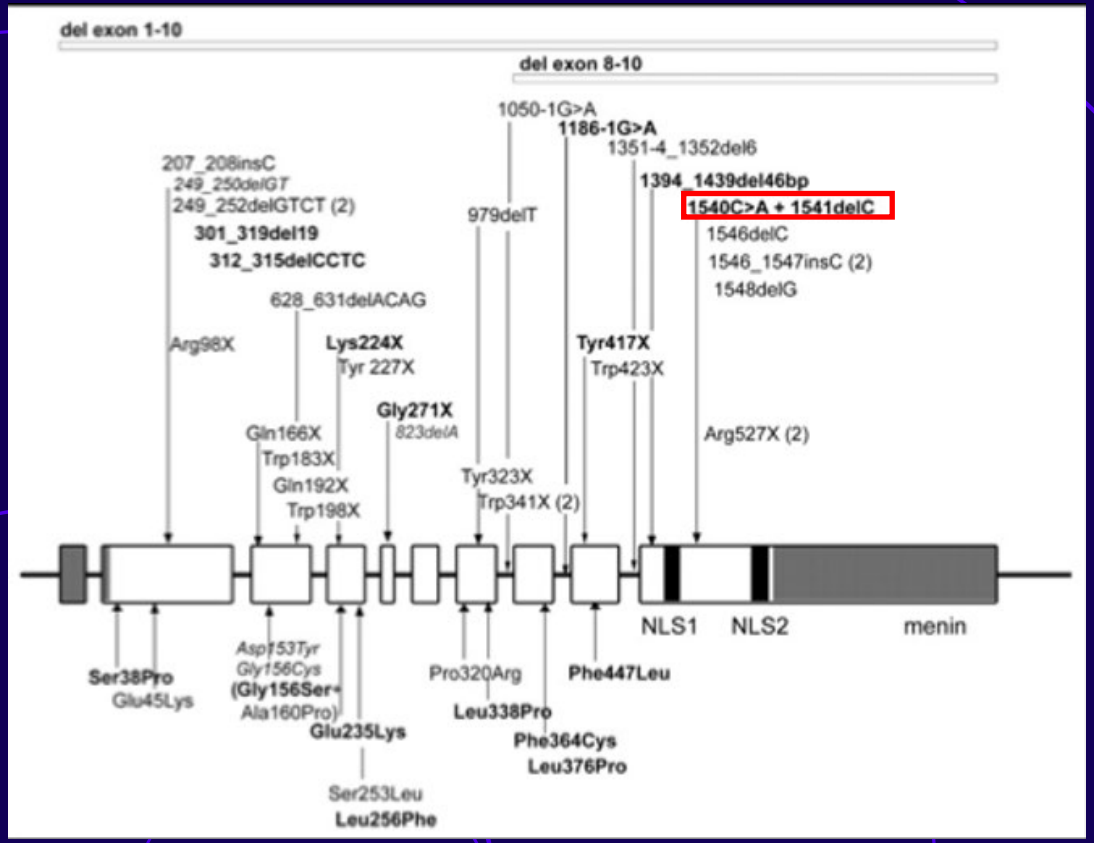
“The pancreas was markedly abnormal with a hyperechogenic pancreatic duct and multiple 2- to 3-mm hyperechoic lesions throughout the pancreas. In addition, there was a mass lesion in the tail of the pancreas, which measured 12 mm in diameter, round, well-defined, variably hypoechoic with Doppler flow. In the head of the pancreas and anterior to the pancreatic duct, there were two additional well-defined solid lesion measuring 10 mm in diameter, round, well-defined, and variably hypoechoic, and immediately inferior to this a smaller lesion measuring 5 mm in diameter. Adjacent to the superior mesenteric artery, there was **a cluster of cysts, consistent with branch duct IPMN**, and there was no ductal communication demonstrated.”

A fork in the road

Localizing the lesion?

Test(s) requested:	MEN1 Gene / Multiple Endocrine Neoplasia Type 1 (MEN1)
Result:	**POSITIVE. Heterozygous for the c.1540_1541delCCinsA Mutation** This individual is heterozygous for a deletion of two nucleotides and an insertion of 1 nucleotide in exon 10 of the MEN1 gene. The normal sequence with the bases that are deleted in braces and the base that is inserted in brackets is: AGGA{CC}[A]CCCC. This mutation is denoted c.1540_1541delCCinsA at the cDNA level or at the protein level as p.Pro514ThrfsX45.
Interpretation:	The c.1540_1541delCCinsA mutation in the MEN1 gene has been reported previously in association with Multiple Endocrine Neoplasia Type 1 (Tham et al., 2007), and is consistent with the diagnosis in this patient. The deletion and insertion causes a frameshift starting with codon Proline 514, changes this amino acid to a Threonine residue and creates a premature Stop codon at position 45 of the new reading frame, denoted p.Pro514ThrfsX45. This mutation is predicted to result in premature protein truncation.

The problem with novelty



Genotype-phenotype correlation?

c1540_1541delCCinsA, *n* = *5*?

- Paternal grandfather died in his late 60s of an unspecified GI malignancy
- Father died in his late 40s of metastatic atypical bronchial carcinoid
- Uncle died in his early 50s from pituitary macroadenoma
- From the Tham paper:

	Proband tumors (age at dx/surg/referral)	*Tumors in family members*		*Mutation type*		*Mutation in sequence*	*Effect on protein*	
38	HPT-h, PIT (PRL), ADR-un (?/40/62)	*HPT-h, malignant schwannoma (†); hypercalcemia*		frameshift deletion/insertion	10	1540_1541delinsA (i.e. 1540C>A + 1541delC)	Pro514Thr CCC>ACC and 515fs	not reported

MEN1 pancreatectomy: the Mayo Clinic experience

- 52 MEN 1 patients underwent 56 operations for suspected PNETs
- Pre-operative data included:

  Imaging

  EUS

  CT

  Octreoscan

MEN1 pancreatectomy: the Mayo Clinic experience

Operative and post-operative data:

- Surgical report
- Gross pathology
- Immunohistochemistry

The question: How well do pre-operative investigations correlate with operative findings?

Correlating pre- and post-op

	Neuroendocrine tumor on pathology	Other pathology
+ Octreoscan	26	1
- Octreoscan	5	0

Sensitivity = 84%
PPV = 96%

	Neuroendocrine tumor on pathology	Other pathology
+ CT	34	1
- CT	8	0

Sensitivity = 81%
PPV = 96%

	Neuroendocrine tumor on pathology	Other pathology
+ EUS	35	0
- EUS	0	0

Sensitivity = 100%
PPV = 100%

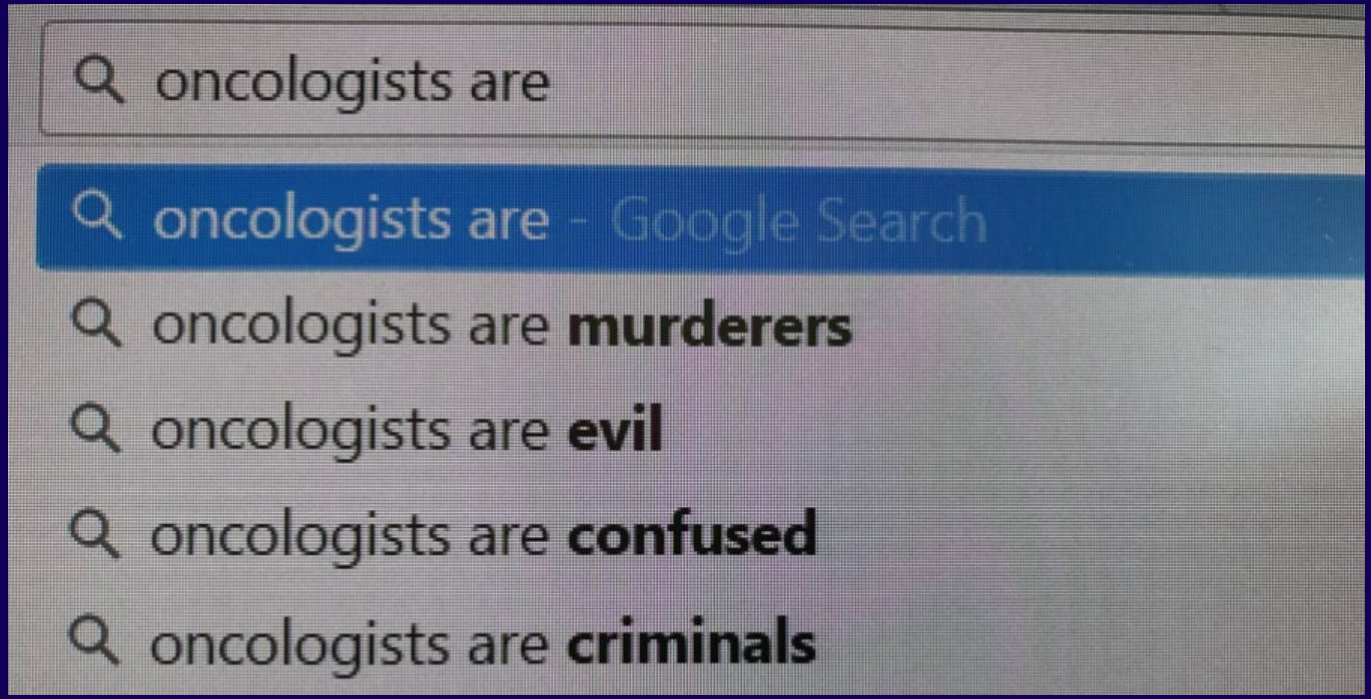
Proof positive

- July 2017: dominant PNET in head of pancreas grew to 3.1cm from 1.7cm the year prior
- August 2017: Whipple procedure removed this mass and innumerable tumorlets

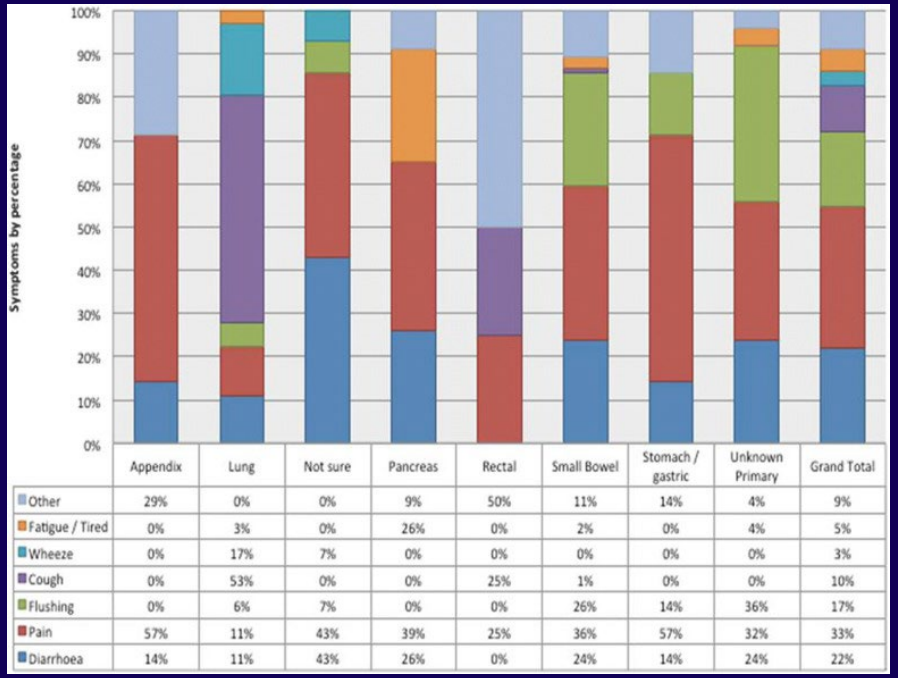
How our patients react to their diagnoses

- 97% use the Internet to search for information about cancer
- 94% search on Google
- Results yielded:
    - Most accurate about etiology (70%) and symptoms (67%)
    - Least accurate about prevention (55%), treatment (55%), and prognosis (43%)
    - Tradeoffs between readability and reliability
    - Patients with rarer cancers are particularly vulnerable to the surfacing of misinformation
    - Searching about specific medications leads to pharmaceutical websites ~20% of the time

Search engine optimization?



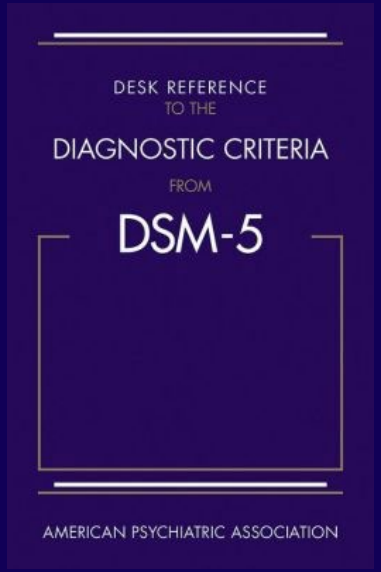
The tortuous journey to a label

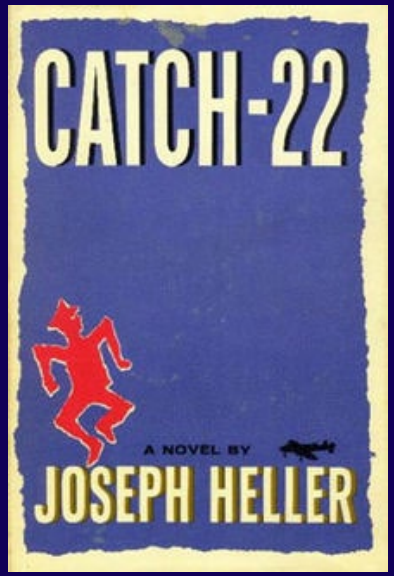


	Appendix	Lung	Not sure	Pancreas	Rectal	Small Bowel	Stomach / gastric	Unknown Primary	Grand Total
Other	29%	0%	0%	9%	50%	11%	14%	4%	9%
Fatigue / Tired	0%	3%	0%	26%	0%	2%	0%	4%	5%
Wheeze	0%	17%	7%	0%	0%	0%	0%	0%	3%
Cough	0%	53%	0%	0%	25%	1%	0%	0%	10%
Flushing	0%	6%	7%	0%	0%	26%	14%	36%	17%
Pain	57%	11%	43%	39%	25%	36%	57%	32%	33%
Diarrhoea	14%	11%	43%	26%	0%	24%	14%	24%	22%

The time from first symptom to diagnosis was 53.8 months, which is a very long time especially when considering the number of respondents that regarded their primary symptom as being severe or very severe in nature. A significant delay is likely to be occurring due to incorrect initial diagnosis. Commonly, functional bowel disorders were the initial diagnosis in a number of cases.

The folly of self-diagnosis





A 30-year-old doctor starting his specialized training in oncology convinces himself he has a tumor syndrome

Nerves or something worse?

The New York Times Magazine

WORLD | U.S. | N.Y. / REGION | BUSINESS | TECHNOLOGY | SCIENCE | HEALTH | SPORTS | OPINION

Take a Fit Test
Get your scores in games that challenge Memory, Attention, and more

Memory Matrix 55%
Speed Match 75%
Train of T 30

DIAGNOSIS

Nerves or Something Worse?

By LISA SANDERS, M.D.
Published: December 2, 2011 | 10 Comments

It felt like a knife slicing through his right side. The young man lay in bed and tried not to move. He'd had this pain off and on for years — usually when he was nervous, and he was very nervous that Sunday morning. He was supposed to start a new job the next day.

TWITTER
LINKEDIN
COMMENTS (10)
PRINT
REPRINTS
SHARE

Enlarge This Image

The patient's chest X-rays.

Multimedia

Graphic

Readers' Responses

WELL
Think Like a Doctor
How this diagnosis unfolded, thanks to Well readers' responses.

Readers' Comments

1. THE PATIENT'S STORY

The pain had never been that bad before. A hot shower helped, but not for long; afterward, he couldn't bend at the waist without gasping. Slowly the pain began to ease, and the next day, he was well enough to start his new position — as a doctor, training for a specialty in cancer.

Although he felt comfortable with his self-diagnosis of a jittery stomach, his wife — also a doctor — did not. At her insistence, he made an appointment with the primary-care doctor he'd been assigned at the Mayo Clinic.

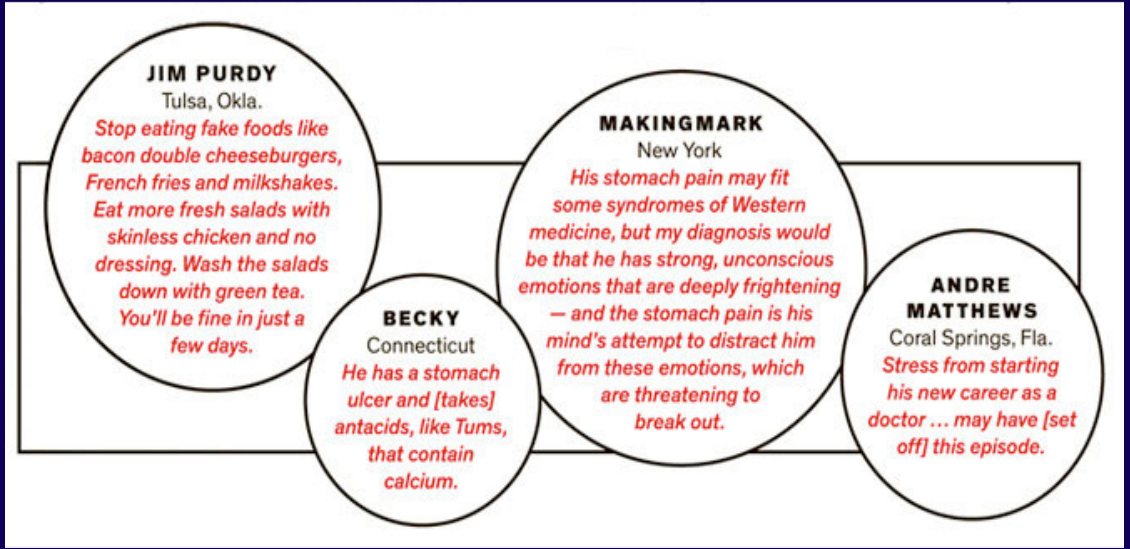
2. THE DOCTOR'S STORY

When Dr. Eric Tangalos met his new patient, his impression was that he was a pretty healthy guy. Tall and slender, he had a ready smile and an earnest, easygoing manner. "Tell me what brought you in," he asked the patient.

3. THE PATIENT'S LIST

a) Abdominal pain: Normally it was intermittent and manageable, but it became quite severe that one time. He

The downfall of Dr. Google



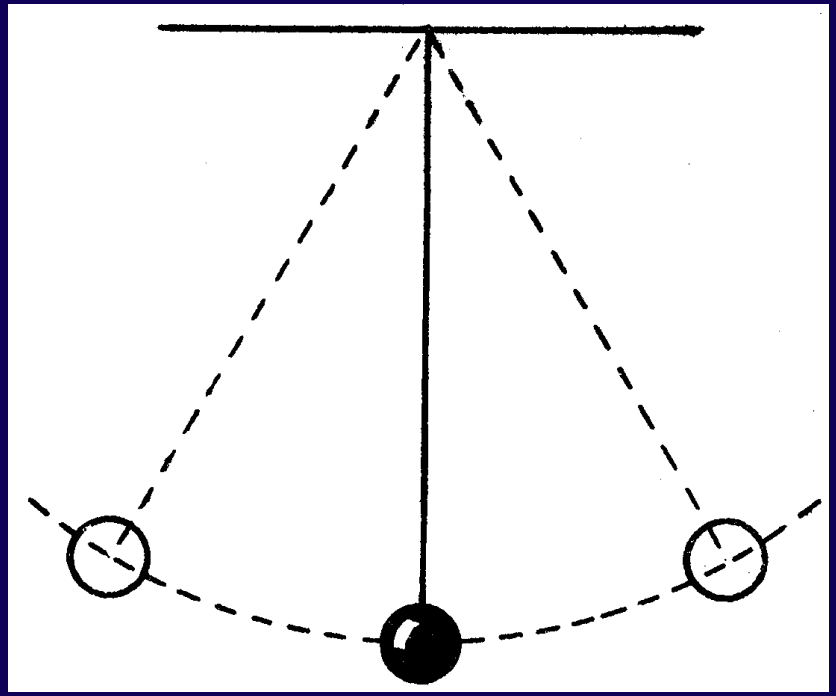
The paradox of choice

Patients vs. paywalls

Associate Officer of Knowledge & Research Services at the Bill & Melinda Gates Foundation

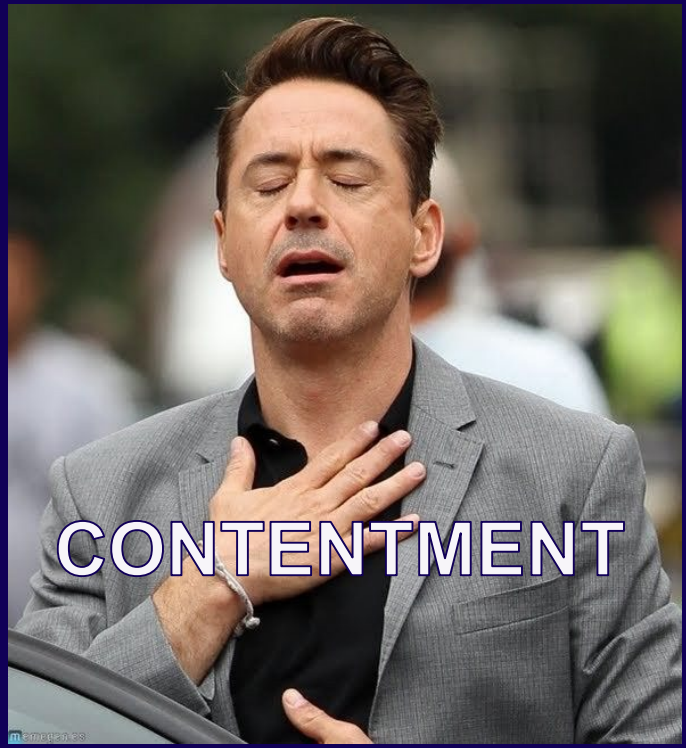
Elsevier's director of scholarly communications

The pitfall and the pendulum



Paternalism SDM *A la carte* oncology

Taming the firehose

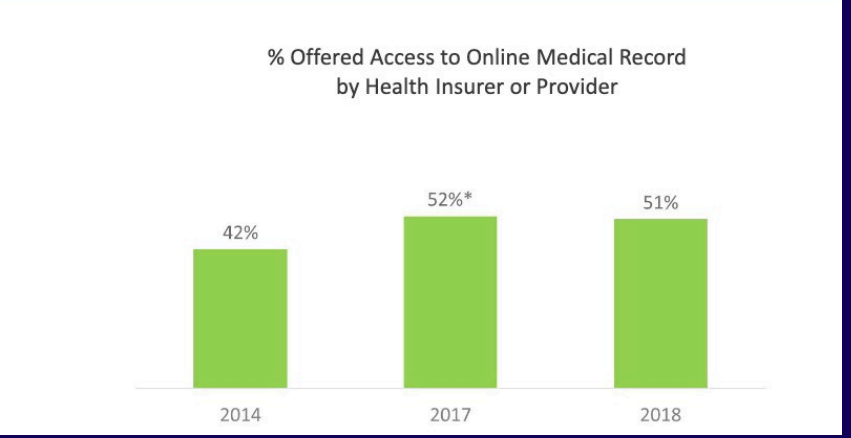


Too long, too soon, or just right? The Goldilocks problem of results release

- 94% of institutions as of a 2018-2019 AAAR survey had patient portals
- 78% have automatic radiology report release into portal
- Mean delay of release is 4 days (range: 0-7 days)

The double-edged sword of ‘Open Notes’

About half of individuals were offered access to an online medical record in both 2017 and 2018



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
OFFICE FOR CIVIL RIGHTS

The Office of the National Coordinator for Health Information Technology

21ST CENTURY CURES ACT & THE HIPAA ACCESS RIGHT

Empowering Patients by Improving Patient Access to Electronic Health Information (EHI)

Since April, 2021, federal program rules addressing "Interoperability, Information Blocking, and ONC Health IT Certification" require healthcare providers to offer patients access to virtually all the health information in their electronic medical records. This is to be free of charge, and it includes the progress notes prepared by doctors, nurses, PAs, and a broad range of therapists. Learn more about the Rule.

"Discuss what you write, and write what you discuss."

− Patients report important clinical benefits from reading notes

Patients who read notes report that they:

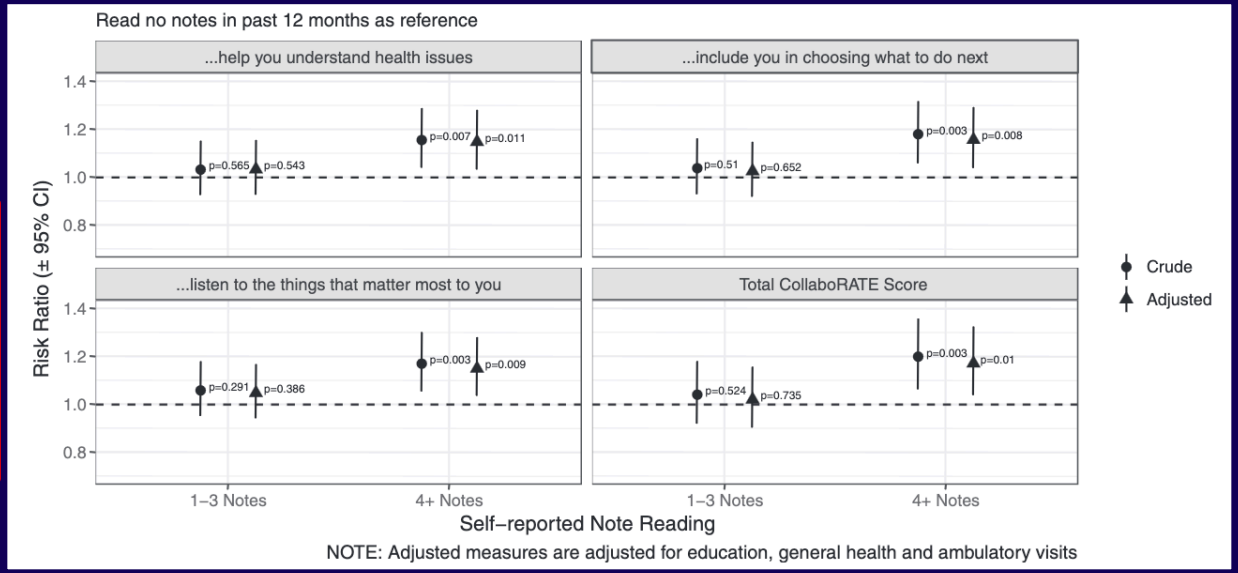
- have improved understanding of their health and medical conditions
- recall their care plan more accurately
- are better prepared for visits
- feel more in control of their care
- take better care of themselves[1]
- take their medications as prescribed more frequently[2]
- have more successful conversations and stronger relationships with their doctors

And keep in mind: Reminding patients that notes are available and providing clearly marked patient portals are important for engaging patients in a practice that is new to them..

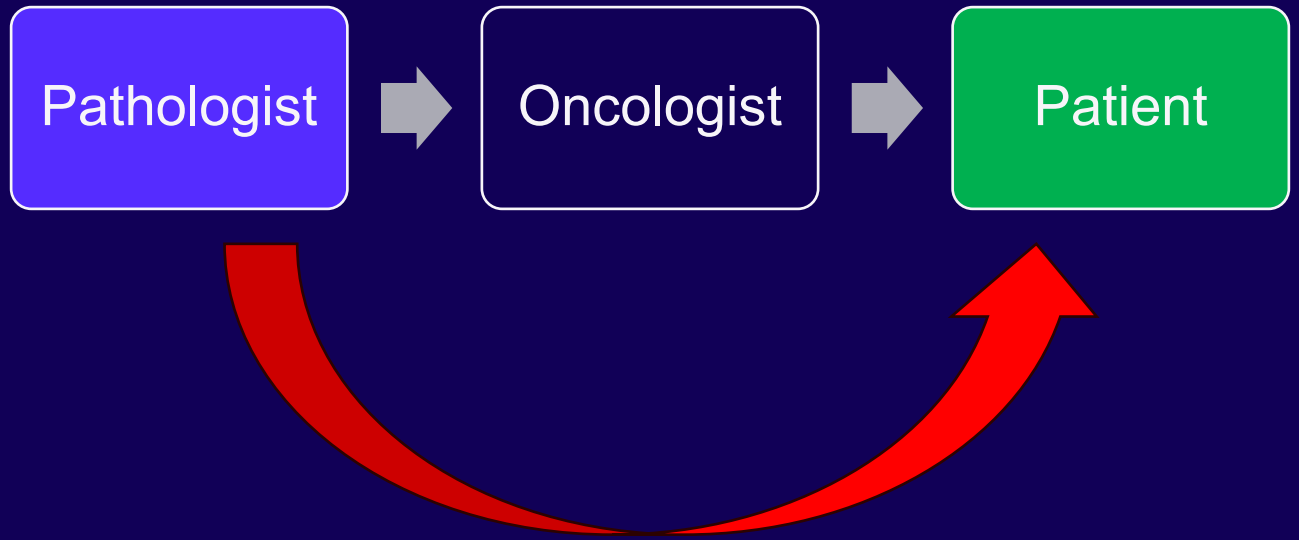
Quantifying patient engagement through note-reading

CollaboRATE is a 3-item measure of the SDM process. Items included are:

1. How much effort was made to help you understand your health issues?
2. How much effort was made to listen to the things that matter most to you about your health issues?
3. How much effort was made to include what matters most to you in choosing what to do next?



Communication is key



Tempus fugit: pressure over precision?

Even more important, "there are several exceptions that can be applied in some instances to individual reports to prevent the immediate release of the report," Dr. Myles says, such as a concern that it would violate patient privacy under HIPAA or cause patient harm. To use the preventing patient harm exception, the physician would have to document a reasonable belief that the delay in release will substantially reduce the risk of harm, and it must be limited to that specific instance. This is generally the responsibility of the ordering clinician, he says, but pathologists could invoke this exception on a case-by-case basis if the pathologist is aware of the circumstances of a specific clinical situation or was involved in a decision to order a test. "But if they did decide to delay release," Dr. Myles says, "they would have to document, in some form that they could retrieve at a later date if they were audited, why the report was not made immediately available to the patient."

Intermountain Health

Paxton A. Results release: new steps under new rules? CAP Today, October 2021.

Applying evidence-based medicine to results release

- 149 surveys of breast cancer patients
- Mean age = 56 years old
- 123 (82.5%) reviewed pathology charts in MyChart

  -- Answering “yes” associated with age (mean 54.5 vs. 61.8 years old, *p=.03*)
- 124 (83.2%) indicated “their pathology report allows them to better understand their diagnosis”
- Only 3 patients commented “the way a pathology report is worded is hard to understand”
- As in other studies, “patient anxiety & confusion were lower among patients accessing results who felt that they’d been **prepared for results by clinicians**”

Johnson KM, Esselmann J, Purdy AC, Jorns JM. Patient Use of Pathology Reports via Online Portals. Arch Pathol Lab Med. 2022 Sep 1;146(9):1053-1055.
Christensen K, Sue VM. Viewing laboratory test results online: patients’ actions and reactions. J Participat Med. 2013;5:e38
Giardina TD, Modi V, Parrish DE, et al. The patient portal and abnormal test results: an exploratory study of patient experiences. Patient Exp J. 2015;2(1):148– 154.

How to Read Your Pathology Report

To diagnose diseases such as cancer, a sample of tissue called a biopsy is taken from a patient and examined by a pathologist to determine if cancer is present.

A pathologist is a medical doctor who specializes in the diagnosis and classification of diseases by looking at tissue or cells under a microscope and by interpreting medical laboratory tests.

The pathologist is also the doctor who examines specimens removed during surgery (resections) for conditions such as cancer, to determine whether a tumor is benign or cancerous, and if cancerous, the exact cell type, grade, and stage of the tumor.

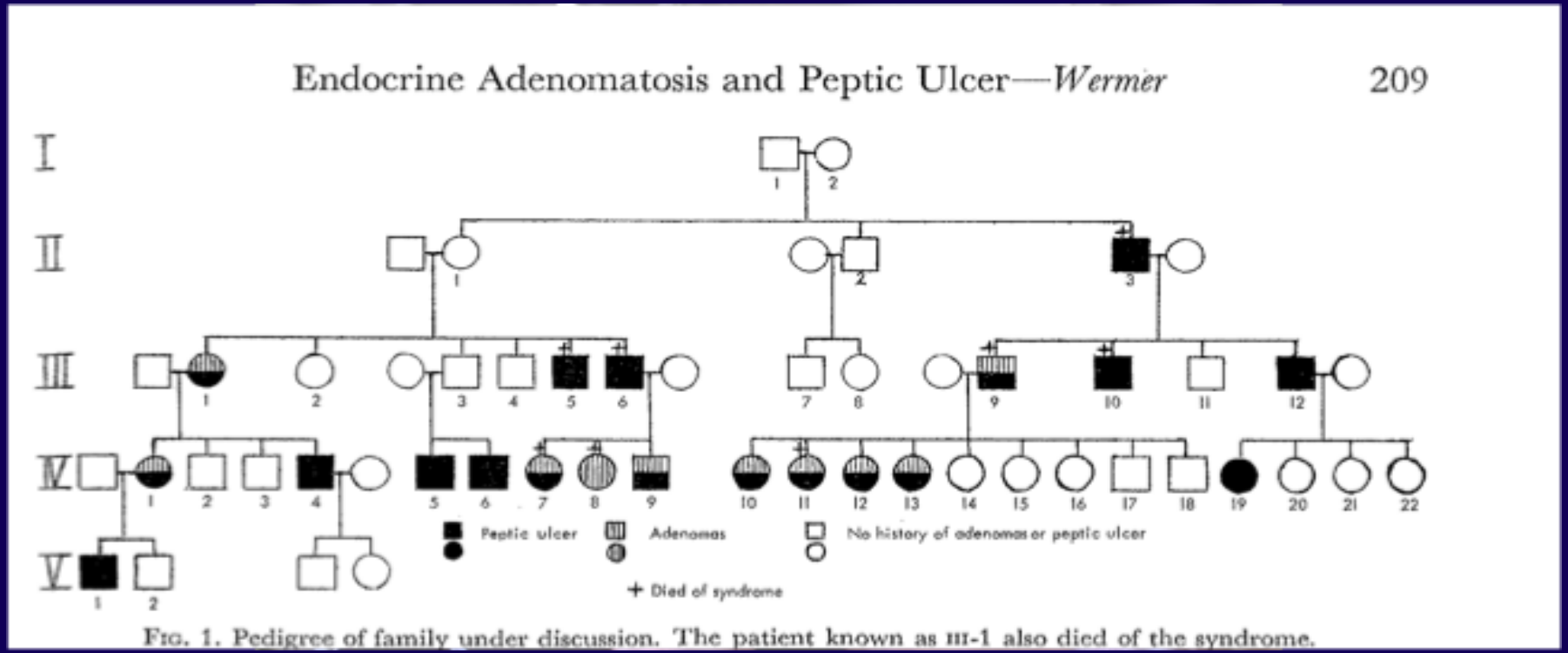
In some cases, the pathologist also performs molecular biomarker analysis and reports genetic alterations that may guide targeted therapy for a specific cancer.

The College of American Pathologists has developed resources to help you understand your pathology report.

Understanding Your Pathology Report: A Patient's Story

https://www.cap.org/member-resources/patient-education/how-to-read-your-pathology-report

Revisiting risk



Endocrine Adenomatosis and Peptic Ulcer—*Wermer* 209

I
II
III
IV
V

Peptic ulcer
Adenomas
No history of adenomas or peptic ulcer
+ Died of syndrome

FIG. 1. Pedigree of family under discussion. The patient known as III-1 also died of the syndrome.

Take-aways

- Patients are the *ultimate* stakeholders in oncology
- There has never been more information available …
- … but that makes curation of both general knowledge and personally applicable data even more crucial
- Think about your ‘audience’
- And know that what you do has a real, *human* impact

Intermountain Health

Thank you!

Intermountain Health

Contact info: mark.lewis2@imail.org
@marklewismd

REFERENCES

Andre T et al. Oxaliplatin-based chemotherapy for patients with stage III colon cancer: Disease Free Survival results of the three versus six months adjuvant IDEA France Trial. 2017 ASCO Annual Meeting.

Barr PJ, Thompson R, Walsh T, Grande SW, Ozanne EM, Elwyn G. The psychometric properties of CollaboRATE: a fast and frugal patient-reported measure of the shared decision-making process. J Med Internet Res. 2014 Jan 3;16(1):e2

Basch E. Overall survival results of a randomized trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment. 2017 ASCO Annual Meeting.

Beaton C, Codd RJ, Holland PA, Gateley CA. Evaluation of the quality and accuracy of information regarding aromatase inhibitors available on the internet. Breast J. 2008 Jul-Aug;14(4):366-8.

Blagden SP, Charman SC, Sharples LD, Magee LR, Gilligan D. Performance status score: do patients and their oncologists agree? Br J Cancer. 2003 Sep 15;89(6):1022-7.

Chang K, Berthelet E, Grubbs E, Hamilton S, Karvat A, Tran E, Wu J, Ingledew PA. Websites, Websites Everywhere: How Thyroid Cancer Patients Use the Internet. J Cancer Educ. 2019 Jul 22.

DesRoches CM *et al*. Patients Managing Medications and Reading Their Visit Notes: A Survey of OpenNotes Participants. Ann Intern Med. 2019 Jul 2;171(1):69-71.

Fossa AJ, Bell SK, DesRoches C. OpenNotes and shared decision making: a growing practice in clinical transparency and how it can support patient-centered care. J Am Med Inform Assoc. 2018 Sep 1;25(9):1153-1159.

Grewal P, Alagaratnam S. The quality and readability of colorectal cancer information on the internet. *Int J Surg*. 2013;11(5):410-3

Holder J, Tocino I, Facchini D, Nardecchia N, Staib L, Crawley D, Pahade JK. Current state of radiology report release in electronic patient portals. Clin Imaging. 2021 Jan 5;74:22-26.

Hwang TJ, Gyawali B. Association between progression-free survival and patients' quality of life in cancer clinical trials. Int J Cancer. 2019 Apr 1;144(7):1746-1751.

Kuenzel U, Monga Sindeu T, Schroth S, Huebner J, Herth N. Evaluation of the Quality of Online Information for Patients with Rare Cancers: Thyroid Cancer. J Cancer Educ. 2018 Oct;33(5):960-966.

Lewis MA, Thompson GB, Young WF Jr. Preoperative assessment of the pancreas in multiple endocrine neoplasia type 1. World J Surg. 2012 Jun;36(6):1375-81.

McLeod C, Norman R, Litton E, Saville BR, Webb S, Snelling TL. Choosing primary endpoints for clinical trials of health care interventions. Contemp Clin Trials Commun. 2019;16:100486.

Montori VM. Shared Decision-Making as a Method of Cancer Care. Health Services Research and Quality Improvement. 2023 ASCO Annual Meeting.

Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, Carbone PP. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982 Dec;5(6):649-55.

Papadakos J et all. Deconstructing Cancer Patient Information Seeking in a Consumer Health Library Toward Developing a Virtual Information Consult for Cancer Patients and Their Caregivers. *JMIR Cancer. 2017 May 24;3(1):e6*

Shklar V, Barnes MC, Chaudhary H, Ukrani J, Staszewski. Implementation of 3-month therapy for stage III colon cancer in a large community practice. 2023 ASCO Annual Meeting.

Trudeau WL, McGuigan JE. Effects of calcium on serum gastrin levels in the zollinger-Ellison syndrome. N Engl J Med. 1969 Oct 16;281(16):862-6.

WERMER P. ENDOCRINE ADENOMATOSIS AND PEPTIC ULCER IN A LARGE KINDRED. INHERITED MULTIPLE TUMORS AND MOSAIC PLEIOTROPISM IN MAN. Am J Med. 1963 Aug;35:205-12.

Weymiller AJ, Montori VM, Jones LA, Gafni A, Guyatt GH, Bryant SC, Christianson TJ, Mullan RJ, Smith SA. Helping patients with type 2 diabetes mellitus make treatment decisions: statin choice randomized trial. Arch Intern Med. 2007 May 28;167(10):1076-82.