

Hello,

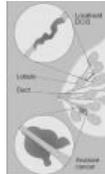
Getting the feeling that, we are **chasing a mirage**, that mirage is the knowledge. **The moment we think we have got sufficient** amount of it, some new developments take place and science like a mirage, moves out of reach.



But you bet the chase is fun. So, let's continue our pursuit for knowledge through discussion of these articles - A) Tumour markers in breast cancer B) Lab tests in acute appendicitis. C) Antioxidants in chocolate D) Use of PCR in paucibacillary smear negative pulmonary Koch's.

What are the issues in tumour markers of breast carcinoma?

Although breast cancer incidence is increasing, the mortality is decreasing mostly as a result of early detection and therapy. But, as anti-neoplastic agents are associated with substantial morbidity, efforts to **individualize**



treatment strategies are desirable. **In this regard, molecular and cellular tumor markers may help in establishing prognosis or prediction of benefit.** Three key issues in tumor marker evaluation are **utility, magnitude, and reliability**, these are discussed in an article from **"The Oncologist"** (2)

What about laboratory tests in acute appendicitis?

In this article, authors studied **897** patients, who underwent appendectomy & **compared** their **initial** WBC count, neutrophils percentage and CRP values with the **final** histopathology **report** of appendix. The authors conclude that



abnormal laboratory findings cannot reliably deliver a **diagnosis of acute appendicitis.** However, acute appendicitis is very unlikely when **leucocyte count, neutrophil percentage and CRP level are simultaneously normal.** (page 3)

Can it really be true, that chocolate can be good for you?

There is **sweet news** for chocolate lovers amongst us. This story from **"Bandolier"**



a premier journal of evidence based medicine , **takes a look at the available evidence for antioxidant properties of chocolate.** (4)

How to clinch the diagnosis in paucibacillary cases of pulmonary Koch's ?

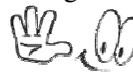
This study from **Indian Journal of Tuberculosis** found that **PCR** using MPB64 primers **has potential**



and can be a **useful adjunct** to **diagnose** clinical tuberculosis, particularly in **smear negative paucibacillary** cases. (Page 5.)

So, this is it for this month. Hope you are **enjoying** the nice whether.

Thanks and Regards,



~Sachin

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(1, Cont.)

Uses and Abuses of Tumor Markers in the Diagnosis, Monitoring, and Treatment of Primary and Metastatic Breast Cancer

N. Lynn Henry and Daniel F. Hayes

Determine utility of marker :

- Evaluate magnitude of effect (none, weak, moderate, strong)
- Analyze reliability of marker
- Technical issues (assay)
- Analytical issues (cutoff points, test/validation sets, multivariate analysis)
- Trial design issues (appropriate patient population)

Determine risk of developing disease:

- Screening for disease
- Establish diagnosis
- Differentiate benign versus malignant disease
- Determine type of malignancy
- Determine prognosis
- For primary disease, predict relapse
- For metastatic disease, predict progression
- Predict survival
- Predict response to therapy
- Hormone therapy
- Chemotherapy
- Novel therapies (e.g., trastuzumab)
- Monitor disease
- For primary disease, predict relapse
- For metastatic disease, follow detectable disease

Conclusions:

- Tumor markers, when well defined, can play a significant role in prediction and prognosis for breast cancer patients.
- Because of the abundance of poorly designed tumor marker studies to date, however, very few markers have been accepted for routine use by groups such as ASCO.
- When designing studies to establish a new tumor marker, or new use for an old marker, it is important to address the utility, magnitude, and reliability of the marker.
- By progressively generating and refining a hypothesis, based on data derived from increasingly well-developed studies, tumor markers with clinical utility can be identified.



Summary of American Society of Clinical Oncology guidelines for use of tumor markers in breast cancer

	Marker	Assess in adjuvant setting	Assess in metastatic setting	Prognostic factor	Predictive factor	Use for monitoring only	
						NED	Met
Tissue-based	ER	Yes	Yes	Weak	Strong ^a	N/A	N/A
	PgR	Yes	Yes	Weak	Strong ^a	N/A	N/A
	Her-2/neu	Yes	Yes	Weak	Strong ^b	N/A	N/A
Circulating	CA 15-3	No	Yes	No	No	No	Yes
	CA 27.29	No	Yes	No	No	No	Yes
	CEA	No	Yes	No	No	No	Yes
	Her-2 ECD	No	No	No	No	No	No

Abbreviations: CA, cancer antigen; CEA, carcinoembryonic antigen; ECD, circulating extracellular domain; ER, estrogen receptor; NED, no evidence of disease; Met: metastatic; N/A: not applicable; PgR, progesterone receptor.

(2, cont)

LABORATORY TESTS IN PATIENTS WITH ACUTE APPENDICITIS

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Background:

- ✓ Laboratory measurements such as **leucocyte count, neutrophil percentage and C-reactive protein (CRP) concentration** are commonly used as diagnostic aids in patients with suspected acute appendicitis.
- ✓ **The present study aimed to clarify the role of these laboratory tests in diagnosing acute appendicitis.**

Methods:

- ✓ The medical records of **897 patients** who underwent appendectomy for suspected acute appendicitis during a 30-month period were retrospectively reviewed.
- ✓ **The laboratory findings were correlated with the histopathology of the excised appendices.**
- ✓ Data were analysed to calculate the **sensitivity and specificity of the individual tests**, as well as the test combinations.

Conclusions:

- ✓ Abnormal laboratory findings **cannot reliably deliver** a diagnosis of acute appendicitis.
- ✓ However, **acute appendicitis is very unlikely when** leucocyte count, neutrophil percentage and CRP level are **simultaneously normal**.

Final diagnoses in 897 patients who were operated on for suspected acute appendicitis:

<u>Appendicitis: (n = 740)</u>	
Inflamed:	544
Perforated:	196
<u>Normal appendix: (n = 157)</u>	
Non-specific abdominal pain:	87
Right colonic diverticulitis:	25
Tubo-ovarian abscess:	8
Enterocolitis:	8
Ruptured ovarian cyst:	5
Others:	18



Distribution of results of the combined tests according to histological findings, and sensitivity and specificity of the combined tests

	Normal appendix (n = 157) negative test/ positive test†	Appendicitis (n = 740) negative test/ positive test	Sensitivity (%)	Specificity (%)
Leucocyte ($\geq 10.39 \times 10^9/L$) and neutrophils ($\geq 74\%$)	27/130	38/702	94.9	17.2
Leucocyte ($\geq 10.39 \times 10^9/L$) and CRP (≥ 8 mg/L)	19/138	13/727	98.2	12.1
Leucocyte ($\geq 10.39 \times 10^9/L$), neutrophils ($\geq 74\%$) and CRP (≥ 8 mg/L)	10/147	6/734	99.2	6.4

†Negative test = test values simultaneously negative, positive test = at least one value positive.



The Case for Chocolate

Note on chocolate:

- ✓ It is made from **cocoa beans**.
- ✓ If hardened, this is **bitter** chocolate. Adding **sugar and cocoa butter** produces **dark** chocolate, and the addition of this to milk concentrate produces **milk chocolate**.
- ✓ Cocoa butter and milk concentrate contain **fats**, a large proportion of which is (**saturated**) **stearic acid**.
- ✓ Chocolate also contains **theobromine and caffeine**,
- ✓ and particularly **antioxidant flavanoids, procyanadins, and flavenols**. These antioxidants are considered to have **significant protective effects against heart disease**.

Chocolate and mechanisms

- ✓ Over **20 small trials** have studied effects of chocolate on physiological and biochemical parameters over the short term.
- ✓ Several reported **lower blood pressure, decreased low density cholesterol oxidation, decreased platelet aggregation, improved endothelial function, and greater antioxidant capacity**.

Flavenoids and heart disease

- ✓ The review reports **11 prospective observational studies** of the association between flavenoid consumption and heart disease or stroke.
- ✓ Studies were conducted in populations of 500 to 40,000 (about 190,000 people in total), followed up for 5 to 28 years.
- ✓ Most reported **some reduction in coronary heart disease mortality**.
- ✓ A meta-analysis indicated a **significant protective effect between flavenoid consumption and risk of coronary heart disease mortality**, with a relative risk of 0.81 (95% confidence interval 0.71 to 0.92).

Comment

- ✓ Many different **polyphenols contribute to antioxidants** in the diet.
- ✓ There is **no absolute need to eat chocolate** to get antioxidants. But **chocolate has lots of them**, and different ones, and is pretty nice on the whole for most of us.
- ✓ Eating too much chocolate is **not a good idea**, though, because of the **sugar and stearic acid** it contains.
- ✓ Like so many other things, a **little chocolate taken regularly is likely to be a good thing; a little of what you fancy**.



A COMPARATIVE STUDY OF THE DIAGNOSIS OF PULMONARY TUBERCULOSIS USING CONVENTIONAL TOOLS AND POLYMERASE CHAIN REACTION

Kavita Modi – Parekh 1, Vikas Inamdar 2, Anagha Jog 3 and Anita Kar4



- ✓ The sensitivity of Polymerase Chain Reaction (PCR) makes it a potential diagnostic test for detection of *M. tuberculosis* in samples with low bacillary load.

Aim:

- ✓ To assess the **efficiency of PCR** as compared to routine diagnostics in detection of *M. tuberculosis* from **sputum samples** of suspects referred to a tuberculosis clinic and those identified during a morbidity survey.

Methods:

- ✓ **Respiratory samples** (sputum with or without saliva) from 144 individuals were examined by **PCR**, using MPB64 primers, **culture and microscopy**. 97 samples were from suspects referred to a tuberculosis clinic, 26 were from suspects identified during a morbidity survey and 21 were from patients with diseases other than tuberculosis. Study was conducted blind.

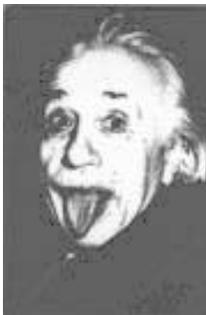
Results:

- ✓ Total cases considered to be **positive for tuberculosis by all criteria was 71**.
- ✓ **PCR detected 98% of 'culture positive', 97% of 'smear positive, culture positive', and 100% of 'smear negative' culture positive samples.**
- ✓ PCR was also **positive for 86% of smear negative samples**, from **tuberculosis suspects** diagnosed on the basis of other routine diagnostics and supporting clinical evidence.
- ✓ Seventeen samples were positive only by PCR but based on clinical parameters **only 7 were considered as true positives**.
- ✓ The **sensitivity of PCR was 91.5% compared to 51% for smear microscopy and 68% for sputum culture**. This was **due to the fact** that PCR could pick up bacterial DNA even from saliva mixed sputum specimens, which are generally not considered appropriate for microbiology.
- ✓ The **specificity of PCR (86%) was found to be lower** than other diagnostic tests mainly due to lack of a suitable gold standard to assess its efficiency. This is an important limitation in evaluation of the test.

Conclusions:

- ✓ **PCR** using MPB64 primers **has potential and can be a useful adjunct to diagnose** clinical tuberculosis, particularly in smear negative paucibacillary cases.
- ✓ However, the **major limitation** of PCR results from the absence of a suitable gold standard by which to evaluate the results.

Parting Thought...



If A equals success, then the formula is: $A = X + Y + Z$, X is work. Y is play. Z is keep your mouth shut.

~Albert Einstein

(End, 5)