A patient with Crohn's disease…

Dr. Batia Weiss
Pediatric Gastroenterology Unit
Edmond & Lily Safra Children's Hospital

שיבא - מרכז רפואי אקדמי מצטיין

בי"ח לילדים
אדמונד ולילי ספרא
המרכז הרפואי ע"ש ח. שיבא, תל השומר
בית החולים של המדינה

Case

- **27-years old** ♀
- **Age 13** – Diagnosis of Ileocaecal (L3) Crohn's disease

- **Age 17** -
  Resection of TI + cecum due to penetrating disease with recurrent UTI due to intestinal pressure on bladder
- **Postop** – treatment with azathioprine for 2 years
- The patient refused azathioprine -> switched to 5-ASA -> non compliance, discontinued after 1-2 years

- **Colonoscopy** at age 22 (5 years postop) –
  15 cm beyond anastomosis - Rutgeerts 1
  Histology- mild chronic active ileitis

- **Symptoms** - mild abdominal pain, occasional soft stools & urgency after meals, stable over the years -IBS?

- **Laboratory tests** – Hb-12.8 gr%, albumin-4.2, CRP - 0.6-2.1mg% (normal)

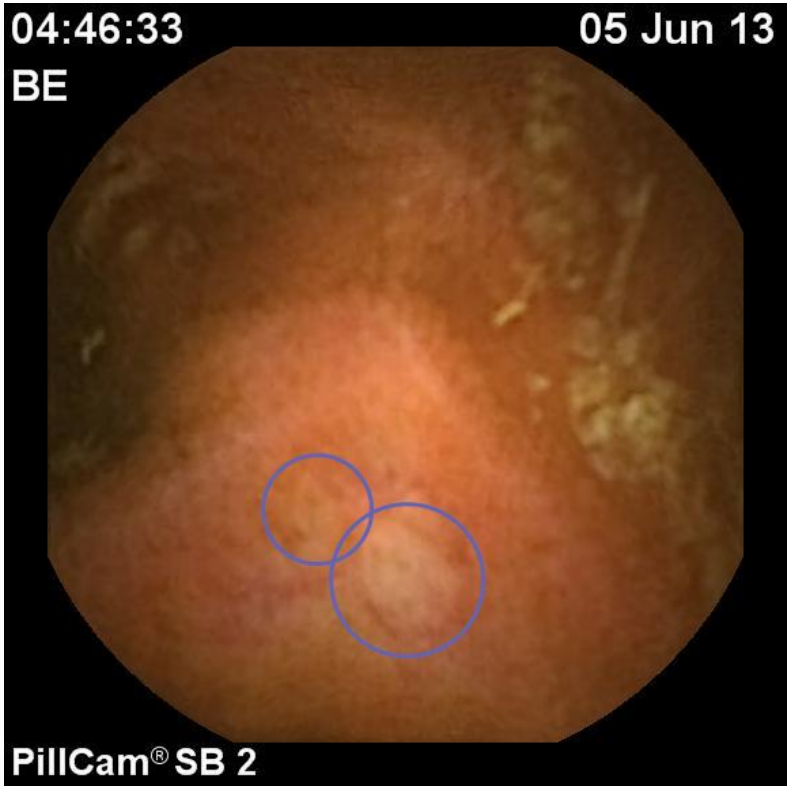
One year later - Things get worse

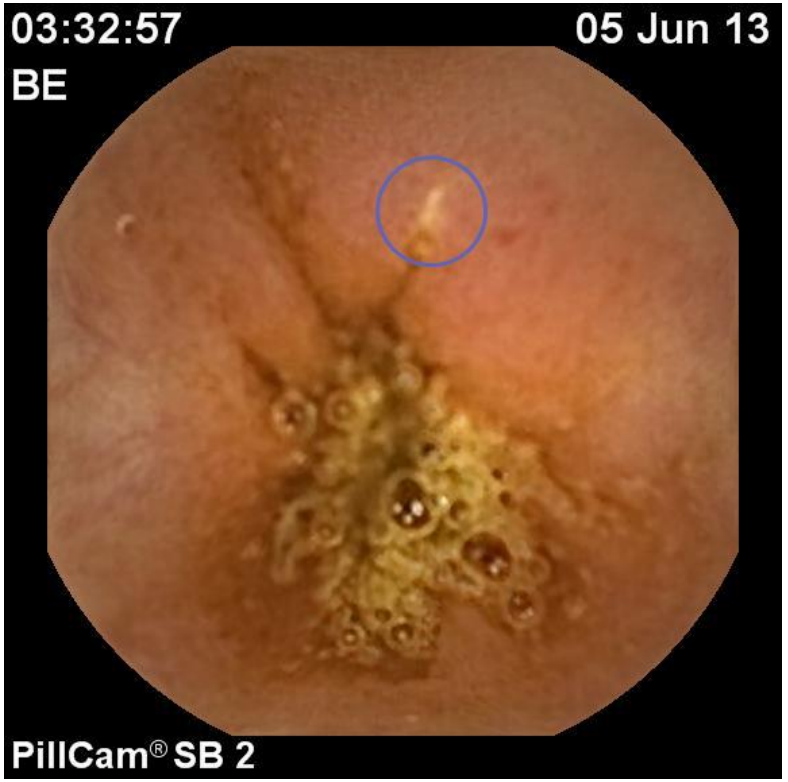
- **CRP** – constant increase 9 -11.9 gr% (X 2-3 normal)
- **Symptoms** -Mild worsening of abdominal pain & episodes Of soft stool
- Hb- 10.7-12 gr%, ferritin- 3-6, albumin- normal
- **Colonoscopy** – mild patchy erythema, anastomosis- normal

  Histology- mild active chronic ileitis. Colonic mucosa- normal
- **MRE** – Enhancement of neo-TI

- **Capsule endoscopy**

Capsule endoscopy





Small bowel cleanliness fair-adequate. Few (<3) apthous lesions and mild erythema seen in ileum. Otherwise normal exam

probably anastomosis

Should the patient be treated?

Which treatment?

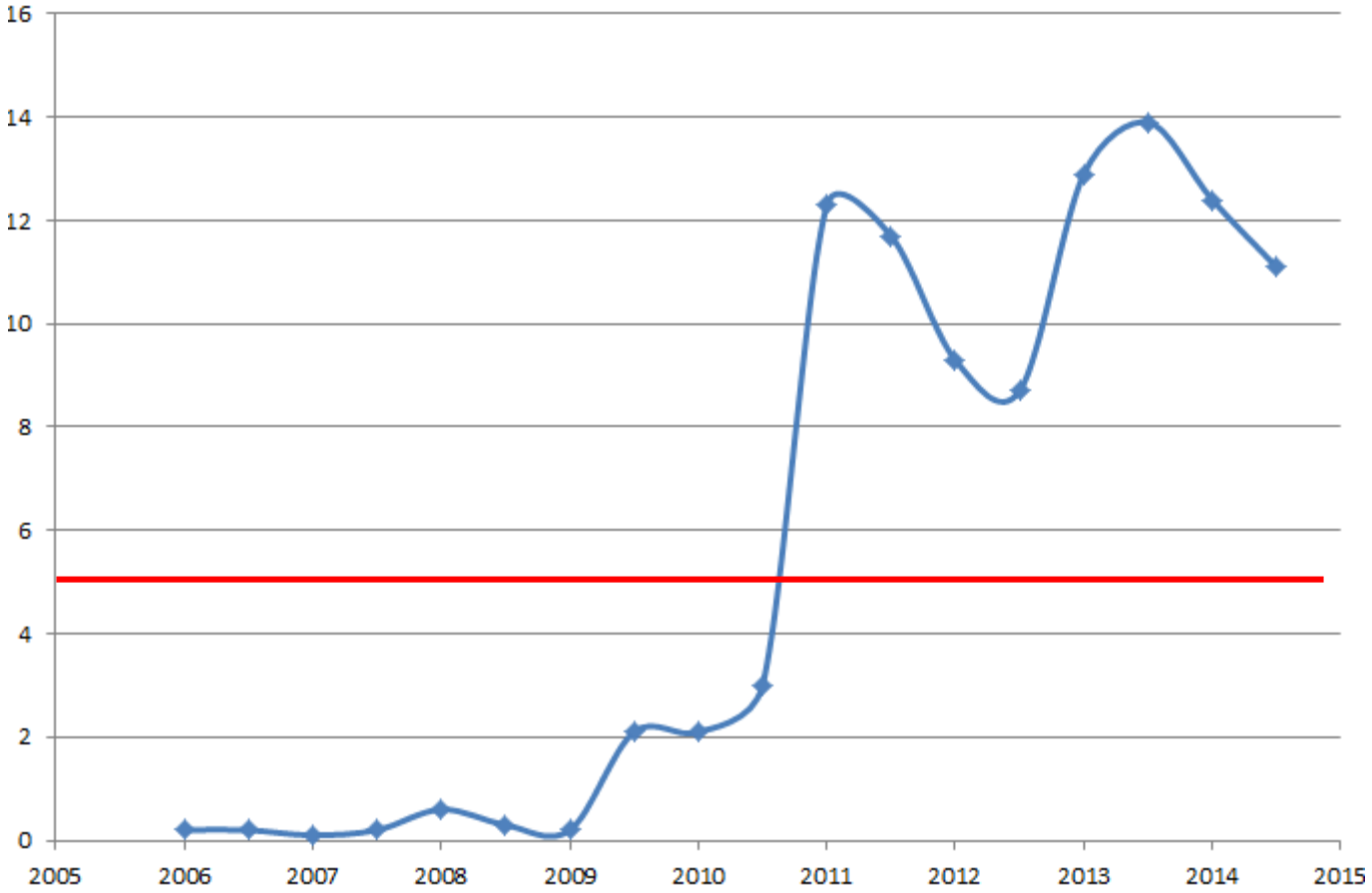
- The patient was offered azathioprine - refused
- Symptoms resolve – back to baseline
- **CRP – constant elevation X 2-3 UNL**

Age 26 years (9 years postop)

- Continuous stable mild symptoms
- **CRP**- **X 2-3 times normal**
- Other labs- ferritin- 3.5-5 (episodic Fe treatment), Hb- 11.5-12.4 gr%.
- **Colonoscopy-** minimal focal edema
- **Histology-** TI: No pathologic change.

  All colonic biopsies: Practically normal

CRP


16
14
12
10
8
6
4
2
0
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015

Extraintestinal evaluation

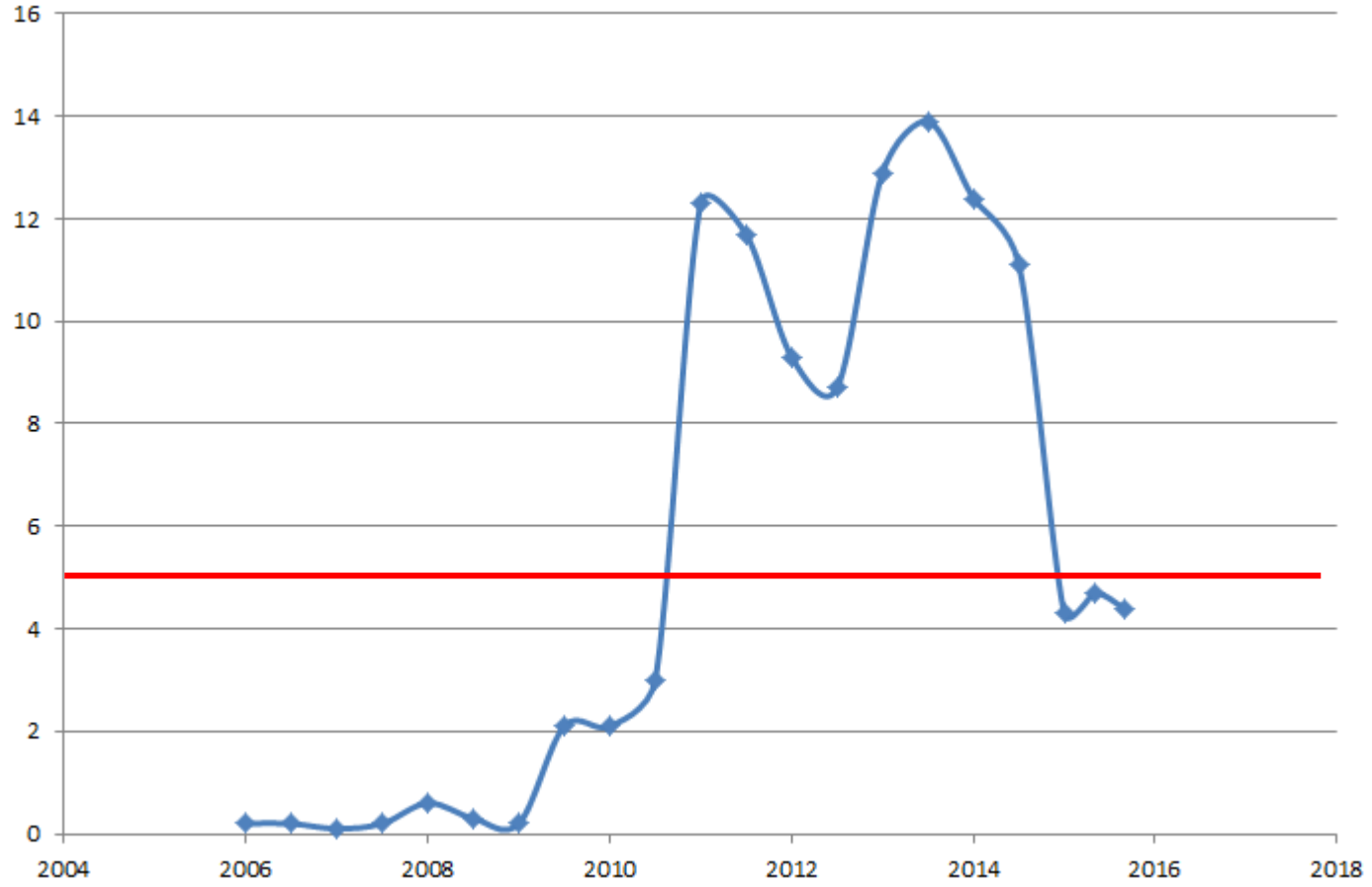
- Pelvic and renal US
- Ophthalmology
- Chest X-ray
- Blood work- CMV EBV
- Autoimmune serology
- Thyroid function

Normal

Should the patient be treated?

Which treatment?

1 year later…



?

"אולי זה מפני שהפסקתי לקחת גלולות? "

Oral contraceptives and CRP

Journal of Thrombosis and Haemostasis, **4**: 77–82

ORIGINAL ARTICLE

Treatment with combined oral contraceptives induces a rise in serum C-reactive protein in the absence of a general inflammatory response

M. VAN ROOIJEN,* L. O. HANSSON,† J. FROSTEGÅRD,‡ A. SILVEIRA,§ A. HAMSTEN§ and K. BREMME*

*Department of Woman and Child Health, Division of Obstetrics and Gynecology, Karolinska Institutet, Karolinska University Hospital

Using high-sensitivity assays, CRP levels <1, 1–3, and >3 mg/dl have been shown to correspond to low, moderate, and high risk of future cardiovascular events respectively.

In the study serum levels of CRP increased after only 2 months of treatment with both COC preparations. The increase was more pronounced with DG/EE; 34% of the women (12 of 35) reached a high-risk CRP level for developing CVD. During LNG/EE treatment 20% of the women reached CRP levels above 3.0 mg/dL.

No effect was noted on serum concentrations of IL-6 or TNFa regardless of treatment.

Hindawi Publishing Corporation
Mediators of Inflammation
Volume 2015, Article ID 379501, 8 pages
http://dx.doi.org/10.1155/2015/379501

Research Article

Effect of Oral and Vaginal Hormonal Contraceptives on Inflammatory Blood Biomarkers

Afshin A. Divani,[1] Xianghua Luo,[2] Yvonne H. Datta,[3] James D. Flaherty,[4] and Angela Panoskaltsis-Mortari[5]

Table 2: Multivariate analysis of the blood inflammatory biomarkers for the selected recruited subjects.

Blood marker	Least square mean (95% CI)				*P* value		
	Nonusers	COC	CVC	Global test	Nonuser versus COC	Nonuser versus CVC	COC versus CVC
MCP-1 (pg/mL)	285 (195, 375)	189 (104, 274)	161 (53, 270)	0.22	0.14	0.12	0.69
IL-6 (pg/mL)	1.1 (0.8, 1.5)	0.9 (0.6, 1.2)	1.1 (0.6, 1.5)	0.64	0.38	0.83	0.55
sTNF-RI (pg/mL)	975 (845, 1105)	950 (829, 1071)	805 (649, 962)	0.25	0.79	0.13	0.14
sTNF-RII (pg/mL)	4310 (3777, 4842)	4295 (3799, 4791)	4311 (3672, 4951)	1.00	0.97	1.00	0.98
sCD40L (ng/mL)	2937 (1843, 4031)	5259 (4240, 6277)	2806 (1493, 4119)	<0.01*	<0.01*	0.89	<0.01*
CRP (mg/L)	0.6 (−0.2, 1.4)	3.6 (2.9, 4.4)	2.9 (2.0, 3.9)	<0.0001*	<0.0001*	<0.001*	0.24
Lymphocytes ($10e^9$/L)	1.93 (1.67, 2.19)	2.31 (2.05, 2.57)	2.27 (1.94, 2.60)	0.14	0.0521	0.15	0.85

Note: a *P* value of <0.05 is indicated by ∗. Multivariate analysis adjusted for age, race, alcohol consumption, regular sleeping habit, and family history of cardiovascular disease (CVD) and stroke.
MCP-1: monocytes chemotactic protein-1, IL-6: interleukin-6, sCD40L: soluble CD40 ligand, sTNF-RI: soluble tissue necrosis factor receptor I, sTNF-RII: soluble tissue necrosis factor receptor II, and CRP: C-reactive protein.

Effects of Third-Generation Oral Contraceptives on High-Sensitivity C-reactive Protein and Homocysteine in Young Women

Sabina Cauci, PhD, Manuela Di Santolo, MS, Jennifer F. Culhane, PhD, MPH, Giuliana Stel, MS, Fabio Gonano, MD, and Secondo Guaschino, MD

Table 3. Relative Risk of Oral Contraceptive Users (n=77) Compared With Non–Oral Contraceptive Users Controls (n=200) for High-Sensitivity C-reactive Protein, Homocysteine and Folate Categorical Values as Estimated by Odds Ratio and 95% Confidence Interval

Measure	OC Users (n=77)	Non–OC Users (n=200)	OR* (95% CI)	P*	Adjusted OR† (95% CI)	P†	Adjusted OR‡ (95% CI)	P‡
High-sensitivity CRP <0.5 mg/L	12 (15.6)	123 (61.5)	0.12 (0.06–0.23)	<.001	0.11 (0.05–0.22)	<.001	0.13 (0.06–0.29)	<.001
High-sensitivity CRP 0.5 to <1.0 mg/L	16 (20.8)	36 (18.0)	1.19 (0.62–2.31)	.60	1.09 (0.56–2.14)	.80	1.36 (0.60–3.07)	.46
High-sensitivity CRP 1.0 to <3.0 mg/L	25 (32.5)	22 (11.0)	3.89 (2.03–7.46)	<.001	4.15 (2.11–8.19)	<.001	3.58 (1.54–8.29)	.003
High-sensitivity CRP 3.0 to <10.0 mg/L	21 (27.3)	17 (8.5)	4.04 (1.99–8.18)	<.001	4.38 (2.07–9.25)	<.001	3.67 (1.39–9.7)1	.009
High-sensitivity CRP ≥3.0 mg/L	24 (31.2)	20 (10.0)	4.08 (2.09–7.95)	<.001	4.35 (2.14–8.86)	<.001	4.23 (1.67–10.67)	.002
High-sensitivity CRP ≥5.0 mg/L	12 (15.6)	12 (6.0)	2.89 (1.24–6.76)	.011	3.48 (1.32–9.13)	.011	3.57 (1.02–12.50)	.046
High-sensitivity CRP ≥10.0 mg/L	3 (3.9)	2 (1.0)	4.01 (0.66–24.50)	.13	3.30 (0.40–27.50)	.27	13.7 (0.48–392.6)	.13
HCY ≥12 micromole/L	15 (19.5)	42 (21.0)	0.95 (0.49–1.85)	.88	0.96 (0.48–1.92)	.92	0.92 (0.38–2.20)	.85
HCY ≥15 micromole/L	5 (6.5)	17 (8.5)	0.79 (0.28–2.23)	.65	0.81 (0.28–2.36)	.69	0.68 (0.17–2.68)	.58
Folate ≤3 microgram/L	9 (11.7)	32 (16.0)	0.74 (0.33–1.64)	.46	0.76 (0.33–1.74)	.51	0.46 (0.16–1.28)	.13

CRP, C-reactive protein; HCY, homocysteine; OR, odds ratio; CI, confidence interval.
Data are n (%) or odds ratio (95% confidence interval).
* Univariable odds ratio.
† Adjusted for age, body mass index, smoking, and white blood cells.
‡ Adjusted for age, body mass index, smoking, white blood cells, cholesterol, triglycerides, albumin, bilirubin, alkaline phosphatase, and lymphocytes.

Obstetrics & Gynecology 2008

Take home

- CRP levels may be elevated with use of COC
- Those patients are at increased risk of cardiovascular events
- In females with IBD –

This effect should be considered when following inflammatory markers, and during treatment decisions

Take into consideration in clinical studies using CRP as part of outcome measures or clinical/endoscopic correlations