שיטות מעבדתיות לאבחון זיהום בחיידק ה.פילורי

פרופסור זמירה סמרה
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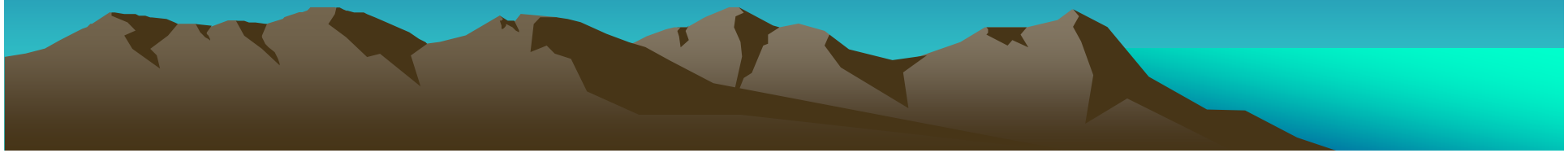
Laboratory Diagnosis

-Serology

-Stool antigen

-Culture



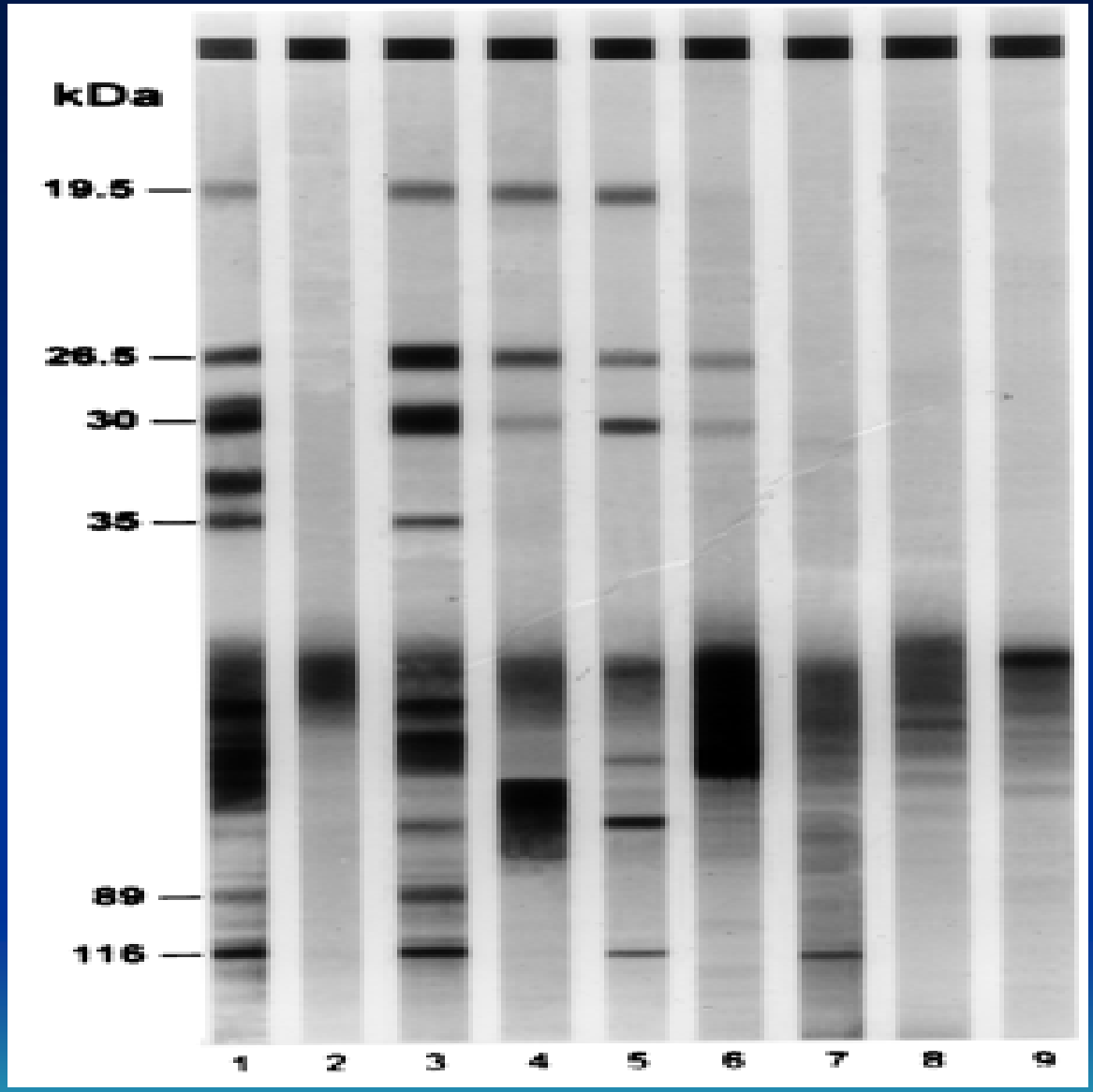
Non-invasive test- Serology

- Laboratory-based serologic testing using ELISA technology to detect IgG antibodies is inexpensive, noninvasive, and well suited to primary care practice.
- Sensitivity and specificity are poor
- 60%-70% sensitivity in symptomatic patients
- Lack of age-range cut-off values
- Not relaiable to follow eradication

  (delayed response)

Non-invasive tests -Serology

- In a patient with a confirmed ulcer in whom the pretest probability of infection is high, it is reasonable to initiate treatment based upon positive serology and to consider confirming a negative serology result with a second non-serologic test.
- In contrast, a negative test is helpful to exclude infection if the pretest probability is low.
- The test was less accurate in children than in adults.
- The reasons for this difference were explained by the lower prevalence of *H. pylori* in children, and the fact that children had lower levels of antibodies to *H. pylori* than adults.


kDa
19.5
26.5
30
35
89
116
1
2
3
4
5
6
7
8
9

Stool antigen assay

- Stool antigen tests for *H. pylori* provide a sensitivity of 89 to 98 percent and a specificity of over 90 percent.
- Stool tests are suitable for the diagnosis and follow-up of infection, provided that an eight-week interval is allowed after therapy.
- Stool tests perform well in children of all ages and may become the noninvasive method of choice for this group of patients.

Stool antigen test in Children

- 264 children aged 2-17 years (mean 9.2 years) were investigated.
- The overall sensitivity was 96%, specificity 96.8%, PPV 93.2% and NPV 98.4%.
- There were no difference among age groups (5, 6-10 and 11 years).
- The test could be used to determine the *H. pylori* status after eradication, although the optimal timing remained to be determined

Kato *Am J Gastroenterol* 2002

Helicobacter pylori and *Clostridium difficile* in Cystic Fibrosis Patients

- We describe the prevalence of *H. pylori* and toxigenic *Clostridium difficile (*CD) infection and its relationship with gastrointestinal symptoms and pancreatic sufficiency (PS) or insufficiency (PI) in cystic fibrosis (CF) patients.
- Stool specimens from 30 consecutive (non-antibiotic treatment period) patients with CF, aged 1–44 y and from 30 healthy similarly aged subjects were tested for the *H. pylori* antigen by specific monoclonal antibodies and for CD toxins by Tox A/B assay and Tox A assay.
- CF patients were assessed clinically and tested for specific *H. pylori* serum antibodies and for mutations.

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Helicobacter pylori and *Clostridium difficile* in Cystic Fibrosis Patients

- In CF patients, the prevalence of *H. pylori* antigen was 16.6% (5/30), compared to 30% (9/30) in controls.
- Fourteen of 30 (46.6%) stool specimens from CF patients tested positive in the ToxA/B assay, and 3 of 14 tested positive for ToxA.
- Almost half of the CF patients were asymptomatic carriers of CD producing mostly toxin B.
- All the healthy controls were negativr for CD toxins

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Bacterial culture and sensitivity testing

- *H. pylori* has historically been difficult to culture, but techniques are improving.
- Culture and antibiotic susceptibility of *H.pylori* provides an important tool for the treating clinician.
- Concerns over metronidazole and macrolide resistanceare growing and a standard definition of t resistance is being established
- The incidence of metronidazole resistance appears to vary with geography and is estimated to range from 80 to 90 percent in tropical countries and to be as high as 50 percent in some European countries
- The incidence of primary macrolide resistance is 4 to 12 percent.

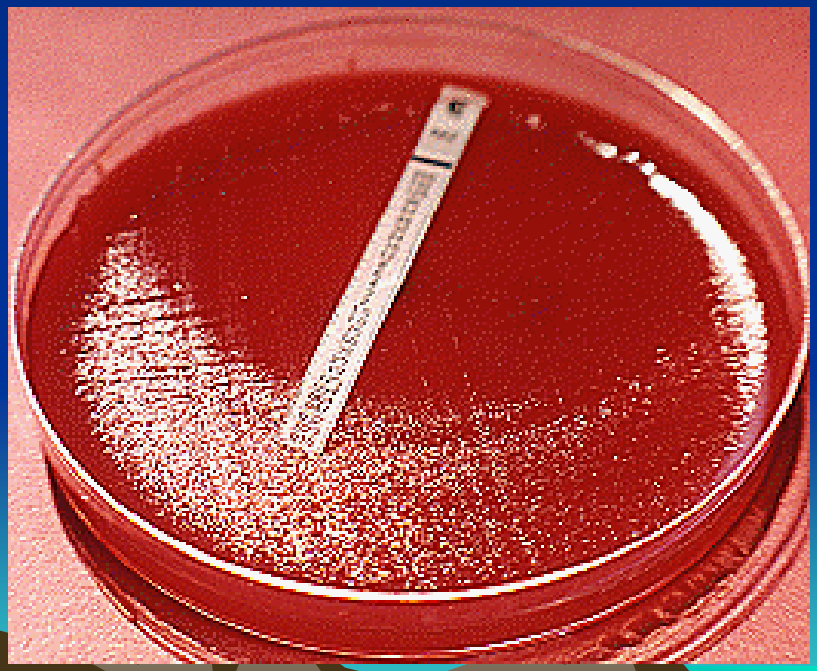
Journal of Antimicrobial Chemotherapy (2002) **49**, 1023–1026
DOI: 10.1093/jac/dkf041

JAC

Resistance of *Helicobacter pylori* isolated in Israel to metronidazole, clarithromycin, tetracycline, amoxicillin and cefixime

Aim

- To assess the in-vitro resistance of *H.pylori* isolates from untreated and treated patients to five antibiotics



Methods

- Bacterial strains:

  138 *H.pylori* isolates cultured from from antral biopsy specimens of 138 dyspeptic adult patients

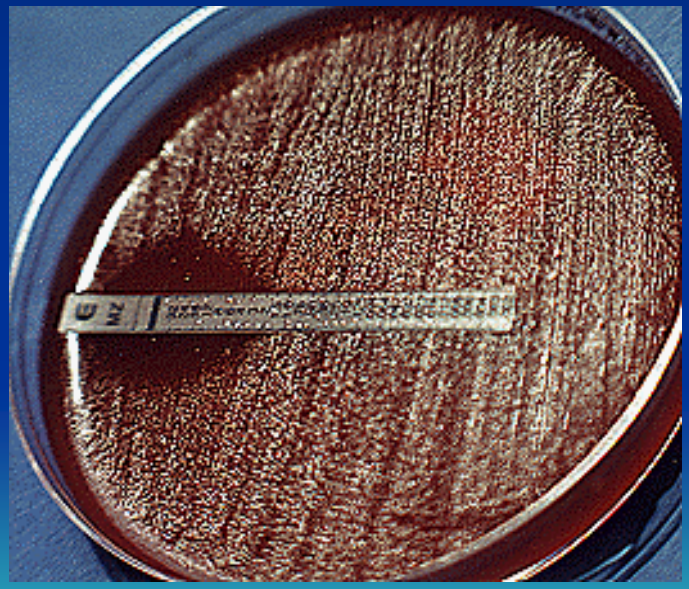
  (71 F/67 M ; median age 55 y)
- 110 were untreated patients
- 28 patients had been treated previously with PPI and 2 or more antimicrobial agents

***J Antimicrob Chemother* 2002;49:1023–6**

Methods

MIC determination:

- The MIC's of amoxicillin, clarithromycin, metronidazole,tetracycline and cefixime were determined by Etest



Methods

- Definitions of resistance:

  MIC defined as resistant strain was as follows:

  -Metronidazole ≥ 8mg/L

  -Clarithromycin ≥ 2mg/L

  -Tetracycline ≥ 4mg/L

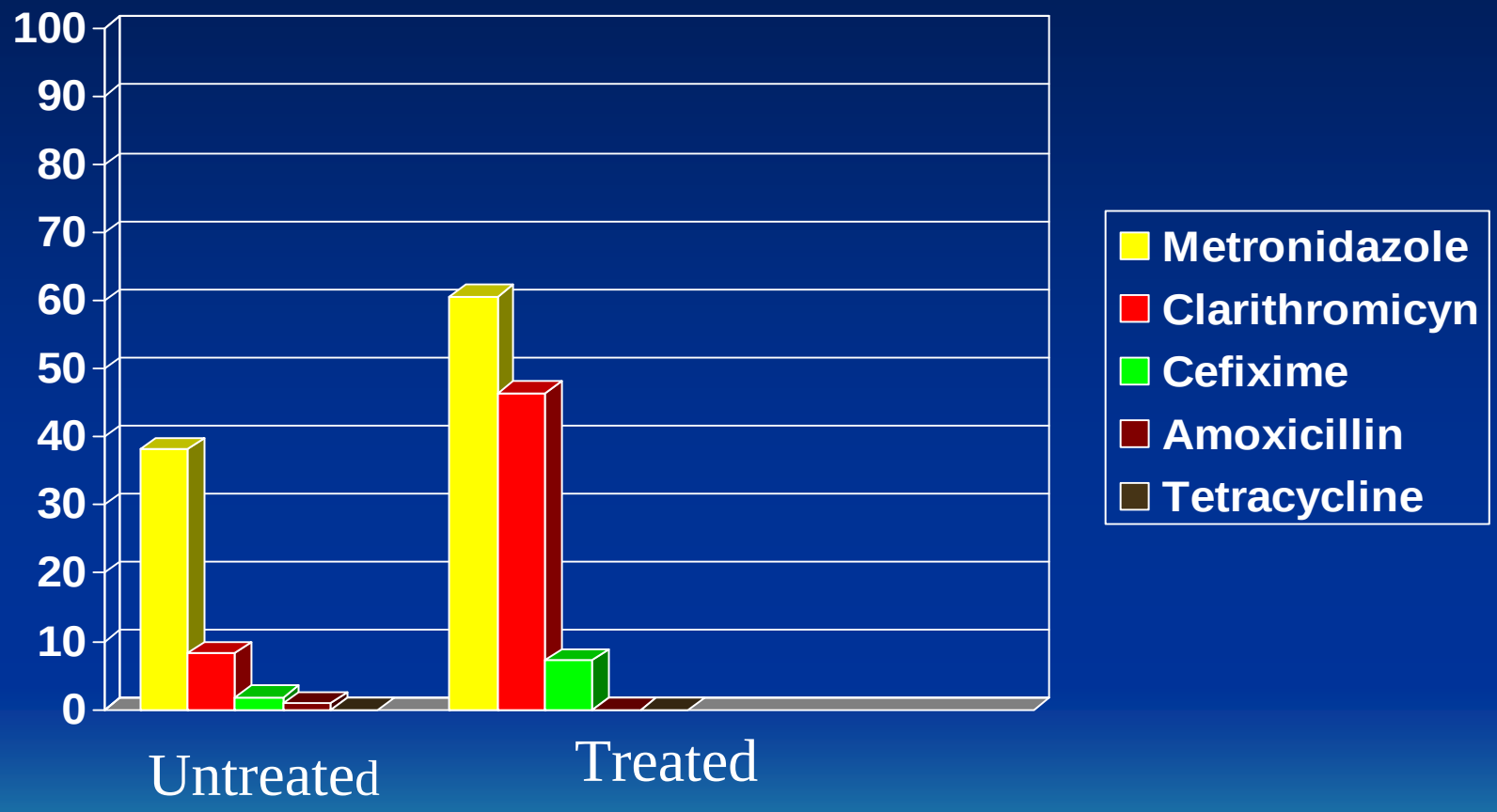
  -Amoxicillin ≥ 1.5mg/L

  -Cefixime ≥ 2mg/L

Prevalence of resistance in *H.pylori* isolates from untreated and treated patients

Antibiotic	Untreated n=110	Treated N=28	N Treatment	OR (95%CI)	P value
Metronidazole	38.2	60.7	1 AM+CL+M 1 CL+MZ 6 AM+CL+MZ 2 CL +MZ 3 AM+CL 2 CL+MZ+TC 7 AM+CL+MZ 7 CL+MZ 1 AM+MZ 2 CL+MZ+TC	2.5 (1-6.4)	0.03
Clarithromycin	8.2	46.4		9.7 (3.2-30)	<0.001
Tetracycline	0	0			
Amoxicillin	0.9	0			
Cefixim	1.87	7.2		4.2 (0.3-59)	0.18

Prevalence of resistance in *H.pylori* isolates from untreated and treated patients



J Antimicrob Chemother 2002;49:1023–6

Results

- Dual resistance was found in 5.5% of untreated patients(6/110) and 32.1% of treated patients(9/28) (P<0.001)
- In eight of the nine isolates from treated patients dual resistance was to metronidazole and clarithromycin.

***J Antimicrob Chemother* 2002;49:1023–6**

Results

- In the treated group, all the clarithromycin-or-metronidazole-resistant isolates were from patients treated previously with clarithromycin or metronidazole, respectively
- No statistically significant association was found between age or gender and resistance to any of the antibiotics studied.

***J Antimicrob Chemother* 2002;49:1023–6**

Conclusions

- There is a high prevalence of both single and dual metronidazole and clarithromycin resistance in isolates recovered from treated patients compared to isolates from untreated patients.

Susceptibility-Guided vs. Empiric Retreatment of *Helicobacter pylori* Infection After Treatment Failure

- Successful eradication of *Helicobacter pylori* after failure of standard triple therapy is difficult because of the higher resistance to metronidazole and clarithromycin.
- We evaluated the efficacy of susceptibility-guided vs. empiric retreatment for *H. pylori* after at least one treatment failure and determined the prevalence of posttreatment antibiotic resistance.
- 49 patients in whom at least one treatment regimen for *H. pylori* eradication had failed underwent gastric biopsy and culture and were retreated according to the in vitro susceptibility results.

Susceptibility-Guided vs. Empiric Retreatment of *Helicobacter pylori* Infection After Treatment Failure

- Findings were compared with those for 49 control patients referred to our center after treatment failure for a 13C-urea breath test.
- *H. pylori* eradication was assessed by urea breath test at least 6 weeks after retreatment in both groups.

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Susceptibility-Guided vs. Empiric Retreatment of *Helicobacter pylori* Infection After Treatment Failure

- Eradication was successful in 42 patients in the guided-therapy group (86%) and 31 patients in the empiric-therapy group (63%).
- Susceptibility-guided therapy was associated with significantly higher eradication success (unadjusted OR=3.5; 95% CI, 1.3–9.4; *P*=0.02). This association held true in stratified and multivariate analyses (OR=3.3; 95% CI, 1.1–10.0; *P*=0.04) .

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Susceptibility-Guided vs. Empiric Retreatment of *Helicobacter pylori* Infection After Treatment Failure

- Susceptibility-guided retreatment was associated with better eradication rates than empiric treatment.
- The difference remained significant in stratified and multivariate analysis.
- Susceptibility-guided retreatment appears to be significantly more effective than empiric retreatment in eradicating *H. pylori* after at least one previous treatment failure.

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Antimicrobial susceptibility study

In vitro activity of levofloxacin against *Helicobacter pylori* isolates from patients after treatment failure

Jacob Yahav[a,d], Haim Shmuely[a,d,*], Yaron Niv[a,b,d], Jacklin Bechor[a,c,d], Zmira Samra[a,c,d]

Table 1

Distribution of MIC values, MIC_{50} and MIC_{90}, for 70 *H. pylori* isolates from 70 patients after both triple and quadruple treatment failure

Antimicrobial agent (mg/L)	≤0.016	0.023–0.094	0.125–0.38	0.5–1.5	2–6	8–32	48–128	≥256	MIC_{50}	MIC_{90}	Range
MET	0	10	10	8	2	6	3	31	24	≥256	≤0.016–≥256
CLA	12	5	3	4	8	12	4	22	12	≥256	≤0.016–≥256
LEV	1	25	27	2	2	13	–	–	0.19	≥32	0.016–≥32
TET	35	26	6	3	–	–	–	–	≤0.016	0.094	≤0.016–0.75
AMP	35	23	11	1	–	–	–	–	≤0.016	0.125	≤0.016–0.75

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Susceptibility of *H. pylori* isolates to CLA, MET, and LEV

CLA	MET	LEV	No. of isolates (%)
S	R	S	8 (11.4)
R	S	S	10 (14.3)
R	R	S	23 (32.8)
R	S	R	4 (5.7)
R	R	R	9 (12.8)
S	S	S	16 (22.9)

S = susceptible; R = resistant.

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Total Resistance

Antibiotic	No of Isolates	% Res.
MET	40/70	57.1
CLA	46/70	65.7
LEV	13/70	18.6
MET+CLA+LEV	9/70	12.8
CLA+LEV	4/70	5.7

תודה רבה