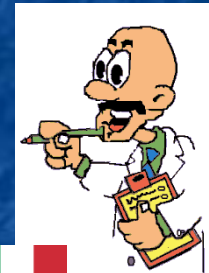


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Antimicrobial susceptibility changes in children with *H. pylori* infection over 13 years in northern Italy

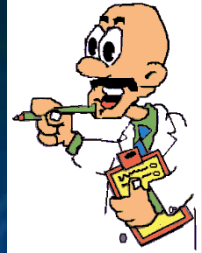
Marco Manfredi MD, PhD
Pediatrician & Gastroenterologist
"Pietro Barilla" Children's Hospital
University of Parma, Parma, Italy



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Helicobacter pylori infection

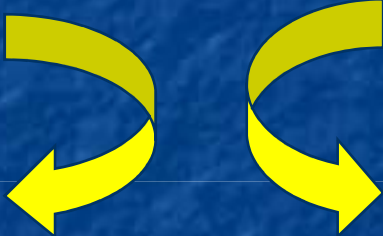
40%-50% developed countries

80% developing countries

GI diseases

Chronic Gastritis

Gastric Cancer

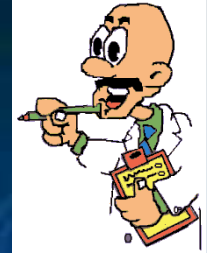


Eradication



Risk of developing GC

European, Asian, American Guidelines



Many efforts have been made in trying eradication

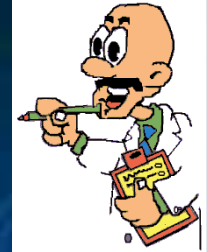
Several difficulties remain to be overcome

Triple therapy = the main eradication therapy

Widespread use/abuse antibiotics (respiratory tract infections)

Maastricht guidelines





Effectiveness of
triple therapy



mainly due to primary resistance towards
antibiotics

80%

clarithromycin over the past 10
years

9.8%

17.5%

Maastricht



clarithromycin

in empirical eradication
therapy

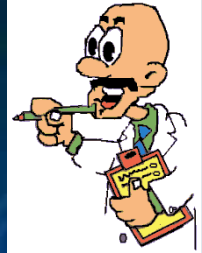


testing
susceptibility
for this antibiotic

before using it
if its resistance prevalence is higher than 15-
20%

Maastricht guidelines





Looking for the best eradication therapy

if the antimicrobial susceptibility is not available

which

1

we should ask to patients

how many antibiotics

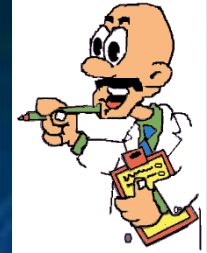
2

they used before



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Gut 2011

ESPGHAN/NASPGHAN
guidelines



antibiotic susceptibility testing for
clarithromycin

before starting clarithromycin-based triple
therapy

in areas/populations with a known high resistance rate
(>20%)

In Italy the clarithromycin resistance is around 25% both in adults and
children

Megraud et al, Gut 2013



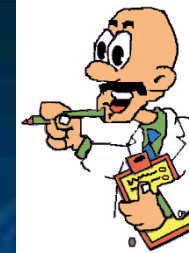
Francavilla et al, J Pediatr 2010





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Culture

common & specific

invasive diagnostic method

antimicrobial susceptibility of *H. pylori*



Thijs JC et al, Am J Gastroenterol 1996

sensitivity



variable (60–90%)



several methodological factors

time from sampling to processing

biopsy site

transport medium

Transportation time

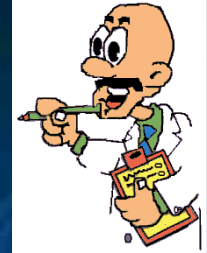
incubation conditions

culture medium



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culture of a single antral biopsy



the detection of *H. pylori* in > 90%

for optimal results

at least

One biopsy

antrum

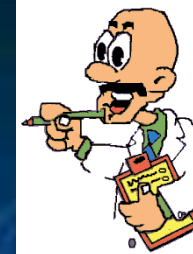
Two biopsies

corpus

Dixon MF et al, Am J Surg pathol, 1996



to ensure a correct diagnosis



in *H. pylori*
eradication

the most common antibiotics
used

in children

amoxicillin

clarithromycin

metronidazole

ESPGHAN-NASPGHAN Guidelines, 2011



Looking for the best eradication therapy

if the antimicrobial susceptibility is not
available

we should ask to
patients

which

1

how many
antibiotics

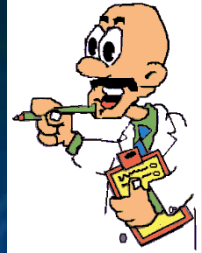
2

they used before



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We wanted to evaluate the variations in primary antibiotic susceptibility over last 13 years in children with *H. pylori* infection in Parma, northern Italy comparing with our previous results obtained in 2001

Street ME, .. Manfredi M, et al, Arch Dis Child 2002

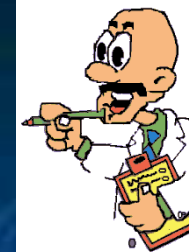


we diagnosed by endoscopy and histological examination
 66 naïve children with *H. pylori* infection



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Symptoms	Endoscopical aspects
Recurrent abdominal pain 27 pts (40.9%)	Nodular Gastritis 52 pts (78.7%)
Epigastric pain 19 pts (28.8%)	Duodenal Ulcer 3 pts (4.5%)
Vomiting 9 pts (13.6%)	Duodenal Erosion 2 pts (3%)
Gastric pyrosis 6 pts (9.1%)	Nodular Duodenitis 9 pts (13.6%)
Anemia 5 pts (7.6%)	

Clinical and endoscopical characteristics of patients

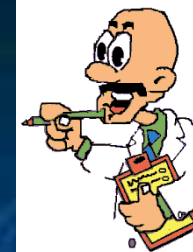
Endoscopic biopsy
specimens

two from the gastric antrum
two from the gastric corpus-
fundus

and microbiological

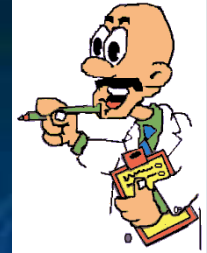
from the antrum

culture



Antibiotic	MIC interpretative values($\mu\text{g/ml}$)	Resistance Rate (years 1998-99)	Resistance Rate (years 2011-12)	p Value
Metronidazole	>16	35 (56%)	15 (33%)	0.014
Clarithromycin	>4	10 (16%)	12 (26%)	0.142
<u>Ampicillin</u>	>4	<u>2 (3%)</u>	<u>0</u>	ns
Tetracyclines	>16	1 (2%)	0	ns
Metronidazole + clarithromycin		5 (8%)	3 (7%)	ns
Total		63/75 (84%)	46/66 (70%)	0.079

Table 3. Differences in antibiotic resistances.



The eradication of *H. pylori* infection represents an enormous challenge in gastroenterology

H. pylori is not so easily attachable

local prevalence of antibiotic resistances

importance

mainly if the antimicrobial susceptibility

~~Culture development~~

therefore we must use an empirical eradication treatment

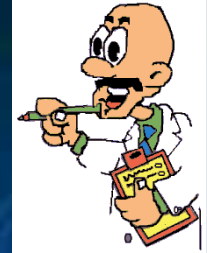
Megraud F et al, Gut 2013





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Culture



Useful, but disadvantages

Difficulty

Sensitivity

High costs

Our study shows a decline of culture development of *H. pylori* over the last 13 years: from 84% in 1998/99 to 70% in 2011/12 with no statistically significant value

Three biopsy samples
RUT positive

Culture can
be negative

62% culture pos

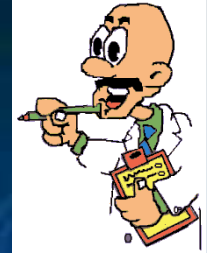


Porowska B et al Aliment Pharmacol Ther
2012



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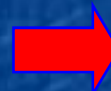
On the contrary

Other Italian researchers obtained a very high culture development rate of 94% in adults



Saracino IM et al, J Gastrointestin Liver Dis 2012

Chronic PPI intake



main cause of culture failure



Selgrad M, Malfertheiner P Aliment Pharmacol Ther 2012

biopsy specimens should also be taken from the gastric body

Culture development

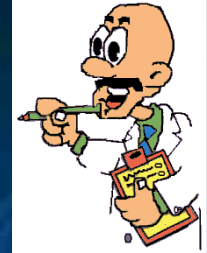


Intrinsic difficulty

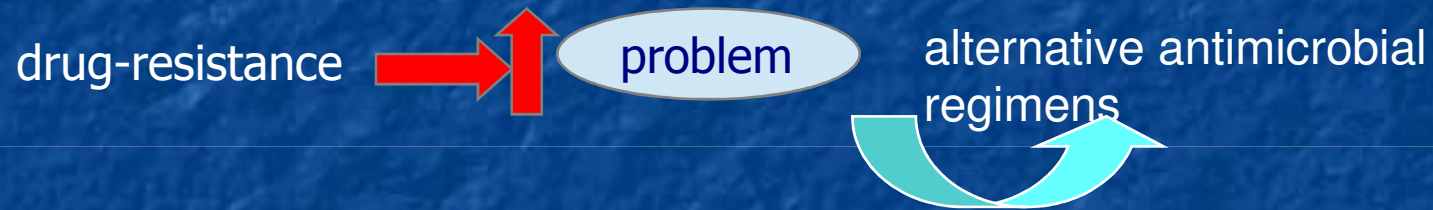


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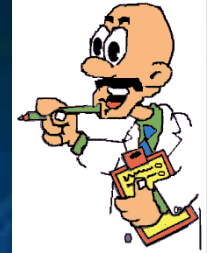
HELICOBACTER pylori THERAPY





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 ESPGHAN/NASPGHAN 

~~clarithromycin~~

In empirical therapy

In areas with R > 20%

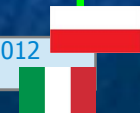
Bismuth-containing quadruple therapy

(B+A+C+M)

A good alternative choices

Sequential therapy

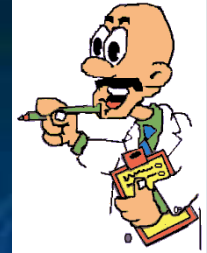
Horvath A et al, Aliment Pharmacol Ther 2012
Francavilla R et al, GUT 2008





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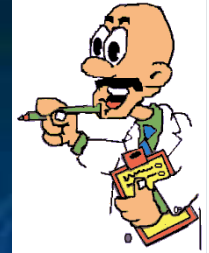
more
attention



to treat by
knowing
the antimicrobial susceptibility
prevalence



for increasing the successful eradication
rate



Therefore

clarithromycin-based
therapy
should be
performed

clarithromycin-susceptible strain

local clarithromycin resistance
rate
is known to be low (< 10%)

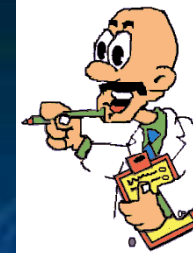
Maastricht guidelines





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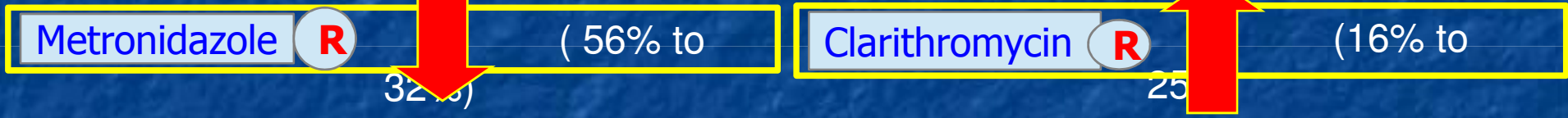


Our studies

2001

today

Street ME, ... Manfredi M, et al, Arch Dis Child 2001



Similar results

Seo JH et al, Pediatr Int 2013



Vecsei A et al, Helicobacter 2010



Amoxicillin (R)

very rare around the world

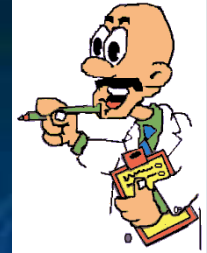
Vakil N, Vaira D, J Clin Gastroenterol 2013





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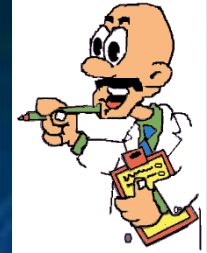
Culture

Not only single biopsy specimen from the antrum

We should taken at least another one sample from the gastric body

Selgrad M, Malfertheiner P Aliment Pharmacol Ther 2012





Conclusion 1

H. pylori culture

could now be substituted by molecular methods

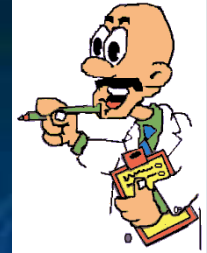
FISH

biopsies

PCR

do not require strict conditions of biopsy specimens transport

can be used to detect the point mutation associated to clarythromycin-resistance



Conclusions 2

Before recommending *H. pylori* eradication therapy

we should know

either

the antibiotic susceptibility of patient

or

the local distribution of antibiotic resistance rates

to have higher successful probabilities



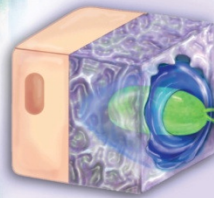
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Helicobacter pylori

Detection Methods, Diseases
and Health Implications



*Bacteriology Research
Developments*



Marco Manfredi
Gian Luigi de'Angelis
Editors

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Editors: Marco Manfredi and Gian Luigi de'Angelis ("Pietro Barilla" Children's Hospital, Univeristy of Parma, Parma, I

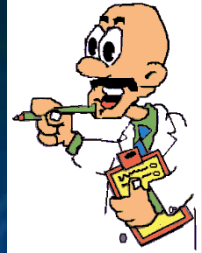
Book Description:

Pediatric gastrointestinal endoscopy has been greatly improving since its introduction and it is continuously evolving due to the 'tools' improvement and the specific training of the staff. Currently this technique can be performed in children of a wide age range, including preterm infants.



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Infection Control & Immunity

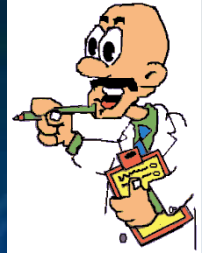
Marco Manfredi MD, PhD

Track 8: Infectious Diseases & Public Health



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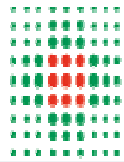
Dante Alighieri drew inspiration for the mountain of Purgatory



"...You can walk at Sanleo, near Urbino, and descend to Noli, near Savone: you can climb Mount Bismantova, south of Reggio, up to the summit, on foot: but here a man had to fly..."

Dante Alighieri
Divina Commedia Purgatory
Canto, IV, 26





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Thank you for
your attention



Infection Control & Immunity

Marco Manfredi MD, PhD

Track 8: Infectious Diseases & Public Health



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Thank you for
your attention



Infection Control & Immunity

Marco Manfredi MD, PhD

Track 8: Infectious Diseases & Public Health