



PREVENTION OF HELICOBACTER PYLORI INFECTION IN AFRICA – THE WAY TO GO

BY

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OUTLINE

Introduction

Discovery and characteristics of H. pylori

Prevalence of H. pylori infection in Africa

Transmission of H. pylori infection

Preventive Measures

Conclusion



INTRODUCTION

In 1982, Warren and Marshall discovered Helicobacter pylori (H. pylori) infection

The discovery of helicobacter pylori has **transformed the therapeutic approach to management** of conditions linked to this infection like gastritis,

- Peptic Ulcer Disease (PUD),
- primary B cell gastric lymphoma of MALT type and
- gastric adenocarcinoma.

Robinwaren J, Marshall B. Unidentified curved bacilli in on gastric epithelium in active chronic gastritis. Lancet 1983; 321 (8336):1273-5

The Clinical Outcomes of Helicobacter pylori Infections





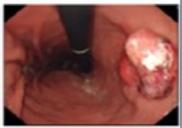
Asymptomatic or chronic gastritis



Chronic atrophic gastritis Intestinal metaplasia



Gastric or Duodenal ulcer

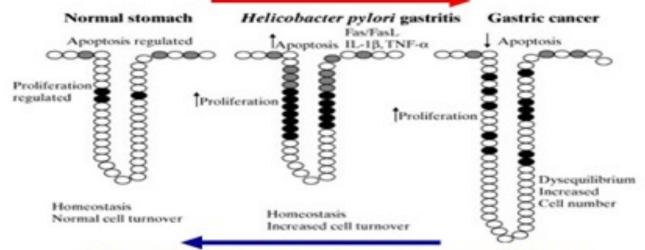


Gastric cancer MALT lymphoma

Е

Inflammatory mediators

COX-2/oxidative stress/ deranged apoptosis



Detouring with anti-inflammatory agents/drugs

COX-2 inhibitor (NSAIDs as anti-inflammatory strategy)

iNOS inhibitor/anti-inflammatory drug, e.g. rebamipide/natural products







 Barry Marshall and Robin Warren (to the right) are the two doctors and scientists, who discovered Helicobacter Pylori in 1982



Microaerophilic, **gram-negative** spiral rods Multiple polar sheathed flagella → highly motile with rapid corkscrew motion



- 100X more potent than other bacterial ureases
- ∘ Breaks down urea to NH₄+ and CO₂ \Rightarrow stomach acidity Ψ \Rightarrow possible for *H. pylori* to survive @ pH 2-3

 Graham DY, Sung JY. Helicobacter pylori. In Feldman M, Friedman LS, Brandt LJ (eds): Sleisenger and Fordtran's Gastrointestinal and Liver Disease, 8th Ed. Saunders Elsevier. Philadephia, 2006; pp1049-1066





HELICOBACTER PYLORI

- More than 90% of gastric cancers are associated with H. pylori infection class 1 carcinogen by
- -the WHO and
- international agency for research on cancer.
- Studies have suggested that eradication of gastric H. pylori can inhibit progression to gastric cancer by reversing gastric atrophy and metaplasia

- Moss SF. The clinical evidence linking Helicobacter pylori to gastric cancer. CellMol Gastroenterol Hepatol. 2017; 3(2): 183-91
- IARC Working groupon the Evaluation of Carcinogenic risks to Humans IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Biological Brisks IARC Monogr Eval Carcinog Risks Hum. 2012; 100 (Pt B): 1-441
- WGO Global Guidelines. Helicobacter pylori. May 2021.



HELICOBACTER PYLORI

- Has tropism for gastric epithelium
- it is found in the gastrum of humans in all parts of the world.

Oraham DY, Sung JY. Helicobacter pylori. In Feldman M, Friedman LS, Brandt LJ (eds): Sleisenger and Fordtran's Gastrointestinal and Liver Disease, 8th Ed. Saunders Elsevier. Philadephia, 2006; pp1049-1066



HELICOBACTER PYLORI

- Infection occurs in childhood and persist into adult life
 - when clinical manifestation typically occurs
 - -in up to 20% of those infected.
- Inflammatory response elicited is robust continues throughout life or until the infection is cured.
 - Graham DY, Sung JY. Helicobacter pylori. In Feldman M, Friedman LS, Brandt LJ (eds): Sleisenger and Fordtran's Gastrointestinal and Liver Disease, 8th Ed. Saunders Elsevier. Philadephia, 2006; pp1049-1066.



It is the most widespread bacterial infection worldwide occurring in 50% of the world's population.

The range is <10% - >90%

prevalence rate is as high as 80% in LMICs especially in Africa

Hooi JKY, Lai WY, Ng WK, Suen MMY. Underwood FE, Tanyingoh D, et al. Global prevalence of Helicobacter pylori infection: systematic review and meta-analysis. Gastroenterology. 2017 Aug 1; 153 (2): 420-9.

Leja M et al.Review: epidemiology of Helicobacter pylori infection. Helicobacter. 2019; 24(Suppl 1): e12635.



H. pylori prevalence rates in the continent vary among regions & communities

These reports are related to individuals that have developed clinical symptoms

Data on H. pylori infection in healthy people & early detection of this bacterium are limited in Africa

Smith et al. Helicobacter pylori infection in Africa: update of the current situation and challenges. Dig Dis. 2022; 40(4):535-44.



The discovery of H. pylori by Warren and Marshall in 1982 was associated with **enigmas** which are being gradually resolved

In Africa, like in some other LICs of the world, **one enigma** is the association of high *H. pylori* prevalence and low incidence of gastric cancer.

Several factors may be responsible in *H.pylori* pathogenesis including environment, diet, host and bacterial genetics

Campbell DI et al. The African enigma: low prevalence of gastric atrophy, high prevalence of chronic inflammation in West African adults and children. Helicobacter. 2001; 6(4): 263-7

Graham DY, Lu H, Yamaoka Y. African, Asian or Indian enigma, the East Asian Helicobacter pylori: facts of medical myths. Jdig Dis. 2009;10(2): 77-84.



It is now well established that **gastric cancer** caused by H. pylori depends on the presence of the **cag** pathogenicity island that encodes CagA classified as a primary carcinogen.

Virulent (type1) – express: s1/m1 of the Vacuolating cytotoxin A

Avirulent (type 2) express: s2/m2

Hatakeyama M. Oncogenicmechanisms of the Helicobacter pylori CagA protein. Nat Rev Cancer. 2004; 4 (9): 688-94.

Fagoones S, PellicanoR. Helicobacter pylori: molecular basisfor colonization and survival in gastric environment and resistance to antibiotics. A short review. If ect Dis. 2019; 51 (6): 399-408



Non-carcinogenic strain with possible benefits is being debated-reduce Asthma.

Others promote DM & Cardiac diseases.

In Africa, there is a knowledge gap in the genotypes of circulating H. pylori strains,

Our study done on patients isolates from Nigeria and South Africa showed that...

Founda EM et al. Helicobacter pylori seropositivity protects against childhood asthma and inversely correlates to its clinical and functional severity. Allergol Immunopathol. 2018; 46 (1): 76-81.

Rayner CK et al. Stomach bugs and diabetes: an outstanding observation or just confounding. Diabetes Care. 2012; 35(3): 463-4

www.nature.com/scientificreports



SCIENTIFIC REPORTS

natureresearch



OPEN Helicobacter pylori patient isolates from South Africa and Nigeria differ in virulence factor pathogenicity profile and associated gastric disease outcome

> Pia Palamides¹, Tolulope Jolaiya², Ayodeji Idowu³, Eva Loell¹, Charles Onyekwere⁴, Rose Ugiagbe⁵, Ifeanyi Agbo⁵, Olufunmilayo Lesi⁶, Dennis Ndububa⁷, Olusegun Adekanle⁷, Manuel Carranza⁸, Reidwaan Ally⁹, Henry Njom³, Isaac A. Adeleye², Ute Harrison¹, Anna Clarke³, Wolfgang Fischer^{1,11}, Stella Smith¹⁰ & Rainer Haas^{1,11} □



Major determinants of infection are

age,

socioeconomic status

country of origin/environment and

host genetics: higher rate of concordance in monozygotic twins

Everhart JE et al. Seroprevalence and ethnic differences in Helicobacter pylori infection among adults in the United States. J Infect Dis 181:1359, 2000.

Webb PM et al. Relationship between infection with Helicobacter pylori and living conditions in childhood: Evidence for person transmission in early life. BMJ 308: 750, 1994.



Socio-economic status in childhood is a major determinant of prevalence and this is reflective of

personal hygiene

environmental sanitation,

living conditions and

level of education.

Webb PM et al. Relationship between infection with Helicobacter pylori and living conditions in childhood: Evidence for person to person transmission in early life. BMJ 308: 750, 1994.

Mendal et al. Childhood living conditions and Helicobacter pylori seropositivity in adult life. Lancet 339: 896, 1992.



TRANSMISSION OF H. PYLORI INFECTION

Humans are the primary reservoir and primary mode of transmission is person to person (Epid & genetic studies)

- 1. Faeco- oral (detection in stool by PCR and culture)
- 2. Oral-oral: found in dental plaques and saliva,

Evidences against: are - low concordance in developed countries amongst couples without children, &

- dentists and dental staff are not at increased risk of infection)

3. Gastro oral route

Malati HM et al. Transmission of Helicobacter pylori infection. Studies in families of healthy individuals. Scand J Gastroenterol 26: 927, 1991.

Parsonnet et al. Fecal and oral shedding of Helicobacter pylori from healthy infected adults. JAMA 282: 2240, 1999

Fergusson et al. Isolation of Helicobacter pylori from saliva. J Clin Microbiol 31: 2802, 1993



TRANSMISSION OF H. PYLORI INFECTION

. 3. Gastro oral route

- epidemics in volunteers undergoing gastric intubations
- transmission from inadequately disinfected endoscopes,
- -higher incidence in those regularly exposed to gastric secretions or vomitus or spit ups from infected children.

Axon AT. Is Helicobacter pylori a transmitted by the gastro-oral route? Aliment Pharmacol Ther 9: 585, 1995.



TRANSMISSION OF H. PYLORI INFECTION

Measures which will interrupt transmission of H. pylori like **improved social economic** status will reduce the burden of the disease in Africa.

Smith SI, Schulz C, Ugiagbe R, Ndip R, Dieye Y, Leja M, Onyekwere C, Ndububa D, Ajayi A, Jolaiya TF, Jaka H, Setshedi M, Gunturu R, Otegbayo JA, Lahbabi-Amrani N, Arigbabu AO, Kayamba V, Nashidengo PA. Helicobacter pylori Diagnosis and Treatment in Africa: The First Lagos Consensus Statement of the African Helicobacter and Microbiota Study Group. Dig Dis. 2024;42(3):240-256. doi: 10.1159/000537878. Epub 2024 Mar 15. PMID: 38493766.



WHAT ARE THE PREVENTIVE MEASURES/STRATEGIES?

Primordial

Primary

Secondary and

Tertiary preventive measures.



PRIMORDIAL PREVENTIVE MEASURES

This involves:

- -Addressing underlying risk factors &
- -Promoting a healthy environment to minimize the emergence of the infection

The interventions include:

- -Initiatives to improve overall hygiene, sanitation and access to clean water.
- -Avoiding contaminated food and promoting a healthy life style
- -Public health campaigns and education



PRIMORDIAL PREVENTIVE MEASURES/STRATEGIES CONTINUED

Others are:

Practice of good hygiene and hand washing using anti bacterial soaps, anti septic washes and hand sanitisers

Institution of good hygiene with food preparation and avoidance of contaminated food and water.

Proper washing and sterilization of endoscopes will prevent transmission from one patient to another



PRIMORDIAL PREVENTION CONTINUED

Proper disposal of waste and sewage

Avoidance of close contact with infected family members and persons as much as possible (e.g., kissing, by sharing eating utensils and drinking glasses) &

Adherence to universal precautions in medical practice and indeed by all will prevent transmission from person to person.



PRIMARY PREVENTIVE MEASURES/STRATEGIES

These are actions taken prior to the onset/development of the disease.

Interventions include immunization and screening

Developing and implementing vaccines against H. pylori is an effective strategy for primary prevention

Efforts should be expedited on production of human vaccines against H. pylori infections.

Sutton P. At last, vaccine-induced protection against Helicobacter pylori. Lancet. 2015; 386:1424-1425.





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Clinical Trial > Lancet. 2015 Oct 10;386(10002):1457-64. doi: 10.1016/S0140-6736(15)60310-5. Epub 2015 Jun 30.

Efficacy, safety, and immunogenicity of an oral recombinant Helicobacter pylori vaccine in children in China: a randomised, double-blind, placebo-controlled, phase 3 trial

Ming Zeng ¹, Xu-Hu Mao ², Jing-Xin Li ³, Wen-De Tong ⁴, Bin Wang ¹, Yi-Ju Zhang ³, Gang Guo ², Zhi-Jing Zhao ¹, Liang Li ³, De-Lin Wu ⁵, Dong-Shui Lu ², Zhong-Ming Tan ³, Hao-Yu Liang ¹, Chao Wu ², Da-Han Li ⁵, Ping Luo ², Hao Zeng ², Wei-Jun Zhang ², Jin-Yu Zhang ², Bo-Tao Guo ², Feng-Cai Zhu ⁶, Quan-Ming Zou ⁷



PRIMARY PREVENTION CONTINUED

Screening can be done with non invasive tests such as stool antigen test, urea breath test and serology.



Involves early diagnosis and prompt treatment:

The interventions are

- early detection and presentation to a health facility
- arriving at a definitive diagnosis and
- institution of optimal therapy.

All patients with chronic GI symptoms that may be associated with H. pylori infection should be tested and treated to prevent exposure to family members and others.

The test ant treat strategy is also recommended in NSAID users & non-ulcer dyspepsia



Also, **post treatment confirmation of H. pylori eradication** using diagnostic tests

monitoring for potential complications like gastric cancer

Regular medical follow ups, adherence to prescribed treatments &

Treatment to prevent recurrence of infection and its complications like peptic ulcer disease, MALT lymphoma and gastric cancer all come under secondary prevention.



Diagnostic tests for H. pylori:

Biopsy based tests (histology, rapid urease test, PCR or culture)

Non invasive test (urea breath test, stool antigen test, serologic test, stool PCR)



Invasive diagnosis with standardized **endoscopic biopsy** is indicated in patients with dyspeptic symptoms **older than 45 years** or in patients with **alarm symptoms**.

The sensitivity and specificity of **histology** for detection of *H. pylori* vary between 53% and 90%.

Dixon MF et al. Classification and grading of gastritis. The updated Sydney system. International workshop on the histopathology of gastritis, Houston 1994. Am J Surg Pathol. 1996;20(10): 1161-81.

Smith SI, Schulz C, Ugiagbe R, Ndip R, Dieye Y, Leja M, Onyekwere C, Ndububa D, Ajayi A, Jolaiya TF, Jaka H, Setshedi M, Gunturu R, Otegbayo JA, Lahbabi-Amrani N, Arigbabu AO, Kayamba V, Nashidengo PA. Helicobacter pylori Diagnosis and Treatment in Africa: The First Lagos Consensus Statement of the African Helicobacter and Microbiota Study Group. Dig Dis. 2024;42(3):240-256. doi: 10.1159/000537878. Epub 2024 Mar 15. PMID: 38493766.



Mucosal biopsies may also be tested for the presence of urease using the **rapid urease tests** consisting of- a urea-rich medium with

- a pH- sensitive dye.

One cross-sectional case-control study in South Africa reported a **100% correlation** between histology and Rapid Urease Test for the diagnosis of *H. pylori* in bleeding and non-bleeding gastric ulcers.

Kgomo MKMK, KsM. The prevalence of Helicobacter pylori infection in bleeding and non-bleeding gastric ulcers: a cross sectional case-control study. J Bioanal Biomed. 2016; 8(4)



Direct detection of *H. pylori* from biopsies using real-time PCR and stool PCR have been demonstrated in Nigeria.

Culturing for antibiotic susceptibility: is not indicated for initial diagnosis but may be done after 3 failed Treatments.

Ajayi A, Jolaiya T, Smith SI. Drect detection of Helicobacter pylori from biopsies of patients in Lagos, Nigeria using reai-time PCR-a pilot study. BMC Res Notes. 202`;14 (1): 90

Smith SI, Schulz C, Ugiagbe R, Ndip R, Dieye Y, Leja M, Onyekwere C, Ndububa D, Ajayi A, Jolaiya TF, Jaka H, Setshedi M, Gunturu R, Otegbayo JA, Lahbabi-Amrani N, Arigbabu AO, Kayamba V, Nashidengo PA. Helicobacter pylori Diagnosis and Treatment in Africa: The First Lagos Consensus Statement of the African Helicobacter and Microbiota Study Group. Dig Dis. 2024;42(3):240-256. doi: 10.1159/000537878. Epub 2024 Mar 15. PMID: 38493766.



Urea breath test (UBT) is regarded as a gold standard for non-invasive method of *H. pylori* diagnosis.

Two different UBTs are available: 13C and 14C

Both provide comparable results. **14C uses radioactive isotopes** with some restrictions when used in children or pregnant woman.

Dore MP, Pes GM. What is new in Helicobacter pylori diagnosis. An overview . J Clin Med. 2021; 10(10): 2091



UBT has advantages of -being non-invasive, -safe, accurate with

- high sensitivity of 95.9% and a specificity of 95.7%.

UBT is also useful for epidemiological and

-follow-up examinations after eradication.

Not readily available in many African countries- Only available in Nigeria, Algeria, Egypt and South Africa.

Palamides P, Jolaiya T, Idowu A, Loell E, Onyekwere C, Ugiagbe R et al. Helicobacter pylori patient isolates from South Africa and Nigeria differ in virulence factor pathogenecity profile and associated gastric diseaseoutcome. Sci Rep. 2020; 10(1): 11409.



The stool enzyme-linked immunosorbent assay (**ELISA**) using monoclonal antibody is an efficient non-invasive test for the diagnosis of *H. pylori* infection.

SAT is a fast, simple, and inexpensive test useful for - epidemiological studies,

- screening programs and
- follow-up examinations after eradication.

The sensitivity and specificity of SAT is 94% and 97%, respectively.

Malfertheiner P, Mégraud F,O'Morain CA, et al. Management of Helicobacter pylori infection—the Maastricht IV Florence Consensus Report. Gut 2012; 61:646–64.

Koletzeko S et al. Evaluation of a novel monoclonal enzyme immunoassay for detection of Helicobacter pylori antigen in stool from children. Gut. 2003; 52(6): 804-6.

Ndip RN et al. Helicobacter pylori in the faeces of asymptomatic children in the Buea and Limbe health districts of Cameroon: a pilot study. Trop Med Int Health. 2004;9(9): 1036-40.



SECONDARY PREVENTIVE MEASURES CONTD

Serology; may be useful for the initial diagnosis of H. pylori infection if there is a high pretest probability,

Low specificity and sensitivity make serologic tests not the preferred test for assessing active infection.

they are also **not useful/practical to assess cure** after antimicrobial therapy as

Paired specimens are required: before specimens frozen and after specimens 6 months after treatment.



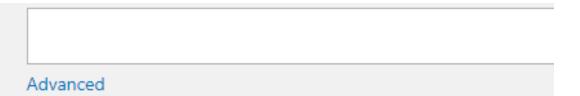
TREATMENT OF H. PYLORI

Resistance to antibiotics by H. pylori determines the efficacy of eradication therapy

The most effective regimens to cure H. pylori infection are combinations of two antibiotics and adjunctive agents (tripple therapy) taken for 14 days.

Meta analyses have confirmed that 1-week tripple therapy produce less than optimal results hence the recommendation of 14 days therapy.







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> Health Sci Rep. 2024 Mar 7;7(3):e1960. doi: 10.1002/hsr2.1960. eCollection 2024 Mar.

Efficacy and tolerability of *Helicobacter pylori* eradication regimes in South Kivu, Eastern of the Democratic Republic of Congo: A single center observational study

Tony A Shindano 1 2 3 4 5, Manix I Masimango 1 6, Antoine S Kishabongo 2 4

Affiliations + expand

PMID: 38455644 PMCID: PMC10918698 DOI: 10.1002/hsr2.1960



TREATMENT OF H. PYLORI CONTD

As established in several international guidelines, eradication therapy is the treatment of choice in infected patients

Advantages of eradication include

reducing the reservoir of infected individuals and preventing transmission,

reducing costs from management of the disease and complications,

halting the progression of mucosa damage &

cure of H. pylori related diseases.

Smith SI, Schulz C, Ugiagbe R, Ndip R, Dieye Y, Leja M, Onyekwere C, Ndububa D, Ajayi A, Jolaiya TF, Jaka H, Setshedi M, Gunturu R, Otegbayo JA, Lahbabi-Amrani N, Arigbabu AO, Kayamba V, Nashidengo PA. Helicobacter pylori Diagnosis and Treatment in Africa: The First Lagos Consensus Statement of the African Helicobacter and Microbiota Study Group. Dig Dis. 2024;42(3):240-256. doi: 10.1159/000537878. Epub 2024 Mar 15. PMID: 38493766.

Malfertheiner P, Megraud F, Rokkas T, Gisbert JP, Liou JM, Schulz C et al. Management of Helicobacter pylori infection—the Maastricht VI/Florence Consensus Report. Gut 2022;71(9):1724-62.

Sugano K, Tack J, Kuipers EJ, Graham DY, El-Omar EM, Miura S et al. Kyoto global consensus report on Helicobacter pylori gastritis. Gut. 2015; 64 (9): 1353-67.



First line therapy for the eradication of *Helicobacter pylori* infection is the combination of amoxicillin, clarithromycin and a proton pump inhibitor (PPI). International guidelines recommend use of this standard triple therapy for 14 days.

Metronidazole is a substitute for amoxicillin, but current guidelines do not recommend the use based on a dramatic increase of resistance to more than 40%.



An alternative first line therapy is the quadruple therapy with amoxicillin, clarithromycin, metronidazole and a proton pump inhibitor.

The recommended second line or salvage therapeutic regimen is with bismuth-based quadruple therapy or levofloxacin-based triple therapy or sequential non-bismuth quadruple therapy.

In the choice of a regimen for second line therapy, attempts should be made to avoid antibiotics previously used.



In the United States, the preferred first line therapy is with a combination of bismuth, metronidazole, tetracycline or amoxicillin, and a PPI (bismuth quadruple therapy).

Current European guidelines stratify by the local clarithromycin resistance rates: less than 15% clarithromycin based triple therapy will be recommended, higher than 15% or unknown bismuth based quadruple therapy will be recommended.



Overall, however, *H. pylori* eradication with the **standard triple therapy** should be employed only in areas with local eradication rates **higher than 85%.**

Our published African guidelines support these recommendations:



Digestive Diseases

Stomach and Duodenum: Review Article

Dig Dis 2024;42:240-256 DOI: 10.1159/000537878 Received: September 28, 2023 Accepted: February 14, 2024 Published online: March 15, 2024

Helicobacter pylori Diagnosis and Treatment in Africa: The First Lagos Consensus Statement of the African Helicobacter and Microbiota Study Group

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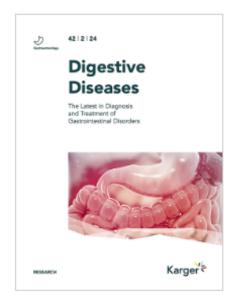


The few available African studies on *H. pylori* susceptibility report divergent antibiotic resistance rates. Resistance to metronidazole is almost 100% in most reports while resistance to amoxicillin ranges from 30% to 85%.



Volume 42, Issue 2

April 2024



RESEARCH ARTICLES | JANUARY 05 2024

Prevalence of Clarithromycin-Resistant Helicobacter pylori Strains in Zambia: A Sub-Saharan African Country 🖯

Subject Area: 🖑 Gastroenterology

Tshegofatso Kebotsamang; Derick Munkombwe; Lalusha Bwalya; Paul Kelly; Violet Kayamba 🕮

Dig Dis (2024) 42 (2): 154-160.

https://doi.org/10.1159/000535454 \(\sigma\) Article history

PubMed:38185098



The lack of consistent resistance data from Africa and the lack of consequent examinations of eradication success emphasize **the need for studies**.

H. pylori Africa Registry has been created.



H. pylori registry has been created

• We invite **Gastroenterologists** working in hospitals in **Africa** to join the project: **Hp-Africa-Registry** and upload patients data so we can fill some of these gaps.



Patients receiving *H. pylori* eradication therapy should be offered a **test to confirm eradication**.

Non-invasive tests are recommended such as UBT and SAT-

The treatment outcome should be **done not less than 4 weeks** after the completion of eradication therapy.

Due to the prolonged effect of antibacterial activity of antibiotics and bismuth compounds.

Succeptibility testing is recommended after 3 failed therapies.



Patients should complete the full course of therapy (antibiotics and acid blockers) to maximize the potential for a cure.

Advantages of eradication include reducing the reservoir of infected individuals and preventing transmission.



TERTIARY PREVENTIVE MEASURES

This involves managing and preventing complications and rehabilitation.

Interventions here include

Treating complications like peptic ulcer disease, MALT lymphoma and gastric cancer

Regular medical follow ups and adherence to prescribed treatments.



CONCLUSION

I will like to conclude with these 2 recommendations by the The First Lagos consensus statement of the AHMSG:

1. The reinfection with *H. pylori* after successful eradication should be studied in Africa.

2. The widespread implementation of programs focused on personal hygiene, environmental hygiene and improved living conditions has the potential to prevent the transmission of H. pylori and reduce the prevalence in Africa.



THANK YOU