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Review Article

A review on Stomach cancer and it's prevention

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Abstract:
Stomach cancer, or gastric cancer, remains one of the most fatal malignancies globally, with a significant burden in both incidence and mortality. Although its prevalence has declined in some developed regions due to better screening and reduced Helicobacter pylori infections, it continues to be a major health concern in low- and middle-income countries. This report provides an in-depth analysis of stomach cancer, focusing on its pathophysiology, risk factors, diagnostic advancements, treatment options, and preventive strategies. With particular emphasis on public health approaches and recent innovations in oncology, the report aims to bridge existing gaps in awareness, early diagnosis, and effective management. The integration of modern therapeutic technologies, public education, and healthcare policies are crucial to reducing the disease burden. The future of gastric cancer control lies in a combination of targeted therapies, early detection programs, and global collaboration.
Keywords: Stomach cancer, gastric cancer, Helicobacter pylori, prevention, diagnosis, chemotherapy, pathophysiology, public health

Chapter 1: Introduction

Background

Stomach cancer, also known as gastric cancer, is one of the leading causes of cancer-related deaths worldwide, despite a declining incidence in some regions. It arises predominantly from the gastric mucosa and is characterized by late diagnosis and poor prognosis. According to the Global Cancer Observatory (GLOBOCAN), stomach cancer ranked fifth in incidence and fourth in mortality among all cancers in 2020, accounting for over 1 million new cases and nearly 770,000 deaths globally [1].

Stomach cancer is more prevalent in East Asia, Eastern Europe, and parts of Central and South America. Its incidence is influenced by numerous factors including Helicobacter pylori (H. pylori) infection, dietary habits, genetic predisposition, smoking, and alcohol consumption. Males are affected nearly twice as often as females, and most cases occur in individuals over 50 years of age [2].

Classification of Stomach Cancer

Stomach cancer is commonly classified based on its histological features and anatomical location:

- Histological Classification (Lauren Classification):
    - Intestinal type: Resembles gland-forming adenocarcinomas, usually linked to environmental factors.

- Diffuse type: Poorly differentiated, more aggressive, and often affects younger individuals.

- Anatomical Location:
  - Cardia (upper stomach)
  - Body (middle)
  - Antrum (lower stomach)

Global and Indian Scenario

Stomach cancer incidence shows geographical variation. High-risk regions include Japan, Korea, and China, where screening programs have been implemented. In India, it is the fifth most common cancer among males and seventh among females, with hotspots observed in the southern and northeastern states [3].

Country/Region	Incidence Rate (per 100,000)	Mortality Rate (per 100,000)
Japan	27.5	11.4
South Korea	39.6	13.8
India	5.4	4.9
Global Average	11.1	8.5

Significance of the Study

Despite improved diagnostic modalities and therapeutic approaches, the prognosis of stomach cancer remains poor due to late-stage diagnosis. The 5-year survival rate remains below 30% in most countries without early detection programs [4]. There is a pressing need to focus on preventive strategies, early detection, and patient awareness to reduce the disease burden.

Objectives of the Project

The present project aims to:

1. Describe the pathophysiology and risk factors associated with stomach cancer.
2. Explore the diagnostic approaches and current treatment modalities.
3. Analyze preventive measures and recent advancements in the field.
4. Discuss future trends and public health interventions for effective control.

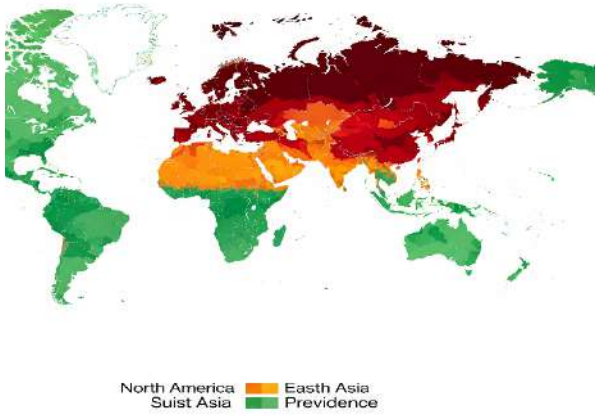

Fig.1 Global Map of Stomach Cancer Incidence

Chapter 2: Pathophysiology of Stomach Cancer

Introduction

The pathophysiology of stomach cancer involves a complex interplay of environmental, genetic, and molecular mechanisms that culminate in the malignant transformation of gastric epithelial cells. The majority of stomach cancers are adenocarcinomas, which arise from the glandular epithelium of the stomach lining. These can further be classified into intestinal and

diffuse types based on morphological and biological behaviors.

Cellular and Molecular Changes

Stomach cancer development typically follows a multistep cascade of histological changes known as the Correa cascade. This progression includes:

1. Chronic Gastritis →
2. Atrophic Gastritis →
3. Intestinal Metaplasia →
4. Dysplasia →
5. Carcinoma

This sequence is mainly associated with Helicobacter pylori infection, which induces chronic inflammation and promotes genetic instability in gastric mucosal cells [5].

Genetic and Epigenetic Mechanisms

Several genetic alterations are central to the pathogenesis of gastric cancer:

- TP53 mutations: Common in both intestinal and diffuse types, resulting in impaired apoptosis.
- CDH1 mutations: Typically associated with hereditary diffuse gastric cancer (HDGC), affecting E-cadherin-mediated cell adhesion.
- Microsatellite instability (MSI): Characterized by hypermutability due to mismatch repair deficiency.
- Epigenetic changes: Hypermethylation of promoter regions of tumor suppressor genes such as MLH1, p16, and APC contributes to tumor progression [6].

Role of Helicobacter pylori

H. pylori play a critical role in gastric carcinogenesis through:

- Secretion of cytotoxin-associated gene A (CagA) and vacuolating cytotoxin A (VacA), leading to epithelial injury.
- Promotion of chronic inflammation and immune evasion.
- Induction of oxidative stress and DNA damage in gastric cells.

It has been classified as a Group I carcinogen by the World Health Organization [7].

Tumor Microenvironment (TME)

The gastric tumor microenvironment includes a mixture of immune cells, fibroblasts, extracellular matrix proteins, and cytokines. Components of the TME support cancer cell proliferation, angiogenesis, immune suppression, and metastasis:

- Tumor-associated macrophages (TAMs): Promote tumor growth and angiogenesis.
- Myeloid-derived suppressor cells (MDSCs): Suppress anti-tumor immunity.
- VEGF overexpression: Stimulates angiogenesis necessary for tumor expansion [8].

Angiogenesis and Metastasis

Tumor growth beyond a few millimeters requires angiogenesis. Vascular endothelial growth factor (VEGF) is a critical mediator of new blood vessel formation. Once the tumor invades deeper gastric layers, it can spread through:

- Lymphatic dissemination → regional lymph nodes
- Hematogenous route → liver and lungs
- Peritoneal seeding → advanced cases

Pathological Features

Type	Histology	Behavior
Intestinal	Gland-like, well-differentiated	Slower progression
Diffuse	Poorly cohesive, signet ring cells	More aggressive and infiltrative
Mixed	Features of both intestinal and diffuse types	Variable

Chapter 3: Risk Factors and Etiology

Introduction

Understanding the risk factors and etiology of stomach cancer is vital for both prevention and early detection. Gastric cancer arises from a multifactorial origin involving a combination of environmental exposures, infectious agents, lifestyle choices, and genetic susceptibility. This chapter categorizes and elaborates on the modifiable and non-modifiable risk factors contributing to the development of stomach cancer.

Infectious Agents

- Helicobacter pylori: The single most important risk factor for non-cardia gastric cancer. Chronic infection promotes gastritis and precancerous lesions [9].
- Epstein–Barr Virus (EBV): Associated with about 10% of gastric cancers. EBV-positive tumors exhibit high lymphocyte infiltration and PD-L1 expression [10].

Dietary and Lifestyle Factors

- High salt intake: Salt damages the gastric mucosa, enhances H. pylori colonization, and increases nitrosamine production.
- Low intake of fruits and vegetables: Reduces protective antioxidants and dietary fiber.
- Smoked and processed meats: Contain nitrates/nitrites that are converted to carcinogenic compounds.
- Smoking and alcohol consumption: Associated with increased risk, particularly for upper gastric cancers [11].

Lifestyle Factor	Effect on Risk	Evidence
High salt diet	↑ Risk (2–3× higher)	WHO, WCRF [12]
Fruits & vegetables	↓ Risk	EPIC study, WCRF [12]
Processed meat	↑ Risk	IARC classification [13]
Tobacco smoking	↑ Risk	Strong evidence (RR: 1.5–2.0)

Occupational and Environmental Exposures

- Exposure to coal dust, rubber processing chemicals, and asbestos has been linked with higher gastric cancer incidence in certain industrial settings.
- Consumption of contaminated water or food with mycotoxins and aflatoxins may also contribute [14].

Genetic and Familial Factors

- Hereditary Diffuse Gastric Cancer (HDGC): Caused by mutations in the CDH1 gene.
- Familial adenomatous polyposis (FAP) and Lynch syndrome also increase gastric cancer risk.
- A positive family history of gastric cancer in first-degree relatives increases the risk by 2-3 fold [15].

Pre-malignant Gastric Conditions

- Chronic atrophic gastritis: Especially autoimmune types.
- Intestinal metaplasia and gastric dysplasia are established precursors.
- Gastric polyps, especially adenomatous types, have malignant potential [16].

Demographic and Geographic Factors

- Age and Sex: Risk increases significantly after age 50. Males are more commonly affected.
- Ethnicity: Higher incidence observed in East Asians, South Americans, and Eastern Europeans.
- Geography: Higher in developing nations due to dietary, hygienic, and infection-related factors.

Risk Factor Interactions

The presence of multiple risk factors can amplify carcinogenic effects. For instance, H. pylori infection combined with high salt intake or smoking significantly elevates the risk compared to individual exposure alone [17].

Risk Prediction Models

Efforts are ongoing to develop tools integrating genetic, clinical, and environmental factors to stratify gastric cancer risk and guide screening strategies. These include:

- ABC method (Anti-H. pylori antibody & serum pepsinogen levels)
- Kyoto classification using endoscopic findings

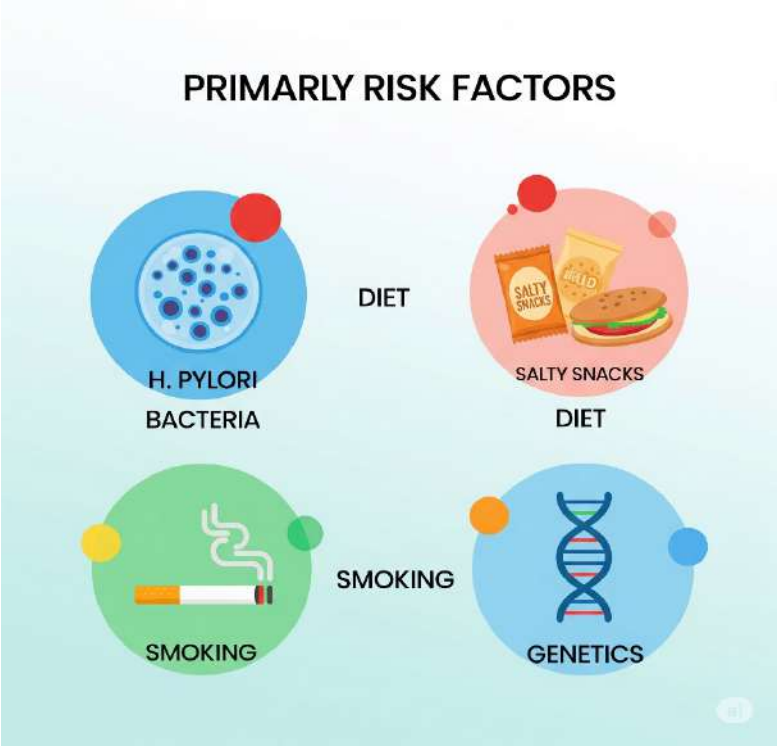

Fig.2 Major Causes and Risk Factors of Stomach Cancer

Chapter 4: Diagnosis and Staging

Introduction

Early detection of stomach cancer significantly improves prognosis and expands treatment options. However, most cases are diagnosed at advanced stages due to non-specific early symptoms. This chapter discusses the clinical presentation, diagnostic methods, staging systems, and recent advances in the detection of gastric cancer.

Clinical Features and Symptoms

Early gastric cancer is often asymptomatic or presents with vague symptoms such as:

- Indigestion or heartburn
- Mild abdominal discomfort
- Bloating and early satiety

As the disease progresses, more definitive signs appear:

- Persistent upper abdominal pain
- Nausea and vomiting
- Unintentional weight loss
- Hematemesis or melena
- Anaemia-related fatigue [18]

Diagnostic Approaches

- Upper Gastrointestinal Endoscopy (EGD): Gold standard for visualizing lesions and obtaining biopsies.
- Endoscopic Ultrasound (EUS): Essential for assessing tumour depth (T staging) and nearby lymph nodes.
- Biopsy and Histopathology: Confirms malignancy, determines type

(intestinal/diffuse), and grades differentiation.

Imaging Studies

- CT scan: Evaluates tumour size, nodal involvement, and distant metastasis.
- PET-CT: Detects metabolically active lesions; useful in staging and recurrence detection.
- MRI: Occasionally used for liver metastases or in patients allergic to contrast media [19].

Diagnostic Tool	Purpose	Strengths
EGD with Biopsy	Visual and tissue diagnosis	Direct confirmation, biopsy capability
EUS	Tumor depth & regional lymph nodes	Best for local staging (T and N)
CT scan	Distant metastasis and organ involvement	Widely available, fast
PET-CT	Metastatic spread and recurrence	Functional imaging

Laboratory Tests

- Complete blood count (CBC): May reveal anaemia.
- Tumour markers:
  - Carcinoembryonic antigen (CEA)
  - Carbohydrate antigen 19-9 (CA 19-9)
  - CA 72-4 These markers are not diagnostic but help monitor disease progression and response to therapy [20].

Staging of Stomach Cancer

Staging helps guide treatment and determine prognosis. The AJCC/UICC TNM system is the most widely used:

- T (Tumour): Depth of invasion
- N (Nodes): Regional lymph node involvement
- M (Metastasis): Distant spread

Summary of TNM Staging

Stage	Description
Stage I	Limited to mucosa/submucosa, minimal lymph nodes
Stage II	Invasion into muscularis with nodal involvement
Stage III	Serosa invasion and/or multiple lymph nodes
Stage IV	Distant metastasis (liver, lung, peritoneum)

Endoscopic Screening Programs

Countries with high incidence (e.g., Japan, South Korea) have national screening programs that include:

- Periodic endoscopy for individuals over 40
- Use of serum pepsinogen and H. pylori serology for risk stratification

These programs have successfully improved early detection rates and survival outcomes [21].

Molecular and Genetic Testing

- HER2 Testing: HER2-positive gastric cancers benefit from trastuzumab.
- MSI and PD-L1 expression: Help identify candidates for immunotherapy.
- Next-Generation Sequencing (NGS): Enables precision oncology in advanced cases [22].

Chapter 5: Current Treatment Approaches

Introduction

Treatment for stomach cancer depends on the stage, location, histological type, and molecular characteristics of the tumour, as well as the overall health of the patient. Early-stage cancers may be curable with surgery alone, while advanced stages often require multimodal therapy. This chapter outlines the current

standard of care, including surgical, medical, and radiation therapies.

Surgical Treatment

Surgery remains the main curative treatment for localized gastric cancer. Types of surgical procedures include:

- Subtotal (Distal) Gastrectomy: Removal of the lower part of the stomach.
- Total Gastrectomy: Complete removal of the stomach, often with oesophagojejunostomy reconstruction.
- Lymphadenectomy: Removal of lymph nodes; D2 lymphadenectomy is standard in East Asia [23].

Minimally invasive techniques, such as laparoscopic or robotic surgery, are increasingly used with comparable oncological outcomes in early-stage cancers.

Endoscopic Treatments

- Endoscopic Submucosal Dissection (ESD): Enables en bloc removal of superficial cancers without lymph node involvement.
- Endoscopic Mucosal Resection (EMR): Suitable for very early-stage lesions.

These are preferred for patients with T1a tumours confined to the mucosa and no nodal risk [24].

Chemotherapy

Systemic chemotherapy is used in various stages:

- Neoadjuvant (pre-operative): Shrinks tumours before surgery to improve respectability.
- Adjuvant (post-operative): Reduces recurrence risk.
- Palliative chemotherapy: Used in advanced/metastatic cases.

Common regimens:

- ECF (Epirubicin, Cisplatin, Fluorouracil)
- FLOT (5-FU, Leucovorin, Oxaliplatin, Docetaxel)
- XELOX (Capecitabine, Oxaliplatin)

Studies such as the MAGIC and CLASSIC trials have demonstrated the benefit of perioperative chemotherapy [25].

Radiotherapy

Radiation therapy is typically used in:

- Adjuvant settings with chemotherapy (e.g., chemoradiation per INT-0116 trial)
- Palliative settings to relieve obstruction, bleeding, or pain

Intensity-modulated radiotherapy (IMRT) improves precision and reduces toxicity [26].

Targeted Therapies

Advancements in molecular profiling have enabled targeted approaches:

- HER2-targeted therapy: Trastuzumab improves survival in HER2-positive advanced gastric cancer.
- VEGF inhibitors: Ramucirumab targets angiogenesis.

Target	Drug	Indication
HER2	Trastuzumab	HER2-positive advanced cancer
VEGFR-2	Ramucirumab	Second-line metastatic setting
PD-1	Nivolumab	Advanced/refractory gastric cancers

Immunotherapy

Immune checkpoint inhibitors (ICIs) have emerged as promising options:

- Nivolumab and Pembrolizumab show benefit in PD-L1 positive and MSI-high tumors.
- Ongoing trials are assessing ICIs in earlier lines of therapy.

Palliative Care

For advanced or incurable cases, palliative treatment focuses on:

- Symptom relief
- Nutritional support (feeding tubes or parenteral nutrition)
- Pain and psychological management

Multidisciplinary Approach

Optimal care involves coordination among surgeons, medical oncologists, radiologists, nutritionists, and palliative care teams. Treatment plans are often discussed in tumor board meetings.

Chapter 6: Preventive Strategies and Public Health Measures

Introduction

Stomach cancer remains a significant cause of morbidity and mortality globally, particularly in developing regions. Preventive strategies aimed at mitigating modifiable risk factors, early detection, and health promotion can significantly reduce the incidence and improve outcomes. This chapter outlines primary, secondary, and tertiary prevention strategies and the role of public health initiatives in combating stomach cancer.

Primary Prevention

Primary prevention focuses on eliminating or reducing risk factors before the onset of disease.

- Helicobacter pylori Eradication: Recognized as a key preventive intervention, especially in high-risk populations. Studies have shown that eradication can reverse precancerous lesions and reduce gastric cancer incidence [27].
- Dietary Modifications:
  - Increase intake of fresh fruits and vegetables.
  - Reduce consumption of salt-preserved, smoked, and processed foods.
- Smoking Cessation and Alcohol Moderation: Associated with reduced gastric cancer risk.
- Occupational Safety: Reducing exposure to carcinogens in industrial settings through regulation and protective equipment.

Secondary Prevention

Secondary prevention targets early detection to enable curative treatment.

- Screening Programs: Routine endoscopic screening is practiced in high-incidence countries like Japan and South Korea.
- Risk Stratification Tools: Include H. pylori status, serum pepsinogen levels, and family history.
- Endoscopic Surveillance: For individuals with gastric dysplasia or intestinal metaplasia.

Country	Screening Strategy	Effectiveness
Japan	Biennial EGD for age > 40	Detects early cancer; improved survival
South Korea	Endoscopy or UGIS every 2 years	Increased early detection
China	Community-based pilot projects	Demonstrated feasibility

Tertiary Prevention

Tertiary prevention involves reducing complications and recurrence in diagnosed cases.

- Adjuvant Chemotherapy and Radiation: Minimize risk of relapse.
- Nutritional Rehabilitation: Essential post-gastrectomy to prevent malnutrition.
- Regular Follow-Up: Involves physical exams, imaging, and tumour marker monitoring to catch recurrences early.

Vaccination and Prophylactic Measures

- While no vaccine for H. pylori is available yet, development is underway and could represent a significant breakthrough.
- Genetic counselling and prophylactic gastrectomy are considered for patients with CDH1 mutations (HDGC) [28].

Health Education and Community Outreach

Public health campaigns play a vital role in raising awareness about stomach cancer risk factors and symptoms:

- Health promotion in schools and community centres
- Posters and media campaigns targeting diet and lifestyle
- Involvement of primary care physicians in screening initiatives

Global Initiatives and Policy Recommendations

- World Health Organization (WHO): Recommends population-based strategies for salt reduction and H. pylori eradication.
- WCRF/AICR: Provides dietary and lifestyle guidelines for cancer prevention.
- National cancer control programs are being strengthened to incorporate gastric cancer in high-risk countries.

Challenges and Future Directions

- Limited access to endoscopy in low-income countries
- Inadequate funding and awareness in rural areas
- Development of cost-effective, non-invasive biomarkers for screening
- Integration of AI and digital tools to optimize early detection

Chapter 7: Recent Advances and Future Trends

Introduction

Recent scientific and technological innovations have led to considerable advances in the understanding and management of stomach cancer. From precision diagnostics to targeted therapies, the treatment landscape is rapidly evolving. This chapter explores key breakthroughs, emerging research, and future directions in the fight against gastric cancer.

Advances in Molecular Profiling and Genomics

- The Cancer Genome Atlas (TCGA) has classified gastric cancer into four molecular subtypes: EBV-positive, MSI-high, genomically stable, and chromosomal instability.
- Genetic profiling has enabled personalized treatment decisions, such as using trastuzumab in HER2-positive cancers and immune checkpoint inhibitors in MSI-high cases [29].

Precision Medicine and Liquid Biopsy

- Liquid biopsies (circulating tumour DNA, exosomes) offer a non-invasive way to monitor disease progression and treatment response.
- These tools facilitate real-time surveillance and early detection of recurrence.

Immunotherapy Breakthroughs

- Checkpoint inhibitors (e.g., nivolumab, pembrolizumab) have shown promising outcomes, especially in MSI-high and PD-L1-positive tumours.
- Trials like KEYNOTE-062 and CheckMate-649 support the use of immunotherapy in frontline treatment for advanced cases [30].

Trial	Drug(s)	Findings
CheckMate-649	Nivolumab + chemotherapy	Improved OS in advanced gastric/GEJ adenocarcinoma
KEYNOTE-062	Pembrolizumab	Beneficial in PD-L1 positive patients

Novel Drug Delivery Systems

- Research is exploring nanoparticles, liposomes, and micelles for targeted delivery of chemotherapeutic agents.
- These systems aim to enhance drug efficacy and minimize systemic toxicity.

Artificial Intelligence (AI) in Diagnosis

- AI-powered image analysis is being integrated into endoscopy to identify precancerous lesions with greater sensitivity and specificity.
- Machine learning algorithms also aid in risk stratification and prognosis modeling [31].

Vaccines and Preventive Research

- Trials for H. pylori vaccines are underway, with a goal to eliminate the root cause of many gastric cancers.
- Therapeutic cancer vaccines targeting tumour antigens are also in experimental phases.

Future Outlook

The future of gastric cancer care lies in individualized therapy, non-invasive diagnostics, and global policy integration. A combination of scientific research, technological integration, and public health outreach will be necessary to reduce disease burden.

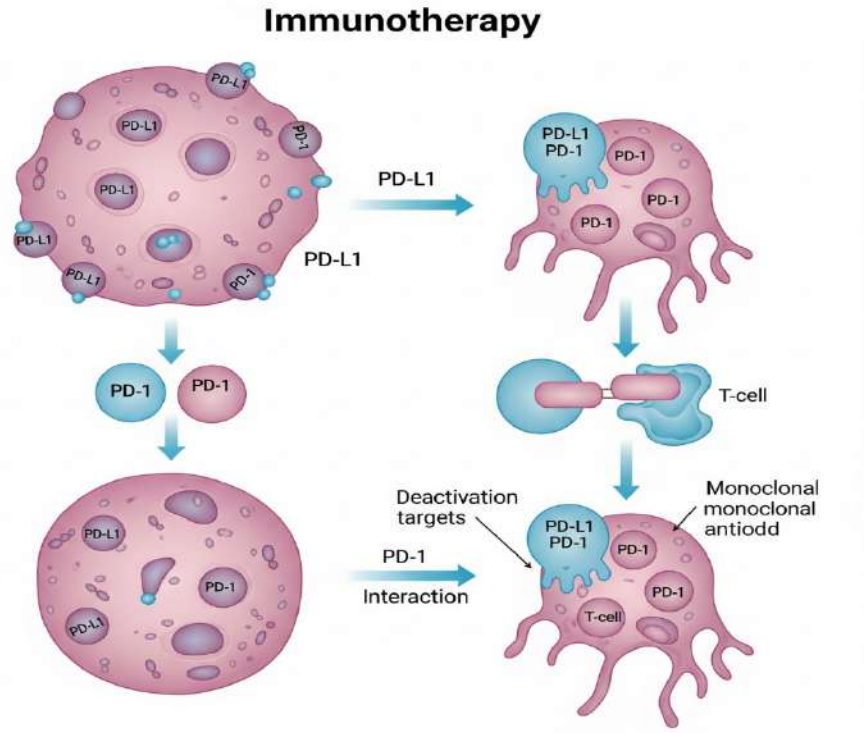

Fig.3 How Immunotherapy Helps Your Body Target Cancer

Chapter 8: Conclusion

Stomach cancer remains a formidable global health challenge due to its complex etiology, late diagnosis, and variable treatment responses. This comprehensive project has examined the pathophysiological basis, risk factors, diagnostic modalities, current treatment protocols, preventive strategies, and recent scientific advancements that shape the management of this malignancy.

The role of Helicobacter pylori, dietary patterns, and genetic predisposition have been emphasized as central to both understanding and preventing gastric carcinogenesis. Early detection remains pivotal, underscoring the importance of robust screening programs, particularly in high-risk regions. Treatment

strategies continue to evolve—from conventional surgery and chemotherapy to targeted and immune-based therapies guided by molecular markers.

Recent advances, especially in genomics, AI-assisted diagnostics, and immunotherapy, hold great promise for more personalized and effective care. These innovations, combined with preventive public health strategies, can contribute significantly to reducing the burden of stomach cancer worldwide.

Moving forward, interdisciplinary collaboration, increased access to healthcare, and investment in translational research will be crucial in the global effort to combat this disease. Policymakers, clinicians, researchers, and communities must work collectively to ensure early detection, equitable treatment access, and continuous innovation in gastric cancer care.

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