



Journées Francophones
d'Imagerie Médicale

*Infectious Agents and Cancers:
Prevalence and Importance
in Public Health in India.*

Antoine GESSAIN

Unité d'Epidémiologie et Physiopathologie des Virus Oncogènes

Institut Pasteur

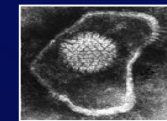
JFIM 15th edition, Mumbai nov 4th 2016

Cancers: Global Burden and Causes

14 millions of new cancers in 2012 worldwide

Cancer is a complex group of diseases with many possible causes and/or associated risk factors: variability according to age, sex, geographical origin ...

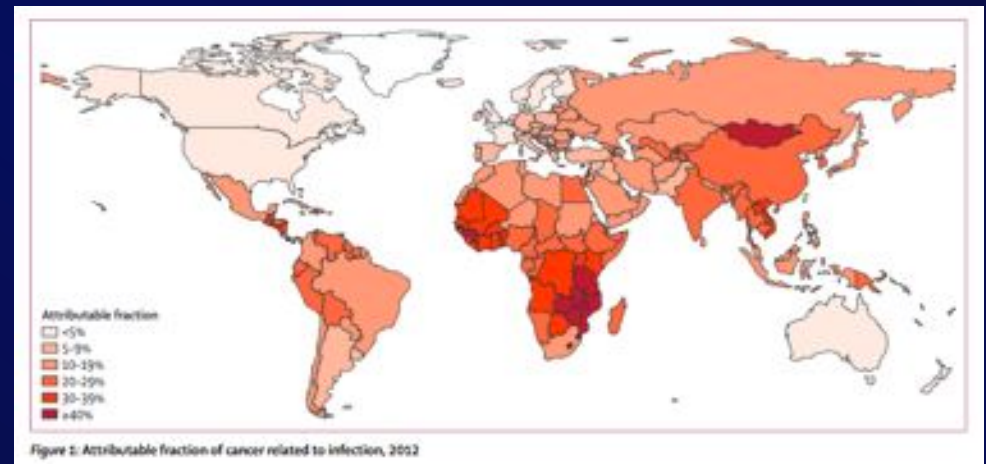
- **Tobacco: 25-30%** in developed countries
- Alcohol: 3%
- Professional exposition (chemical products): 4-5%
- Environmental exposures (air, soil, water) to different types of chemicals: 1-4%
- Alimentary contamination (% variable)
- **Diet, nutrition and physical activity: 30%**
- Genetic factors: 2-4%
- **Certain types of infections: 15%**



It is estimated that 35-50% of the cancer cases worldwide can be prevented by control of potentially modifiable factors

Microbes/Infectious agents and cancers

- Of 14 millions of new cancers in 2012,
2.2 millions were attributable to carcinogenic infections
 - 15.4 % worldwide
- 3-10 % developed countries (France, UK, Australia, USA)
- >20 % in most developing countries
- >30 % several African countries



- 30% of these cancers occurred in individuals aged < 50 years
 - 71% are associated to viruses.



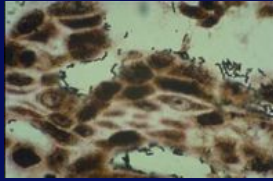
International Agency for Research on Cancer in Lyon, France
(IARC)

has identified with expert groups **12 biological agents as proven carcinogenic agents.**

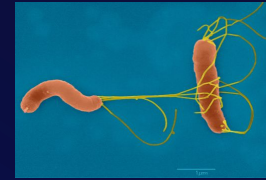
8 Viruses (EBV, HHV-8, HBV, HCV, HTLV-1, HIV, HPV, Merkel Cell polyomavirus).

1 Bacteria (*Helicobacter pylori*).

3 Parasites (*Clonorchis sinensis*, *Opistorchis viverrini*, *Schistosoma haematobium*).

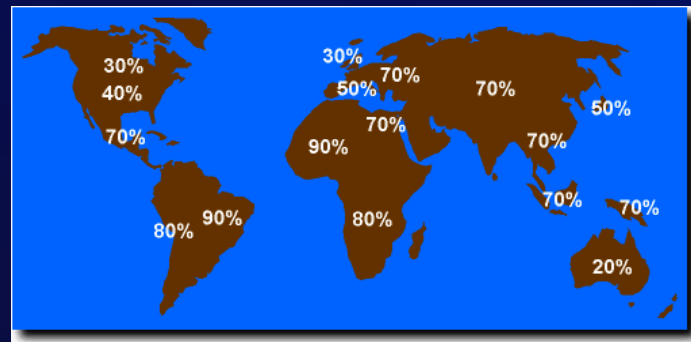


Gastric Cancer

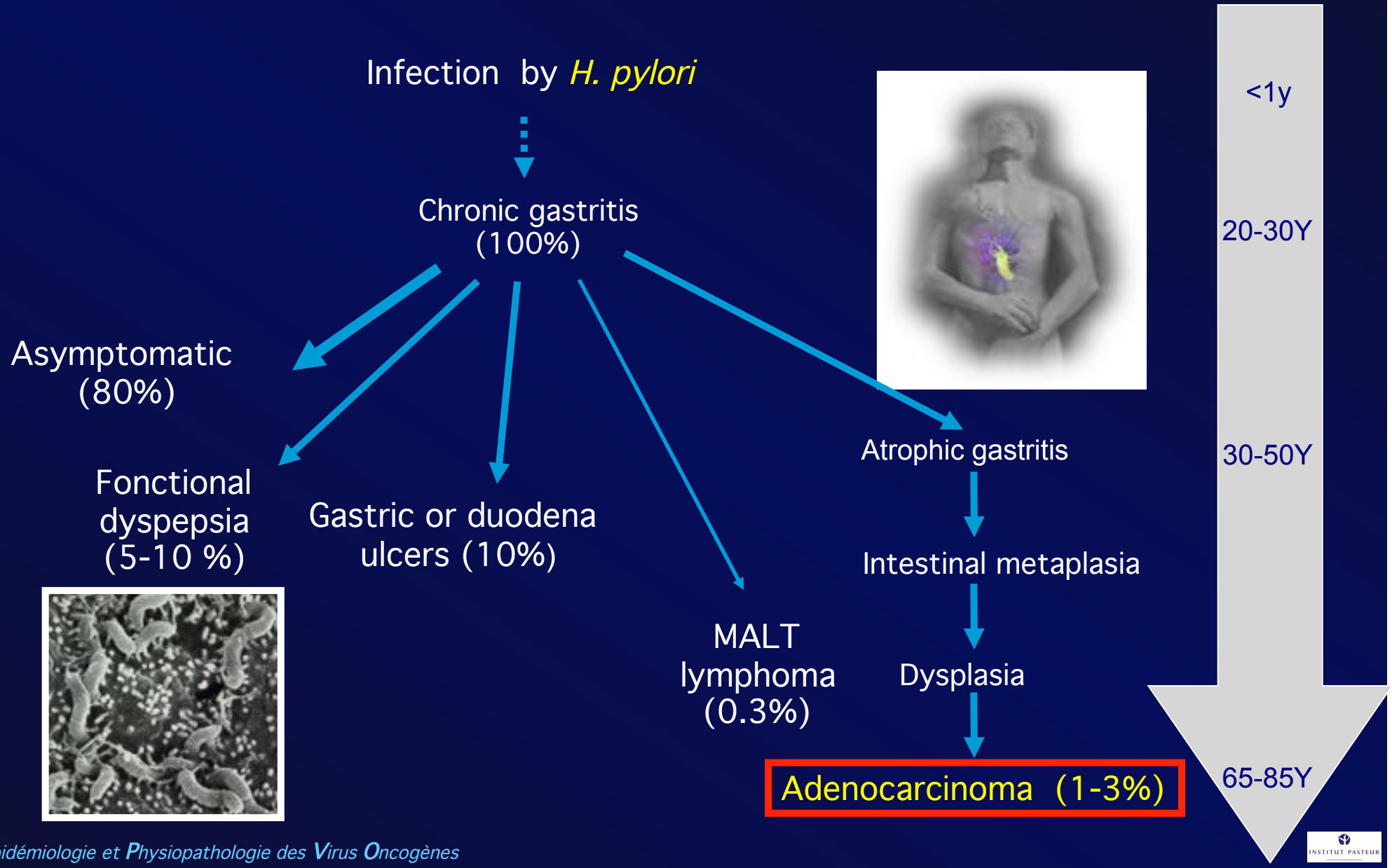


- > 700 000 new cases/each year
- Fifth most common cancer worldwide and second mortality caused by cancer (++ in developing countries)
- 5 year survival: 10-15 %
- Role of *Helicobacter Pylori* bacteria in the genesis of gastric diseases, including gastric cancer

Very high prevalence, half of the world population great variability according to geography (socio-economic level)

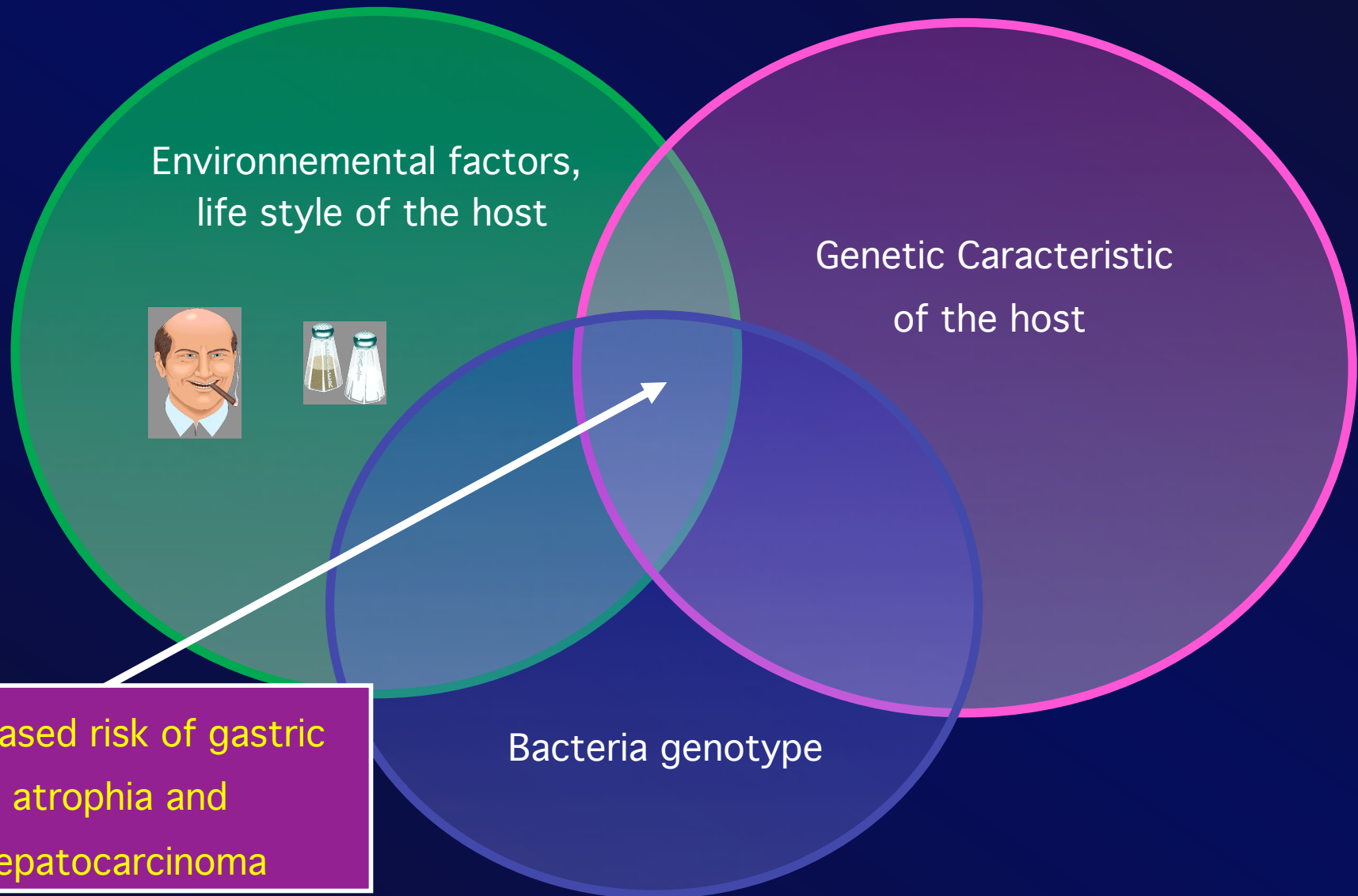


Robin Warren et Barry Marshall
Nobel Prize in 2005

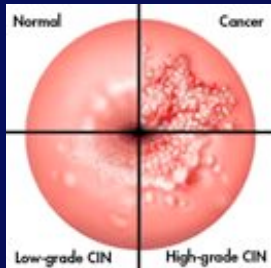


Multiple Steps, Multifactorial Carcinogenesis

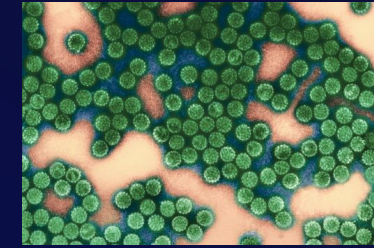
as for other cancers associated to infectious agents



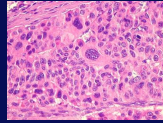
Increased risk of gastric atrophy and hepatocarcinoma



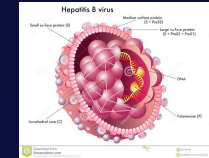
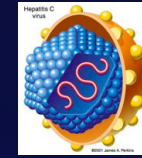
Cervix Uteri Carcinoma



- Worldwide, cervical cancer is both the 4th-most common cause of cancer and deaths from cancer in women (after breast, colorectal, and lung).
- In 2012, 530,000 cases with 266,000 deaths.
- About **80% of cervical cancers occur in developing countries.** (2,5 new cases/100 000 women in Israël and 55/100 000 women in Zimbabwe).
- Attributable part to **Human papillomaviruses** is 100%.
- Virtually all cervical cancer cases are linked to genital infection with HPV of high grade 16/18/31/33/35...with the role of viral integration.

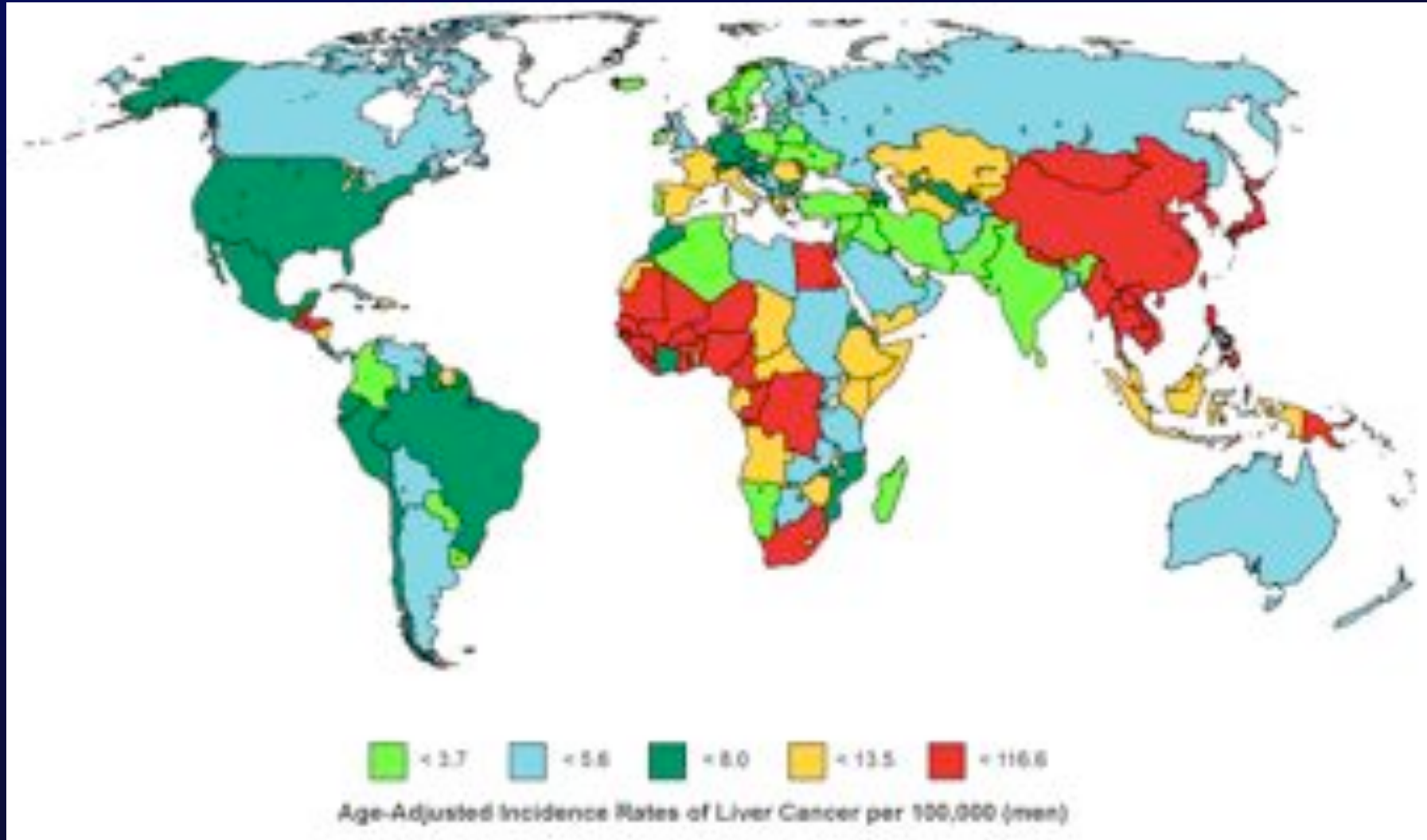


Hepatocarcinoma



- Hepatocarcinoma (HCC) is the fifth most common tumor in the world.
- 780 000 new cases in 2012 with 660 000 deaths, about half of them in China.
- The most important **risk factors vary widely from country to country.**
- In countries where **Hepatitis B** is endemic, such as China, HBV is the predominant cause of HCC whereas in countries, such as the US, where HBV is rare because of high vaccination rates, the major cause of HCC is cirrhosis (often due to **Hepatitis C Virus**, obesity or **alcohol** abuse).
- Multifactorial cancer with also co-factors as alcohol and **aflatoxin**

Age-adjusted incidence rate of Hepatocarcinoma (Africa and Asia; China++)



JFM Burkitt's lymphoma and Epstein-Barr virus (EBV)

Viral isolation in 1964 from a culture of BL cells

EBV-associated cancers with variable attributable risk:

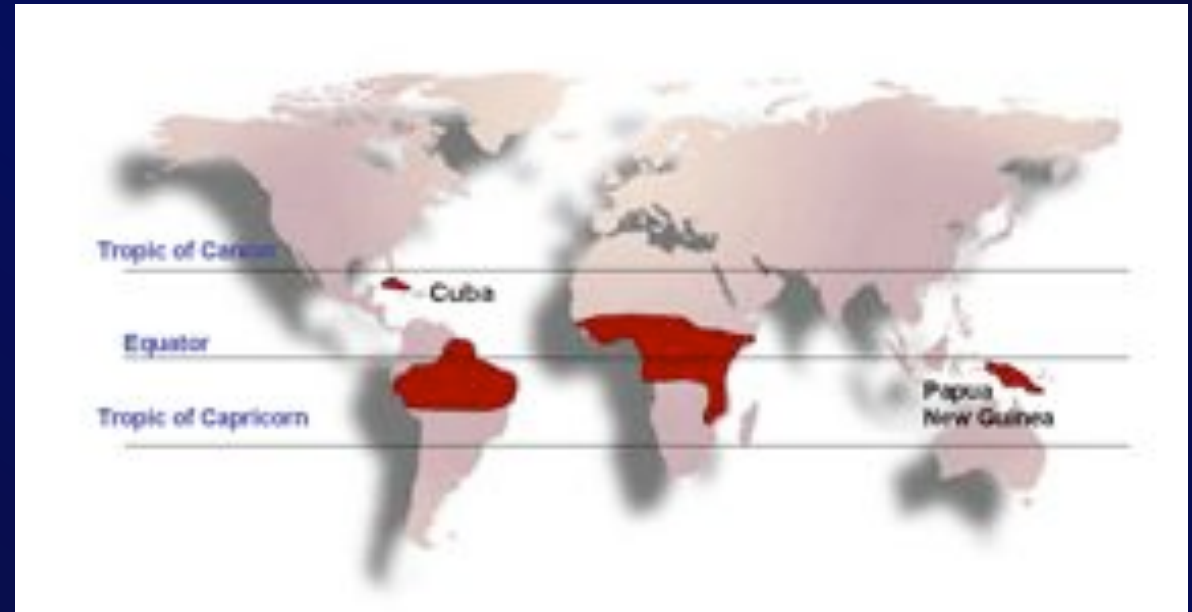
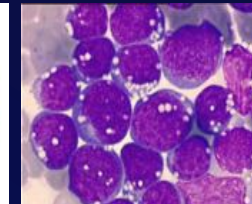
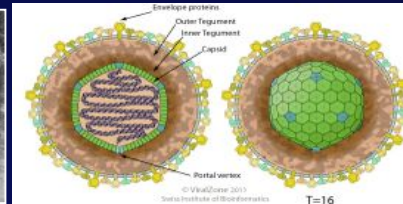
Burkitt's lymphoma
10 000 cases (10-100%)

Hodgkin lymphoma,
60 000 cases (10-70%)

NPC (Nasopharyngeal
Carcinoma), 80 000 cases
(80-100%)

Non Hodgkin lymphoma (AIDS/
immunosuppression)

Rare other cancers
Epidémiologie et Physiopathologie des Virus Oncogènes

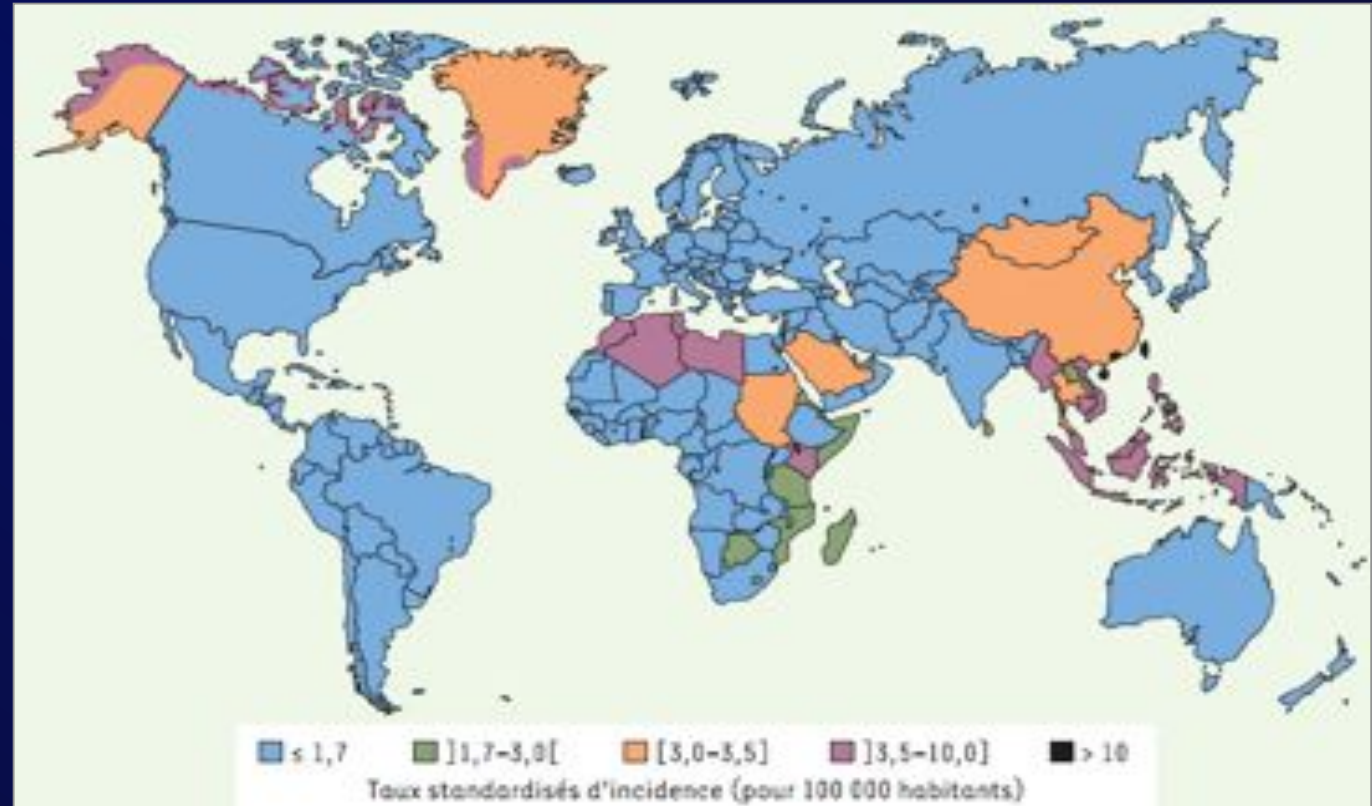
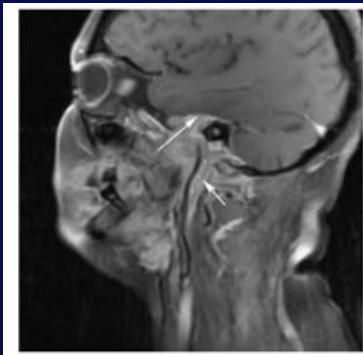
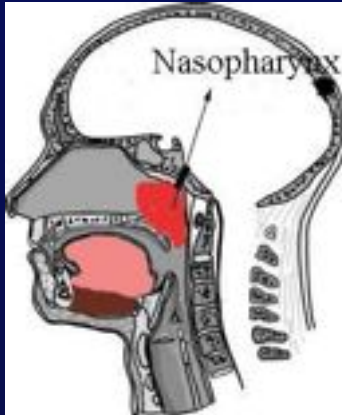
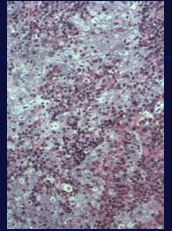


- Endemic form nearly always associated with EBV:
(Malaria is a **Cofacteur majeur**).
- Sporadic form: EBV-associated in only 10% à 20% of cases.

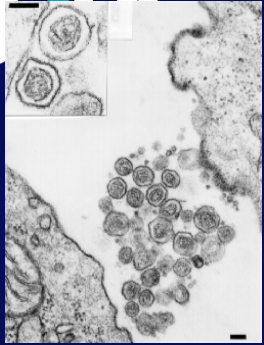


EBV and Nasopharyngeal Carcinoma (NPC)

80 000 cases/year

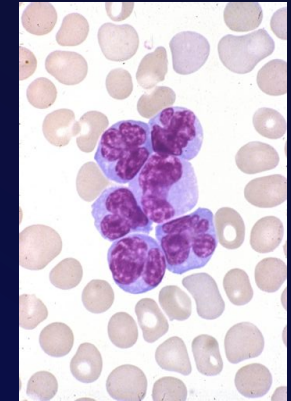


- Multifactorial cancer always associated to EBV
- Major public health problem in different areas (China/Canton, Eskimos, Maghreb)
- Major co-factors: alimentary habits (dried fish, nitrosamine,...) and genetic

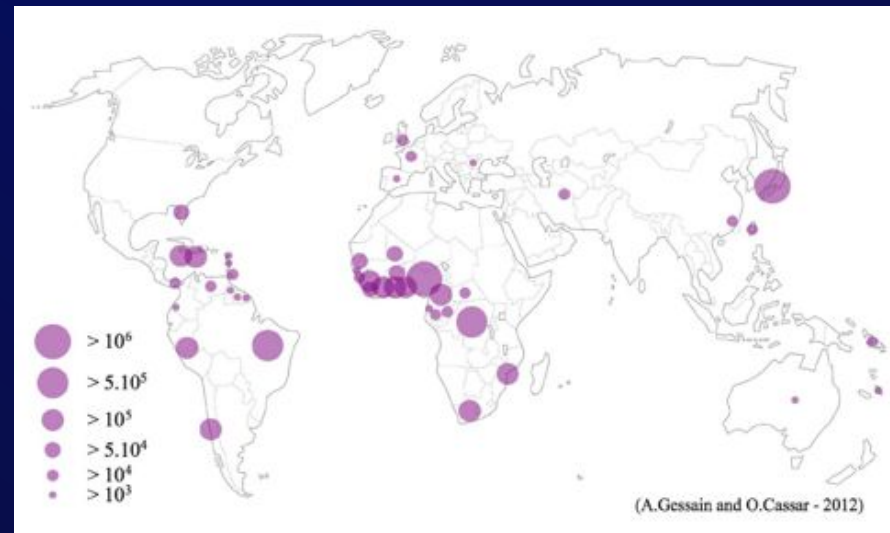
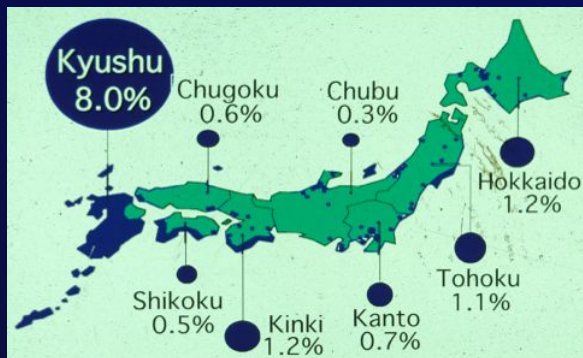


Adult T cell Leukemia/Lymphoma and the Human retrovirus HTLV-1

- First human retrovirus to be isolated
- Causally associated with a very severe leukemia/lymphoma
- Median survival < 6 months (acute leukemic form)
- High endemic foci, including Japan with 1000 cases/year



ATLL cells



TSP/HAM

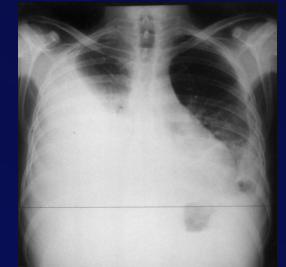
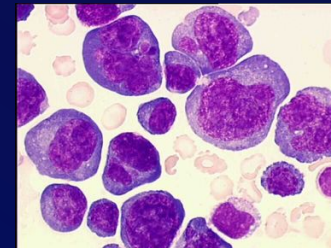
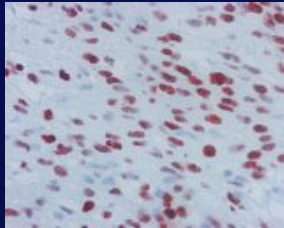
1) Age of infection (breast feeding ++). 2) Genetic factors. 3) Other cofactor : *S. Stercoralis*,.

Poor therapy. Prevention++.

Other viruses associated with human cancers

Human herpes virus 8 (HHV-8)/ Merkel Cell Carcinoma polyomavirus (MCPyV)

HHV-8 is associated with all Kaposi sarcoma forms (45 000 new cases/year), primary effusion lymphoma and some forms of multicentric Castlemann's diseases (role of HIV++).



MCPyV is associated with Merkel Cell Carcinoma: a rare and aggressive skin cancer.

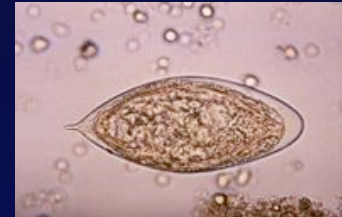


Parasites and Cancers in Humans

Shistosoma haematobium and bladder cancer

7000 cases /year

Africa and Middle East (Egypt++)



Opisthorchis viverini, Clonorchis sinensis (liver flukes) induce an inflammatory reaction, epithelial hyperplasia and sometimes even **cholangiocarcinoma**

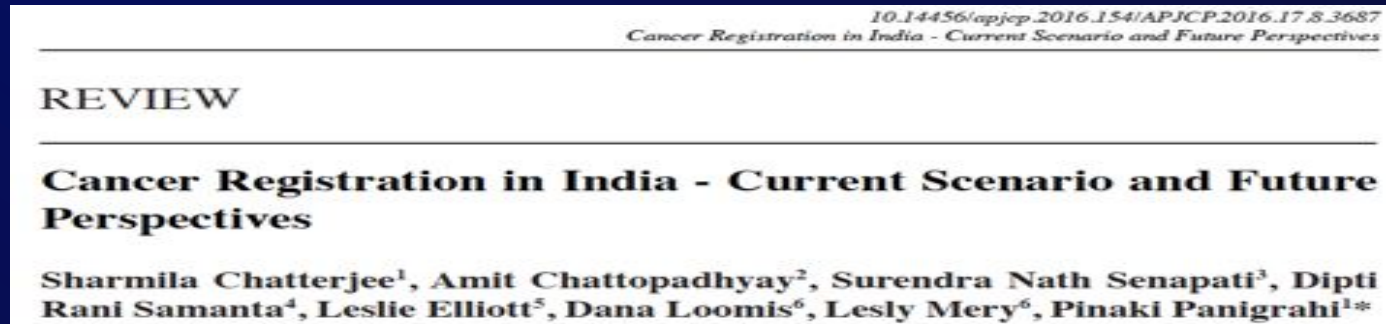
1300 cases/year

Thailand, the Laos, Vietnam and Cambodia (OV)

Japan, China, Taiwan, and Southeast Asia (CS)



What is the Situation of Cancers in India? (especially for Infectious-Related cancers)



Cancer registration in India was initiated in 1964 and expanded since 1982, through the **National Cancer Registry Program (NCRP)**.

NCRP currently has twenty-six population based registries and seven hospital based registries.

Cover **less than 15% of the population (mostly in urban areas++)**.

Potential concerns about some Indian registries include accuracy, detail of information, and speed in updating the databases.



India has one of the highest cancer incidence and mortality rates in the world

In 2010, about 555,000 people died of cancer in India.

The most common fatal cancers in men: oral (22.9%), stomach (12.6%), and lung cancers (11.4%), while cervical (17.1%), stomach (14.1%), and breast cancers (10.2%); in women

In 2016: 1.45 millions of new cases with 750 000 death.

In 2020: 1.73 millions of new cases with 880 000 death



India contributes to **25 % of the global burden (130 000 cases/year) and mortality of Cervical cancer cases.**

Cervical cancer is the second cancer among females in India with 14% of all cancers (NCRP, 2015).

Around 78-88% of Cervical cancer are HPV-16 or 18 positive.

There is **no organized national cervical cancer screening program** and no national policy for cervical cancer prevention in India, and screening of asymptomatic females is practically non-existent.

HPV vaccines can make a major breakthrough in the control of cervical cancer for countries like India with high disease load.



Accurate data on hepatocarcinoma in India are not available.

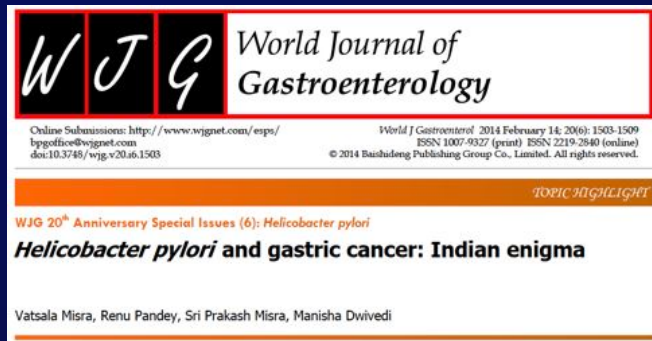
Estimation: 30 000 to 50 000 cases/year.

Possible increase of incidence and regional differences.

The major factors responsible for HCC development in India is **chronic HBV infection, HCV infection and alcohol consumption.**

India has around **35-40 million HBV carriers.**

Prevention of viral infection **by universal vaccination against HBV should be adopted in India,** as well as therapy fo HCV.



Helicobacter Pylori has been etiologically linked to gastric cancer and is considered as a carcinogenic agent.

H. pylori is very frequent in India (50/80 % of the population), but the incidence of gastric cancer is low.

Gastric cancer is a multifactorial disease which includes host's genetic, dietary (fish, salt in contrast to vegetarian,...) and environmental factors and not *H. Pylori* alone. All these factors need to be considered.

Indian Journal of Dermatology

Indian J Dermatol. 2015 Jan-Feb; 60(1): 103.
doi: 10.4103/0019-5154.147848

Multifaceted Adult T-Cell Leukemia/Lymphoma in India: A Case Series

Anza Khader, Mohamed Shean,¹ Sunitha Balakrishnan,² Betsy Ambooken, Kunnummal Muhammed, and Uma Rajan

From the Department of Dermatology, Government Medical College, Calicut, Kerala, India
¹Department of Medicine, Government Medical College, Calicut, Kerala, India
²Department of Pathology, Government Medical College, Calicut, Kerala, India

Indian Journal of Pathology & Microbiology

HTLV 1 associated adult T cell lymphoma/leukemia a clinicopathologic, immunophenotypic tale of three cases from non-endemic region of south India

Indian Journal of Pathology and Microbiology. 2012;55(1):92-96 DOI 10.4103/0377-4929.94870

Observational Study

Medicine

OPEN

HIV and cancer registry linkage identifies a substantial burden of cancers in persons with HIV in India

Sheela V. Godbole, MD^{1*}, Karabi Nandy, PhD², Mansi Gauniyal, PhD³, Pallavi Nalawade, MCM, MCA⁴, Suvarna Sane, MSC, MPhil⁵, Shravani Koyande, MComm⁶, Joy Toyama, MS⁷, Asha Hegde, MBBS, MBA, Dip. in HIV Epidemiology⁸, Phil Virgo, BS⁹, Kishor Bhatia, PhD, FRCPATH¹⁰, Ramesh S. Paranjape, PhD¹¹, Arun R. Ribbud, MD, MPH¹², Sam M. Mbulaitwe, MBChB, MPhil, MMed¹³, Ronald T. Mitsuyasu, MD¹⁴

HTLV-1 and ATLL is quite rare in India and under-reported as well as HHV-8 and Kaposi's sarcoma except in HIV infected persons.

Conclusion

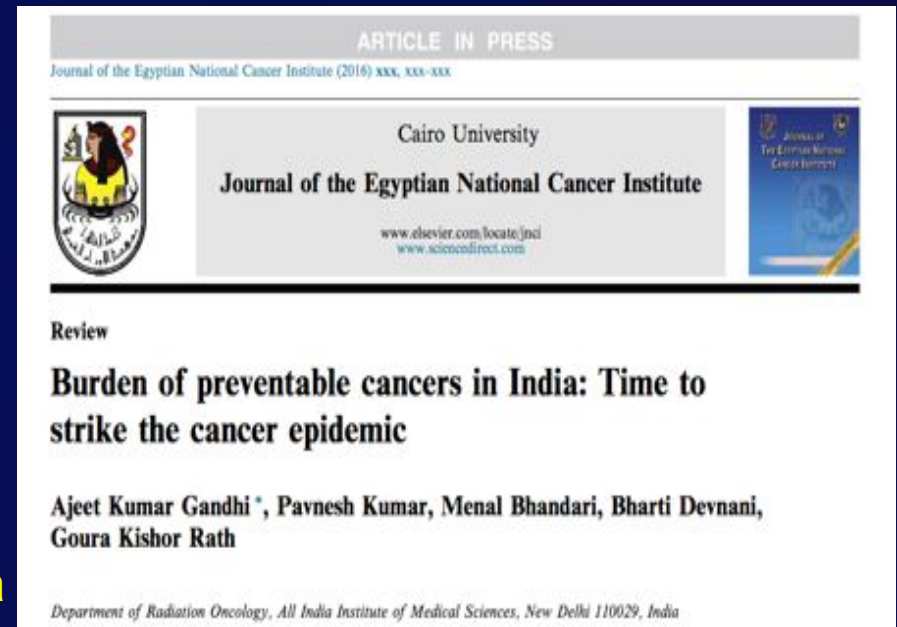
Cancer (including those associated with infectious agents) is already an
Important public health problem in India.

However, cancer incidence will continue to grow in the future.

We can really speak about «a cancer epidemic».

This is due to:

- 1) Increase in the population size
- 2) Increase of life expectancy
- 3) Increase of proportion of elderly population
- 4) Absence of any screening program in India



What can be done?

Primary and Secondary Prevention

Primary: Prevention of the infection by Vaccination against HPV and HBV.

National program should be developed.

Secondary: Medical Education from the bottom to top, from the general population and primary health structures, to nurses and medical school, will allow **an earlier and better diagnosis** and thus a **better medical care**.

This can and should be done for **cervical cancer++**, **Nasopharyngeal Carcinoma**, and **Gastric cancer**.

आपका ध्यान के लिए धन्यवाद

Thank you very much for your attention