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

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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 Pylory* 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
Infection by *H. pylori*

- **Chronic gastritis** (100%)
  - Asymptomatic (80%)
  - **Fonctional dyspepsia** (5-10%)
- **Gastric or duodenum ulcers** (10%)
- **Atrophic gastritis**
- **Intestinal metaplasia**
- **MALT lymphoma** (0.3%)
- **Dysplasia**
- **Adenocarcinoma** (1-3%)

Infection by *H. pylori* is associated with various pathologies, including chronic gastritis, which is the most common. Other conditions such as gastric or duodenal ulcers, atrophic gastritis, intestinal metaplasia, MALT lymphoma, dysplasia, and adenocarcinoma can also occur. The diagram highlights the progression of these pathologies with age ranges provided in years.
Multiple Steps, Multifactorial Carcinogenesis
as for other cancers associated to infectious agents

Environmental factors, life style of the host

Genetic Characteristic of the host

Bacteria genotype

Increased risk of gastric atrophy and hepatocarcinoma
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 Israel 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++)
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**

- 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

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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

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

Poor therapy. Prevention++. 

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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 Castleman’ 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++)

*Opistorchis 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.
Cancer in India: the Epidemic

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 for 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 with include 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.
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