Epidemiology and etiology of lymphomas

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Bellinzona



Disclosures

Roche

Celgene

Mundipharma

Janssen

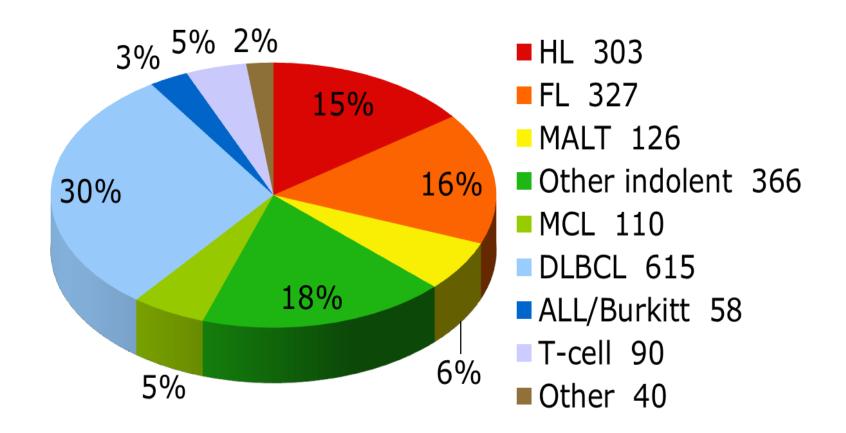
Gilead

Bayer

Millenium

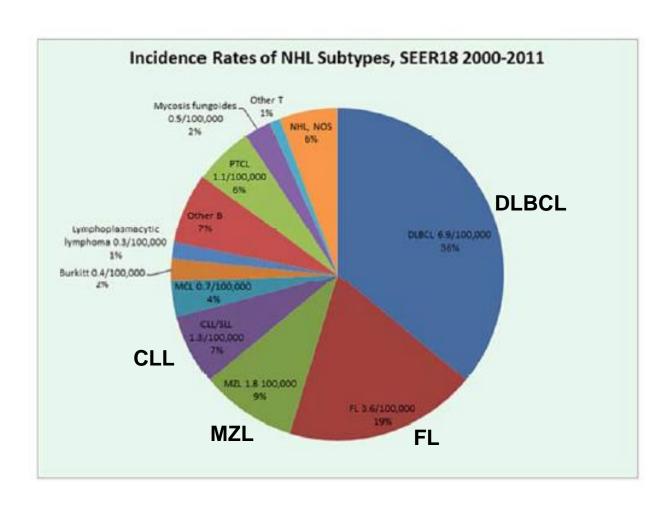


Aggressive: 45% Indolent: 40% Hodgkin: 15%



IOSI LYMPHOID NEOPLASMS DATABASE 1980-2011 [N=2035, Median follow-up: 9.8 years]

Incidence of lymphoma in the USA



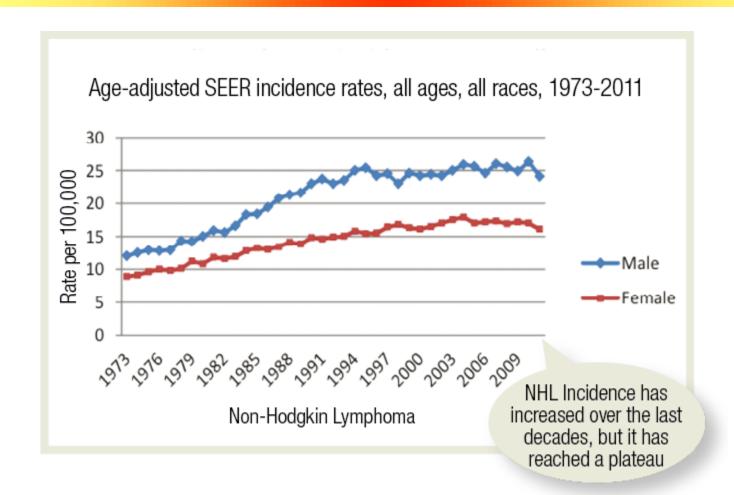


Lymphoma incidence by age

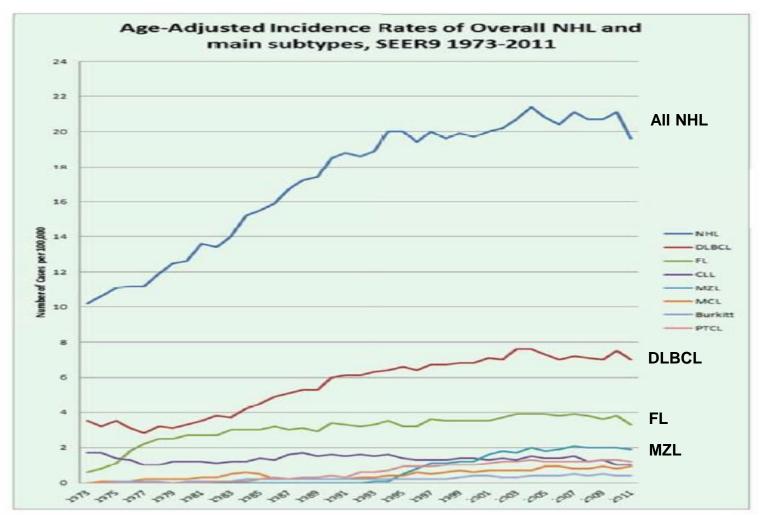
Incidence rates per 100 000 and number of cases (World - Non-Hodgkin Lymphoma, Globocan 2012) 50000 50 The diagnosis of 45000 45 NHL increases with 40000 40 age, and it is more 35000 Number of cases Rate per 100 000 35 frequent in men 30000 30 25 25000 20 20000 15 15000 10000 10 5000 0 - 1415 - 3945-49 50-54 55-59 60-64 65-69 70-74 75 +Age Female cases — - Male rates Female rates



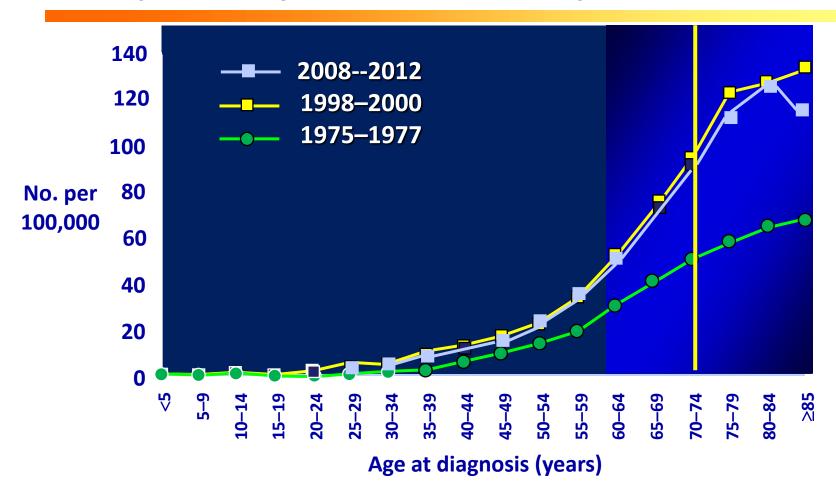
Evolution of NHL incidence



Incidence by histology over time (1975 – 2011)



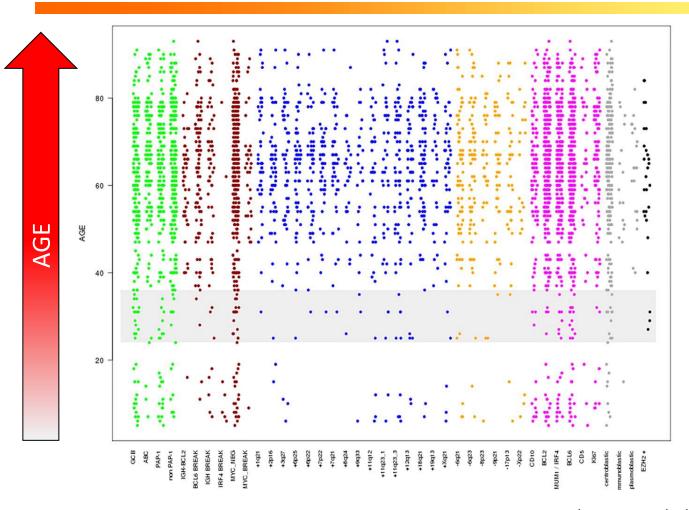
The incidence of NHL increased especially in the elderly (> 60 Years)



Ries et al (eds). SEER Cancer Statistics Review, 1975-2000 Howlader N,et. al. SEER Cancer Statistics Review, 1975-2012,



Age at diagnosis is associated with molecular complexity: n=364 pt German MMML project



Gene expression

Chromosomal translocations/breaks

Copy number gains

Copy number losses

Immunohistochemistry markers

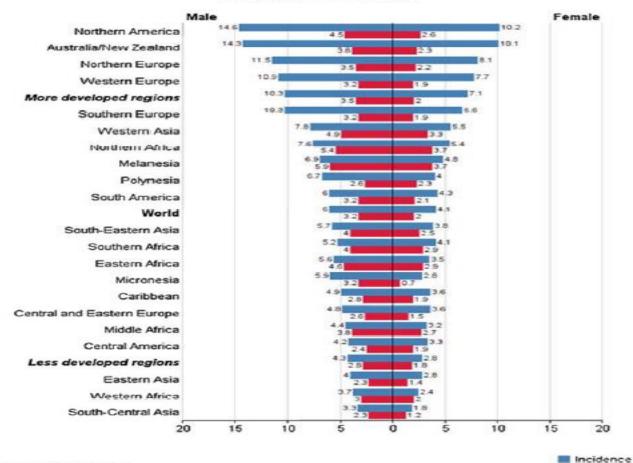
Morphology

EZH2 Tyr 641 mutations



Incidence of lymphoma In the world

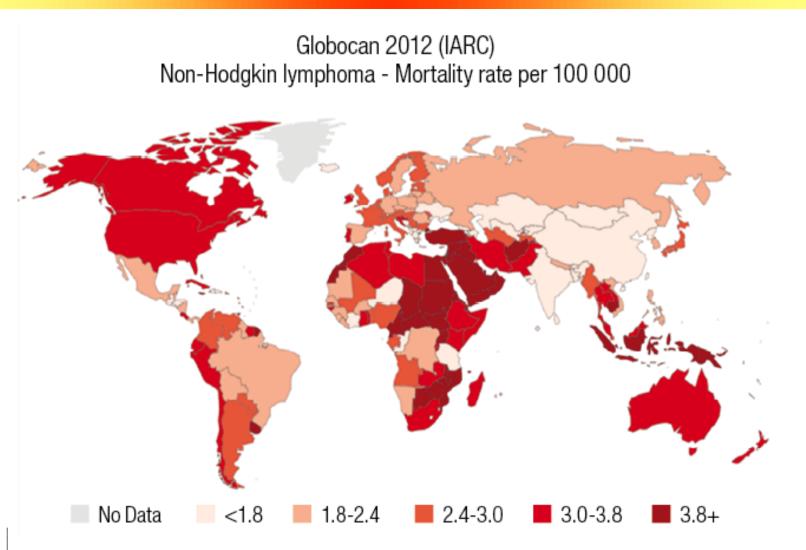
Non-Hodgkin lymphoma ASR (W) per 100,000, all ages





Mortality

NHL mortality in the world



Etiology of lymphoma

- Immune modulation
- Viruses
- Bacterial infections
- Lifestyle factors
- Occupational exposures
- Host factors

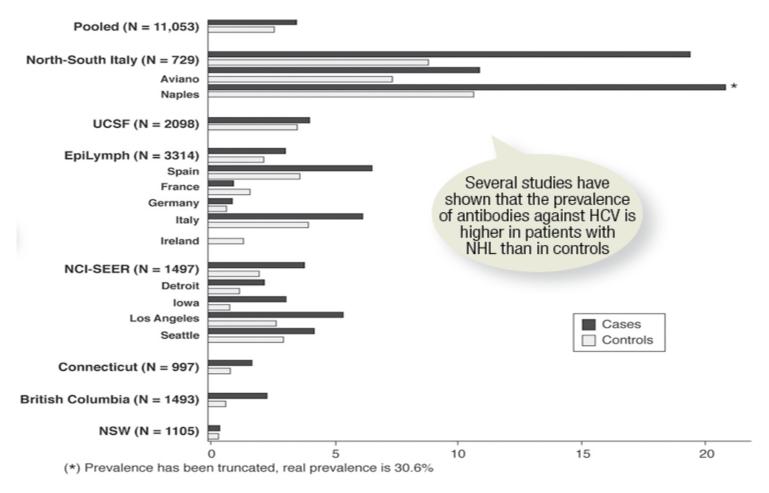
Immune modulation

- > Immunosuppression is the strongest risk factor
- > EBV is an important co-factor
- > HIV infection increase risk x 100 (less since HAART)
 - (Immune surveillance of viruses EBV, HHV8)
- Post-transplant immunosuppression

Viruses

Epstein-Barr Virus (EBV)	Burkitt Hodgkin NHL of immunocompromised patients
Human T-cell Lymphotropic Virus (HTLV-1)	Adult T-cell leukemia/lymphoma
Kaposi Sarcoma-associated Herpesvirus (KSHV)	Kaposi sarcoma Primary effusion lymphoma Multicentric Castelman disease Plasmablastic lymphoma
Hepatitis C Virus (HCV)	Controversial

Hepatitis C could be a predisposing agent

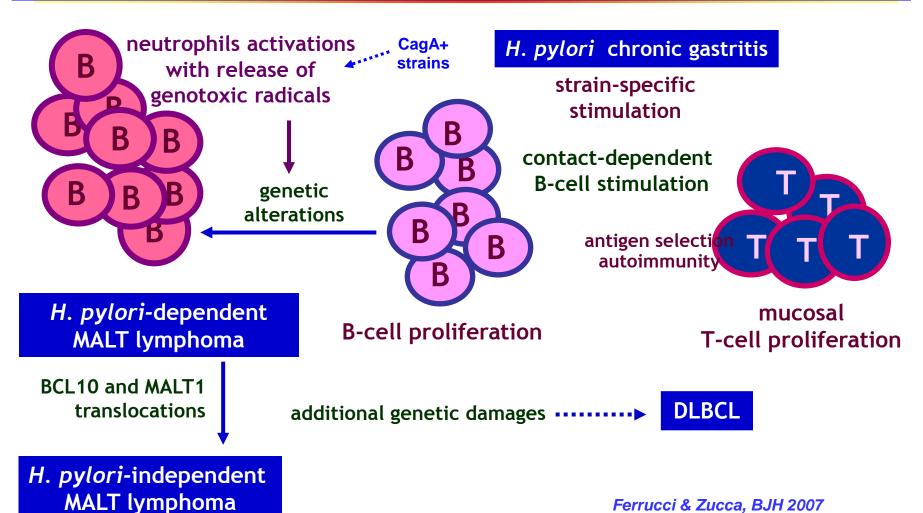




Bacterial infections

Helicobacter pylori	Gastric MALT lymphoma
Borrelia burgdorferi	Primary cutaneous B-cell lymphoma
Chlamydia psittaci	Ocular adnexal marginal zone lymphoma

H. pylori and MALT lymphoma: a model of tumor progression



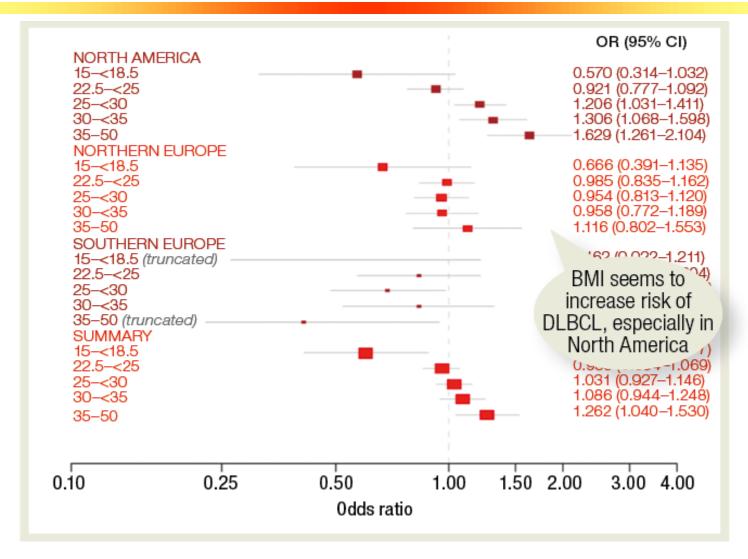
Ferrucci & Zucca, BJH 2007

Lifestile factors

Tobacco	controversial
Alcohol use	controversial
Diet	controversial
Obesity	Possible excess of DLBCL
Hair dyes	Possible excess of FL and CLL
UV radiation	Possible protective effect



Body mass as a risk factor

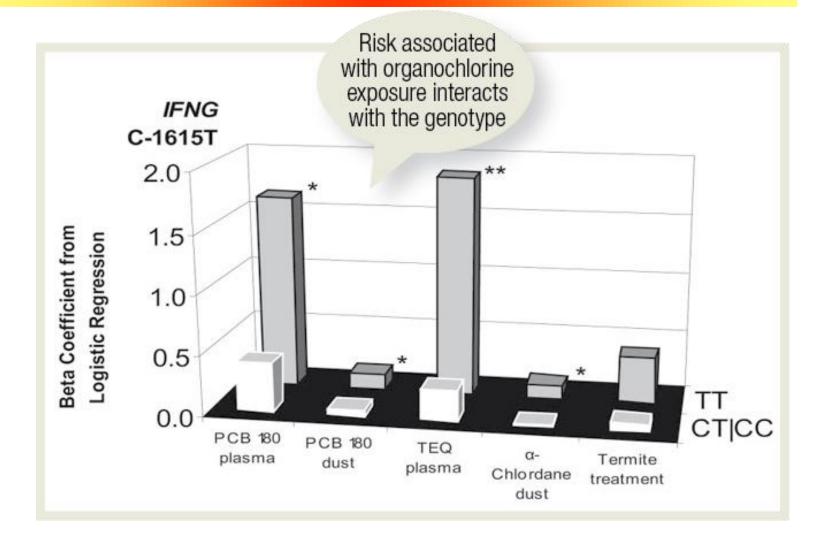


Occupational exposures

Occupation	Agents
Farmers Pesticide applicators Benzene workers Petroleum refinery workers Dry cleaners Firefighters Chemists	Pesticides Benzene Herbicides Organic solvents



Some genotypes are more susceptible to carcinogens

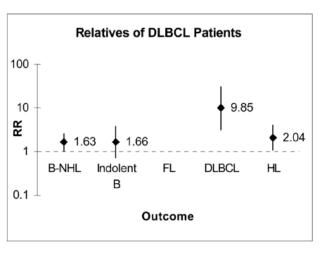


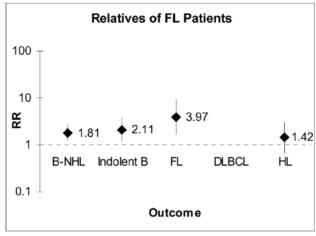
Familial aggregation

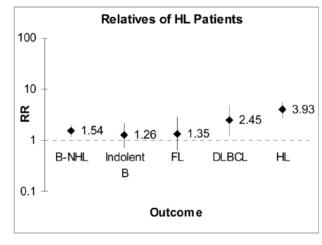
Registry study in Sweden

Risk of lymphoma in first degree relatives of

- 2668 FL
- 2517 DLBCL
- 6963 HL

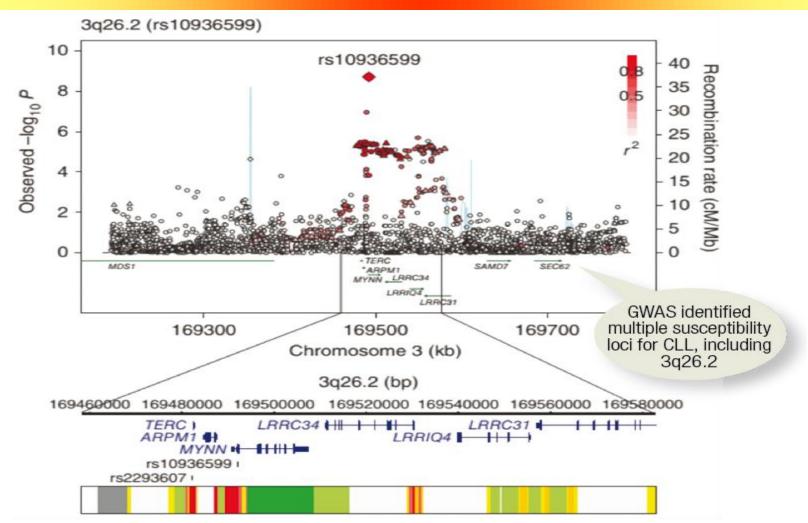








Genetic predisposition for NHL (GWAS: genome-wide association studies)



Lymphoma inducers by histology

Exposure category	Specific exposure	MF/SS	PTCL	MZL	В	LPL/WM	DLBCL	CLASIL	႕	MCL	로	AL A			
Family history of	Any		Х	Х		Х	Х	Х	Х	Х	Х	Х			
haematologic	NHL		Х	Х			Х	Х	Х	Х	Х	X.			
malignancy	Leukemia		Х	Х		Х		Х		Х	m		_		
	Multiple myeloma	X	Х		m	m				Х	m	Х			
	Hodgkin lymphoma	m		Х	m	Х	Х				m	m		3	
Autoimmune disease	Any B-cell activating disease			Х		X	X					m		ľ	
	Sjögren's syndrome	m		Х	m	X				m	m	m			
	Systemic lupus erythematosus	X	X	X	m	Х					m	m		2	
	Any T-cell activating disease	Х	Х											۲	
	Celiac disease	m	Х	m	m						m	m			
	Systemic sclerosis/scleroderma	X	m		Х	m		m		m	Х	m		L a	
HCV seropositivity	-			Х	Х	Х	Х			m	m	m		Γ'	~
Atopic disease	Hay fever				Х	Х	Х		Х	Х		Χ			In OR
	Eczema	X												J- 0	드
	Allergy		Х		Х		Х	Х	Х	Х		Х		0	
Blood transfusion	Transfusion occurring <1990				Х		Х	Х	Х	Х	Х	Х			
Anthropometric factors	Body mass index as a young adult						X		Х		Х	Х		١.	
	Height		Х		X		Х	Х	Х	Х	Х	Х		-1	
Alcohol consumption	Any alcohol	X	Х	Х	Х		Х								
(≥1 drink per month)	Wine		Х	Х	Х		Х					Х		١,	
	Liquor	X	Х	Х	Х		Х		Х		Х			-2	
	Beer	Х	Х	Х	Х	Х	Х				Х				
Cigarette smoking	Duration of smoking	X	Х	Х		Х			Х	Χ		Х		•	
Recreational sun exposure			Х	Х	Х		Х	Х	Х	Х					
Socioeconomic		Х	Х		Х		Х			Х		Х			
status															
Occupational history	Teacher			X	Х	Х									
	Painter	Х			Х										
	General farm worker	X			Χ			Χ			Χ				



Conclusions

- > After 20 y of increase (AIDS), incidence is now stable
- Incidence and histology differs by age and geography
- Infections, environmental and lifestile factors matter
- Host factors have also an importance