Consumo rischioso e dannoso di alcol: prospettive e proposte per lo screening oncologico

Gianni Testino

Centro Alcologico Regionale – Regione Liguria

UO Alcologia e Patologie Correlate, Dip. Medicina Interna, IRCCS San Martino-IST, Genova

WHO Collaborating Centre for research and health promotion on alcohol and alcohol-related health problems

Societa' Italiana di Alcologia

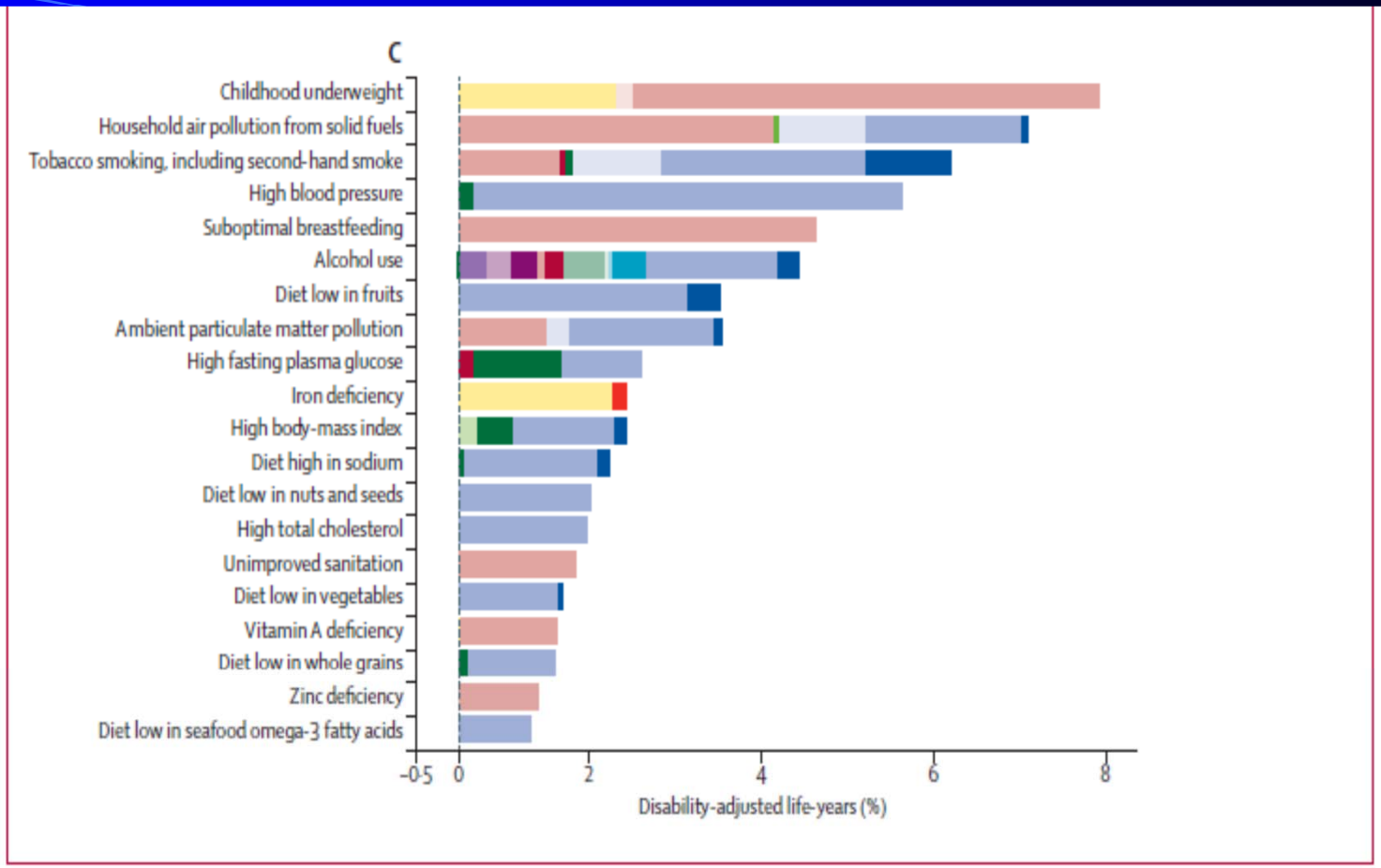


Figure 1: **Burden of disease attributable to 20 leading risk factors in 1990, expressed as a percentage of global disability-adjusted life-years**
For men (A), women (B), and both sexes (C).

Lim ST et al; Lancet 2012, 380: 2224

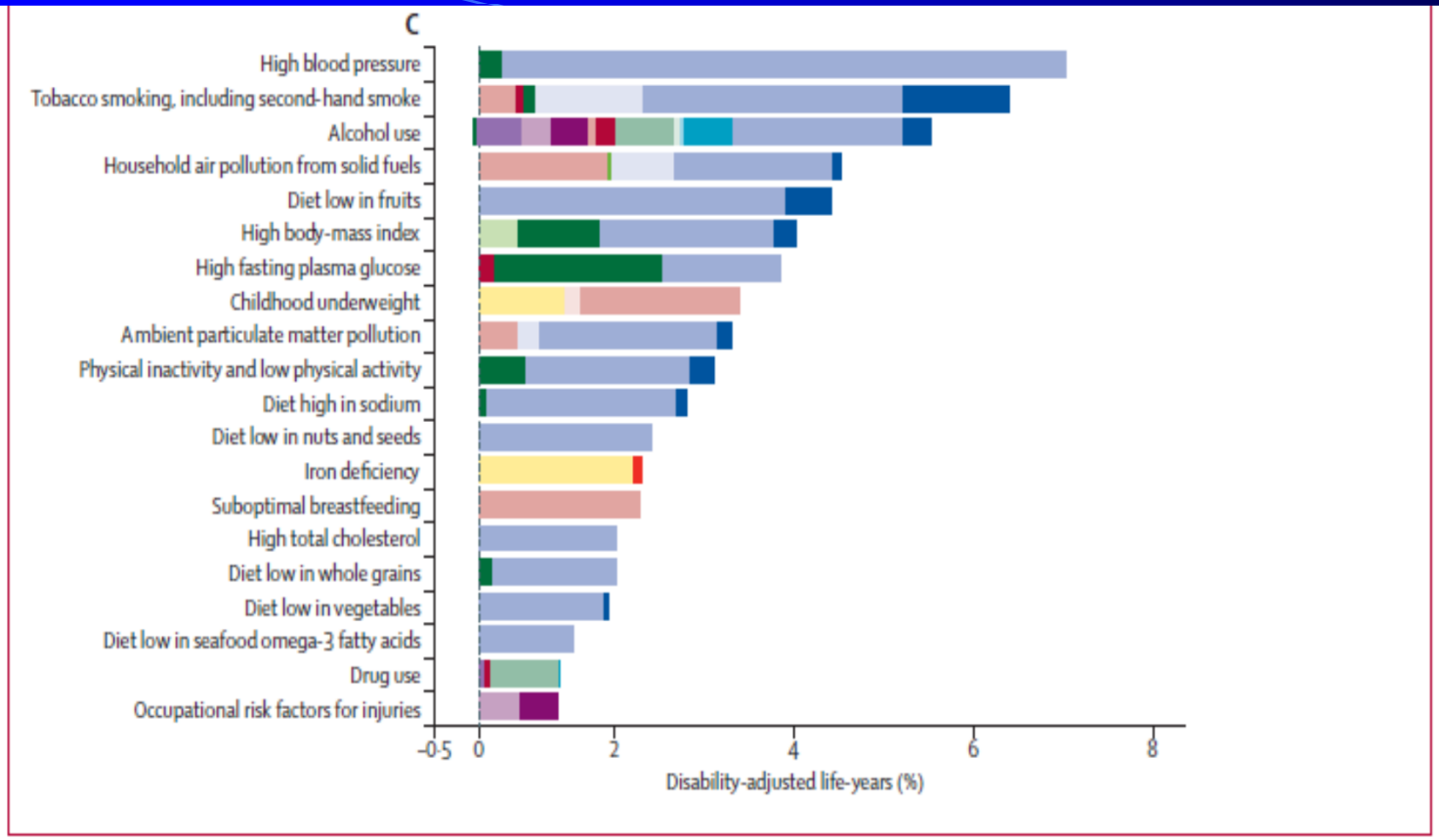


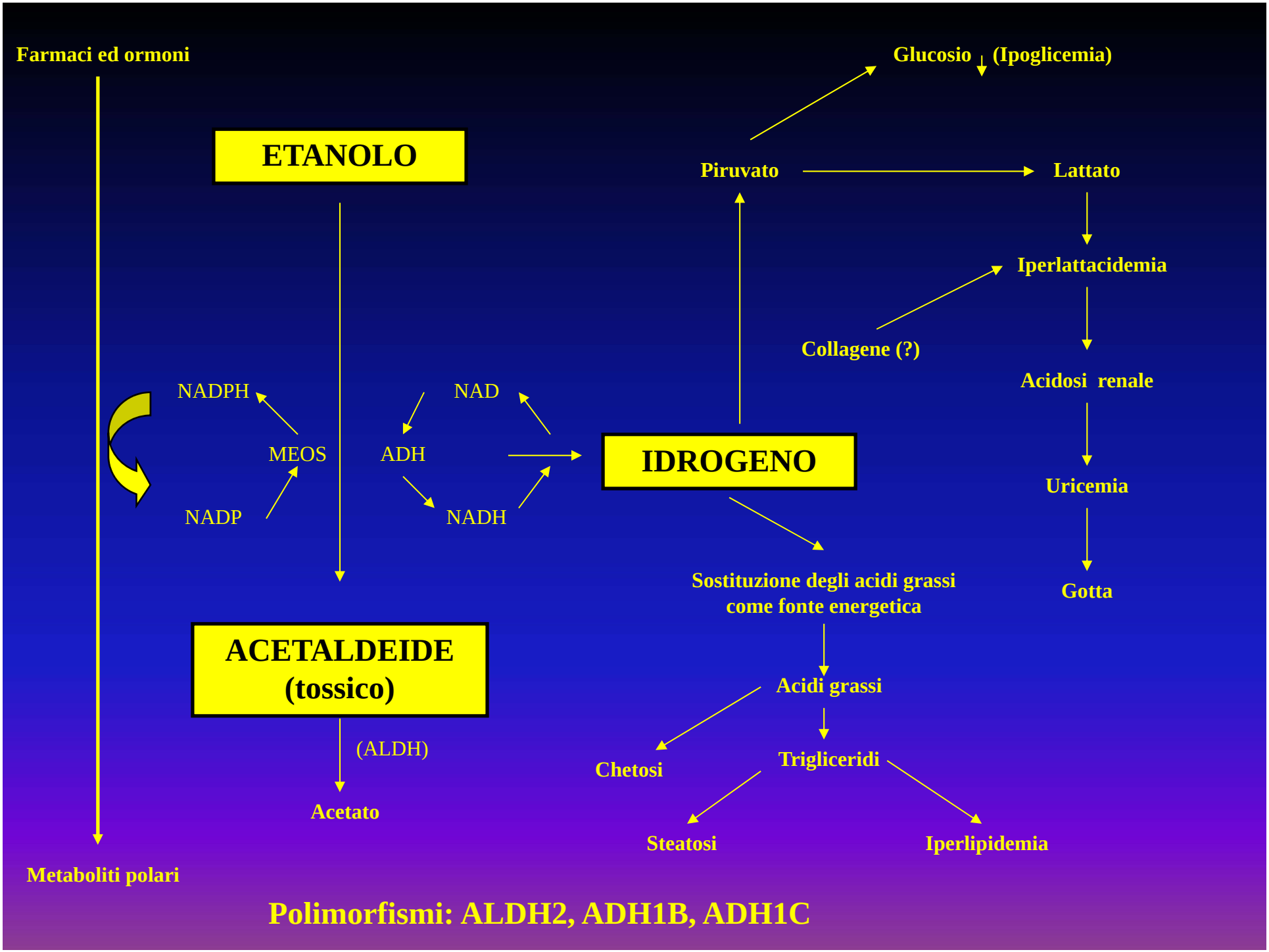
Figure 2: **Burden of disease attributable to 20 leading risk factors in 2010, expressed as a percentage of global disability-adjusted life-years**
For men (A), women (B), and both sexes (C).

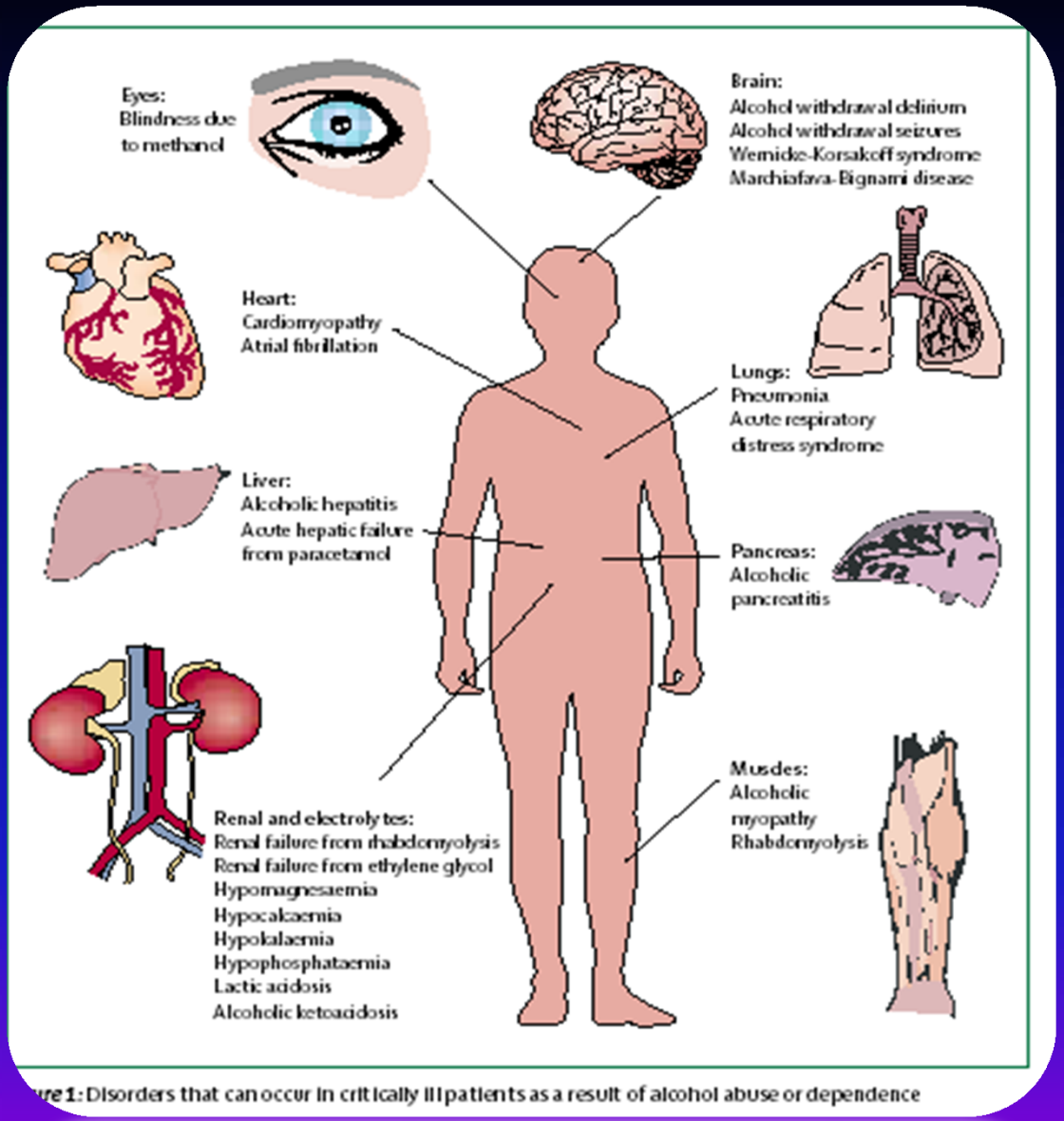
Lim ST et al; Lancet 2012, 380: 2224

CONSUMO DI BEVANDE ALCOLICHE IN SOGGETTI SANI

3 - 5 gr/die	Rischio minimo
Donna < 10 gr/die **Uomo < 20 gr/die**	Basso rischio
Donna 11-40 gr/die **Uomo 21-60 gr/die** **> 65 anni e fra i 16-18 anni >12/die**	Consumo Rischioso
Donna > 40 gr/die **Uomo > 60 gr/die** **Binge Drinking**	**Consumo Dannoso**

E. Scafato et al, Istituto Superiore Sanita' 2010


Farmaci ed ormoni
Glucosio (Ipoglicemia)
ETANOLO
Piruvato
Lattato
Iperlattacidemia
Collagene (?)
Acidosi renale
NADPH
NAD
MEOS
ADH
IDROGENO
Uricemia
NADP
NADH
Gotta
Sostituzione degli acidi grassi
come fonte energetica
ACETALDEIDE
(tossico)
Acidi grassi
(ALDH)
Chetosi
Trigliceridi
Acetato
Steatosi
Iperlipidemia
Metaboliti polari
Polimorfismi: ALDH2, ADH1B, ADH1C



ure 1: Disorders that can occur in critically ill patients as a result of alcohol abuse or dependence

Moss M. and Burnham E. L., The Lancet 2006

Emanuele Scafato (a), Silvia Ghirini (a), Luca Casartino (b)
(a) Centro Nazionale di Epidemiologia, Sorveglianza e Promozione della salute, CNESPS; Centro Organizzazione Mondiale della Sanità Ricerca sull'Alcol, Istituto Superiore di Sanità; (b) Lazioanna, Agenzia di Sanità Pubblica della Regione Lazio

L'assunzione acuta di alcol comporta

- *conseguenze organiche*
  - epatiti
  - esofagite
  - dispepsia
  - gastrite
  - uricemia
  - pancreatite
  - aritmie cardiache
  - traumi
  - reazioni con altre sostanze
  - danni al feto
  - reazioni con i farmaci
- *conseguenze psicologiche*
  - riduzione delle capacità cognitive
  - depressione
  - ansia
  - tentati suicidi
  - problemi psicologici dei figli
  - insonnia
- *conseguenze sociali*
  - violenze familiari
  - disgregazione familiare
  - abuso sui minori
  - incidenti domestici
  - incidenti sul lavoro
  - difficoltà sul lavoro
  - problemi di ordine pubblico
  - gravidanze indesiderate

L'assunzione cronica di alcol comporta per l'

- *conseguenze organiche*
  - steatosi epatica
  - cirrosi
  - demenza
  - epatocarcinoma
  - varici esofagee
  - gastroduodeniti
  - pancreatiti
  - carcinoma bocca, laringite, esofago, fe;
  - danni al sistema nervoso
  - obesità
  - diabete
  - miopatie
  - neuropatie
  - deficienze nutrizionali
  - disfunzioni sessuali
  - impotenza
  - ipogonadismo
  - alterazioni mestruali
  - alterazioni del sistema immunitario
  - patologie oculari
  - patologie dermatologiche
  - danni ai reni
  - ipertensione arteriosa
  - gotta
- *conseguenze psicologiche*
  - insonnia
  - disturbi di personalità
  - amnesie
  - tentati suicidi
  - allucinazioni
- *conseguenze sociali*
  - problemi familiari
  - senza fissa dimora
  - difficoltà sul lavoro
  - instabilità lavorativa
  - incidenti sul lavoro
  - disoccupazione
  - problemi giudiziari
  - problemi finanziari
  - gioco d'azzardo
  - assunzione di altre sostanze
  - poliassunzioni di sostanze nei figli

Scafato et al. Alcol e Salute,

ISS – Centro Collaboratore OMS 2012

WORLD HEALTH ORGANIZATION
International Agency for Research on Cancer
(IARC)
Evaluation of Carcinogenic Risks to Humans

Group 1 Carcinogenic to humans
(arsenic, asbesto, benzene, radionuclide, tobacco smoking …..)

Group 2 A Probably carcinogenic to humans

Group 2B Possibly carcinogenic to humans
(radio frequency elettromagnetic fields from wireless phones ….)

Group 3 Unclassifiable as to carcinogenicity in humans

Group 4 Probably not carcinogenic to humans

IARC; Lancet Oncology, November 2009

	Tumour sites for which there is sufficient evidence	Tumour sites for which there is limited evidence	Tumour sites for which there is evidence suggesting lack of carcinogenicity
Tobacco smoking	Oral cavity, oropharynx, nasopharynx, and hypopharynx, oesophagus (adenocarcinoma and squamous-cell carcinoma), stomach, colorectum,* liver, pancreas, nasal cavity and paranasal sinuses, larynx, lung, uterine cervix, ovary (mucinous)*, urinary bladder, kidney (body and pelvis), ureter, bone marrow (myeloid leukaemia)	Female breast*	Endometrium (postmenopausal*), thyroid*
Parental smoking (cancer in the offspring)	Hepatoblastoma*	Childhood leukaemia (in particular acute lymphocytic leukaemia)*	
Second-hand smoke	Lung	Larynx,* pharynx*	
Smokeless tobacco	Oral cavity, oesophagus,* pancreas		
Areca nut			
Betel quid with added tobacco	Oral cavity, pharynx, oesophagus		
Betel quid without added tobacco	Oral cavity, oesophagus*	Liver*	
Alcohol consumption	Oral cavity, pharynx, larynx, oesophagus, liver, colorectum, female breast	Pancreas*	Kidney, non-Hodgkin lymphoma
Acetaldehyde associated with alcohol consumption	Oesophagus,* head and neck*		
Chinese-style salted fish	Nasopharynx	Stomach*	
Indoor emissions from household combustion of coal	Lung		

*New sites.

Table: Evidence for carcinogenicity in humans of Group 1 agents assessed

IARC; Lancet Oncology, November 2009

	Tumour sites for which there is sufficient evidence	Tumour sites for which there is limited evidence	Tumour sites for which there is evidence suggesting lack of carcinogenicity
Tobacco smoking	Oral cavity, oropharynx, nasopharynx, and hypopharynx, oesophagus (adenocarcinoma and squamous-cell carcinoma), stomach, colorectum,* liver, pancreas, nasal cavity and paranasal sinuses, larynx, lung, uterine cervix, ovary (mucinous)*, urinary bladder, kidney (body and pelvis), ureter, bone marrow (myeloid leukaemia)	Female breast*	Endometrium (postmenopausal*), thyroid*
Parental smoking (cancer in the offspring)	Hepatoblastoma*	Childhood leukaemia (in particular acute lymphocytic leukaemia)*	
Second-hand smoke	Lung	Larynx,* pharynx*	
Smokeless tobacco	Oral cavity, oesophagus,* pancreas		
Areca nut			
Betel quid with added tobacco	Oral cavity, pharynx, oesophagus		
Betel quid without added tobacco	Oral cavity, oesophagus*	Liver*	
Alcohol consumption	Oral cavity, pharynx, larynx, oesophagus, liver, colorectum, female breast	Pancreas*	Kidney, non-Hodgkin lymphoma
Acetaldehyde associated with alcohol consumption	Oesophagus,* head and neck*		
Chinese-style salted fish	Nasopharynx	Stomach*	
Indoor emissions from household combustion of coal	Lung		

*New sites.

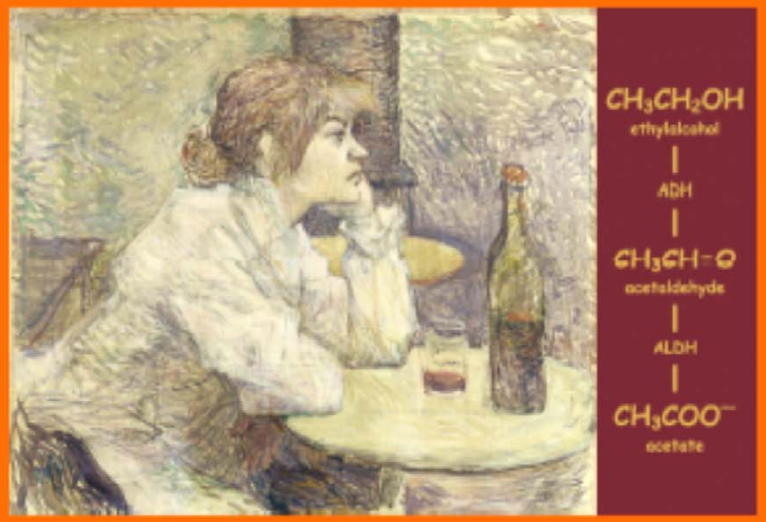
Table: Evidence for carcinogenicity in humans of Group 1 agents assessed

WORLD HEALTH ORGANIZATION
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

VOLUME 96

Alcohol Consumption and Ethyl Carbamate



LYON, FRANCE
2010

WORLD HEALTH ORGANIZATION
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

VOLUME 100

A Review of Human Carcinogens

Part E: Personal Habits and Indoor Combustions

LYON, FRANCE

2012

Agents Classified by the *IARC Monographs*, Volumes 1–104

CAS No	Agent	Group	Volume	Year
000075-07-0	Acetaldehyde associated with consumption of alcoholic beverages	1	100E	2012
	Acid mists, strong inorganic	1	54, 100F	2012
001402-68-2	Aflatoxins	1	56, 82, 100F	2012
	Alcoholic beverages	1	44, 96, 100E	2012
	Aluminium production	1	34, Sup 7, 100F	2012
000092-67-1	4-Aminobiphenyl	1	1, Sup 7, 99, 100F	2012
	Areca nut	1	85, 100E	2012
000313-67-7	Aristolochic acid (NB: Overall evaluation upgraded to Group 1 based on mechanistic and other relevant data)	1	82, 100A	2012
000313-67-7	Aristolochic acid, plants containing	1	82, 100A	2012
007440-38-2	Arsenic and inorganic arsenic compounds	1	23, Sup 7, 100C	2012
000064-17-5	Ethanol in alcoholic beverages	1	96, 100E	2012
000075-21-8	Ethylene oxide (NB: Overall evaluation upgraded to Group 1 based on mechanistic and other relevant data)	1	97, 100F	2012
033419-42-0	Etoposide (NB: Overall evaluation upgraded to Group 1 based on mechanistic and other relevant data)	1	76, 100A	2012
033419-42-0 015663-27-1 011056-06-7	Etoposide in combination with cisplatin and bleomycin	1	76, 100A	2012
	Fission products, including strontium-90	1	100D	2012
000050-00-0	Formaldehyde	1	88, 100F	2012

OMS, IARC 2012

2.19 Synthesis

2.19.1 Oral cavity and pharnyx

Data published since the previous *IARC monograph* (IARC, 2010) support the conclusion that consumption of alcoholic beverages is causally related to cancer of the oral cavity and pharynx. Increasing alcohol consumption increases risk in a dose-dependent manner, does not vary materially by beverage type or sex and the association is not due to chance, bias or confounding.

2.19.2 Larnynx

Data published since the previous *IARC Monograph* (IARC 2010) supports the conclusion that consumption of alcoholic beverages is causally related to cancer of the larynx. Increasing alcohol consumption increases risk in a dose-dependent manner, does not vary materially by beverage type or sex, and chance, bias and confounding can be ruled out.

2.19.3 Oesophagus

Data published since the previous *IARC Monograph* (IARC, 2010) supports the conclusion that consumption of alcoholic beverages is causally related to squamous cell carcinoma of the oesophagus. Increasing alcohol consumption increases risk in a dose-dependent manner, does not vary materially by beverage type or sex, and chance, bias and confounding can be ruled out. There is now a substantial body of evidence that alcoholic beverage consumption is not associated with adenocarcinoma of the oesophagus.

2.19.4 Upper aerodigestive tract

There is evidence that consumption of alcoholic beverages is causally related to cancer of the upper aerodigestive tract, as it is for cancer of the oral cavity and pharynx, larynx and oesophagus separately. Increasing alcohol consumption increases risk in a dose-dependent manner, does not vary materially by beverage type or sex and chance, bias and confounding can be ruled out.

2.19.5 Colon and rectum

Overall, the data published since the previous *IARC Monograph* (IARC, 2010) supports the conclusion that consumption of alcoholic beverages is causally related to cancer of the colorectum. Most of the evidence suggests that consumption of alcoholic beverages is positively associated with both cancer of the colon and cancer of the rectum, and is similar in men and women, although the data are not entirely consistent. Similarly, there is some evidence that risk may only be increased at relatively high levels of intake (i.e. > 30 g/d). There is consistent evidence that risk does not differ by beverage type; whether the risk associated with consumption of alcoholic beverages differs by smoking status or intake of dietary folate is inconsistent.

2.19.6 Liver

The new studies support the previous conclusion that the risk for hepatocellular carcinoma is causally related to the consumption of alcoholic beverages. It is not possible to draw any conclusion concerning consumption of alcoholic beverages and risk of cholangiocarcinoma.

OMS, IARC Volume 100 E, pag 450, 2012

2.19.8 Pancreas

There is accumulating evidence that high alcohol intake (i.e. ≥ 30 g/d) is associated with a small increased risk of cancer for the pancreas. However, the possibility that residual confounding by smoking may partly explain this association cannot be excluded. Whether the risk associated with heavy alcohol consumption differs by beverage type, smoking status or body mass index requires further investigation.

2.19.10 Breast

Occurrence of cancer of the female breast is causally associated with the consumption of alcoholic beverages. Cancer risk increases proportionately according to the amount of alcohol consumed, with an increase in risk of up to 12% for each additional drink consumed regularly each day (equivalent to about 10 g/d). The risk does not appear to vary significantly by beverage type or smoking status. It remains

World Health Organization, IARC, Volume 100 E, pag. 451 2012

There is *sufficient evidence* in humans for the carcinogenicity of alcohol consumption. Alcohol consumption causes cancers of the oral cavity, pharynx, larynx, oesophagus, colorectum, liver (hepatocellular carcinoma) and female breast. Also, an association has been observed between alcohol consumption and cancer of the pancreas.

For cancer of the kidney and non-Hodgkin lymphoma, there is *evidence suggesting lack of carcinogenicity.*

There is *sufficient evidence* in humans for the carcinogenicity of acetaldehyde associated with the consumption of alcoholic beverages. Acetaldehyde associated with the consumption of alcoholic beverages causes cancer of the oesophagus and of the upper aerodigestive tract combined.

There is *sufficient evidence* in experimental animals for the carcinogenicity of ethanol.

There is *sufficient evidence* in experimental animals for the carcinogenicity of acetaldehyde.

Alcohol consumption is *carcinogenic to humans (Group 1).*

Ethanol in alcoholic beverages is *carcinogenic to humans (Group 1).*

Acetaldehyde associated with the consumption of alcoholic beverages is *carcinogenic to humans (Group 1).*

World Health Organization, International Agency for Cancer Research,

Volume 100 E, pag. 476 – Lyon, France 2012

Alcohol Attributable Burden of Incidence of Cancer in Eight European Countries* Based on Results from Prospective Cohort Study

* Denmark, France, Germany, Greece, Italy, the Netherlands, Spain, UK

…among men and women, 10% (95% confidence interval 7 to 13%) and 3% (1 to 5%) of the incidence of total cancer was attributable to former and current alcohol consumption……

Alcohol Attributable Fractions:

upper aerodigestive tract	44% for men and 25% for women
liver	33% for men and 18% for women
colorectal	17% for men and 4% for women
female breast	5%

BMJ 2011; 342: d1564

Alcohol-Attributable Cancer Deaths and Years of Potential Life Lost in the United States

David E. Nelson, MD, MPH, Dwayne W. Jarman, DVM, MPH, Jürgen Rehm, PhD, Thomas K. Greenfield, PhD, Grégoire Rey, PhD, William C. Kerr, PhD, Paige Miller, PhD, MPH, Kevin D. Shield, MHSc, Yu Ye, MA, and Timothy S. Naimi, MD, MPH

Objectives. Our goal was to provide current estimates of alcohol-attributable cancer mortality and years of potential life lost (YPLL) in the United States.

Methods. We used 2 methods to calculate population-attributable fractions. We based relative risks on meta-analyses published since 2000, and adult alcohol consumption on data from the 2009 Alcohol Epidemiologic Data System, 2009 Behavioral Risk Factor Surveillance System, and 2009–2010 National Alcohol Survey.

Results. Alcohol consumption resulted in an estimated 18 200 to 21 300 cancer deaths, or 3.2% to 3.7% of all US cancer deaths. The majority of alcohol-attributable female cancer deaths were from breast cancer (56% to 66%), whereas upper airway and esophageal cancer deaths were more common among men (53% to 71%). Alcohol-attributable cancers resulted in 17.0 to 19.1 YPLL for each death. Daily consumption of up to 20 grams of alcohol (≤1.5 drinks) accounted for 26% to 35% of alcohol-attributable cancer deaths.

Conclusions. Alcohol remains a major contributor to cancer mortality and YPLL. Higher consumption increases risk but there is no safe threshold for alcohol and cancer risk. Reducing alcohol consumption is an important and underemphasized cancer prevention strategy. (*Am J Public Health*. Published online ahead of print February 14, 2013: e1–e8. doi:10.2105/AJPH.2012.301199)

Alcohol use is estimated to account for about 4% of all deaths worldwide.[1] Research over several decades has consistently shown that alcohol increases the risk for cancers of the oral cavity and pharynx, larynx, esophagus, and liver.[2–6] The biological mechanisms by which alcohol induces cancer are not fully understood, but may include genotoxic effects of acetaldehyde, production of reactive oxygen or nitrogen species, changes in folate metabolism, increased estrogen concentration, or serving as a solvent for tobacco metabolites.[5]

The International Agency for Research on Cancer (IARC) and the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) both published comprehensive reviews of the scientific literature on alcohol and cancer risk in 2007.[5–7] In addition to confirming earlier research for the previously mentioned cancers, they con-

TABLE 1—Population-Attributable Fractions for Alcohol-Attributable Cancers: United States, 2009

Cancer Type	BRFSS		NAS	
	Men, % (95% CI)	Women, % (95% CI)	Men, % (95% CI)	Women, % (95% CI)
		Method 1 PAF[45,54–56]		
Oral cavity and pharynx	30 (29, 32)	28 (27, 30)	27 (25, 29)	26 (24, 28)
Larynx	20 (19, 22)	22 (20, 23)	17 (16, 19)	19 (18, 21)
Esophagus	19 (18, 20)	21 (19, 22)	17 (15, 18)	18 (17, 20)
Colon	8 (7, 9)	14 (12, 15)	7 (6, 8)	12 (10, 13)
Rectum	10 (9, 11)	15 (13, 16)	8 (7, 9)	12 (11, 14)
Liver	13 (11, 14)	16 (15, 18)	11 (10, 12)	14 (13, 16)
Female breast	NA	18 (16, 20)	NA	16 (14, 17)
		Method 2 PAF[45]		
Oral cavity and pharynx	66 (63, 69)	37 (34, 41)	64 (60, 68)	38 (36, 40)
Larynx	38 (36, 41)	18 (16, 20)	32 (29, 35)	11 (9, 13)
Esophagus	34 (32, 36)	20 (18, 23)	30 (29, 33)	16 (14, 18)
Colon	5 (4, 6)	3 (2, 4)	4 (3, 5)	2 (1, 3)
Rectum	9 (8, 10)	5 (4, 6)	8 (7, 9)	4 (3, 5)
Liver	16 (15, 17)	9 (8, 10)	15 (14, 16)	8 (6, 10)
Female breast	NA	14 (12, 16)	NA	12 (10, 14)

Note. BRFSS = Behavioral Risk Factor Surveillance System; CI = confidence interval; NA = not applicable; NAS = National Alcohol Survey; PAF = population-attributable fraction.

Nelson DE et al, Am J Public Health 2013

Site of cancer (ICD 7)	Men				Women			
	Obs	Exp	SIR	(95% CI)	Obs	Exp	SIR	95% (CI)
All cancers except non-melanoma skin cancer (140–205 minus 191)	2145	1140.8	1.9	(1.8–2.0)**	601	239.1	2.5	(2.3–2.7)**
Buccal cavity and pharynx (140–148)	227	48.2	4.7	(4.1–5.4)**	42	3.2	13.1	(9.5–17.7)**
Lip (140)	3	14.5	0.2	(0.0–0.6)*	0	0.3	0.0	(0.0–12.7)
Tongue (141)	47	5.7	8.3	(6.1–11.0)**	10	0.5	20.4	(9.8–37.5)**
Salivary glands (142)	6	3.2	1.9	(0.7–4.1)	1	0.4	2.3	(0.0–12.9)
Mouth (143–144)	76	11.0	6.9	(5.5–8.7)**	11	1.0	10.7	(5.3–19.1)**
Pharynx (145–148)	95	13.8	6.9	(5.6–8.4)**	20	1.0	21.1	(12.9–32.5)**
Digestive organs and peritoneum (150–159)	473	297.8	1.6	(1.5–1.7)**	55	38.4	1.4	(1.1–1.9)*
Oesophagus (150)	80	19.6	4.1	(3.2–5.1)**	8	1.1	7.1	(3.1–14.0)**
Stomach (151)	68	49.6	1.4	(1.1–1.7)*	7	3.7	1.9	(0.8–3.9)
Colon (153)	89	87.5	1.0	(0.8–1.3)	14	15.7	0.9	(0.5–1.5)
Rectum (154)	81	66.6	1.2	(1.0–1.5)	4	7.4	0.5	(0.2–1.4)
Liver (155)	64	13.6	4.7	(3.6–6.0)**	8	1.3	6.0	(2.6–11.9)**
Gall bladder (155.1)	9	7.6	1.2	(0.5–2.3)	4	1.7	2.3	(0.6–6.0)
Pancreas (157)	61	36.5	1.7	(1.3–2.2)**	6	4.8	1.2	(0.5–2.7)
Respiratory system (160–164)	661	276.7	2.4	(2.2–2.6)**	96	24.2	4.0	(3.2–4.9)**
Larynx (161)	121	26.1	4.6	(3.9–5.5)**	4	1.0	3.9	(1.0–9.9)*
Lung (162)	523	238.2	2.2	(2.0–2.4)**	90	22.4	4.0	(3.2–5.0)**
Pleura (162.2)	11	6.5	1.7	(0.8–3.0)	1	0.3	3.6	(0.1–19.9)
Urinary system (180–181)	174	156.3	1.1	(1.0–1.3)	16	10.7	1.5	(0.9–2.4)
Kidney (180)	64	44.4	1.4	(1.1–1.8)*	10	4.8	2.1	(1.0–3.8)*
Urinary bladder (181)	110	112.0	1.0	(0.8–1.2)	6	5.9	1.0	(0.4–2.2)
Breast (170)	3	2.2	1.4	(0.3–4.1)	93	75.9	1.2	(1.0–1.5)
Female genital organs (171–176)	–	–	–	–	58	45.8	1.3	(1.0–1.6)
Cervix uteri (171)	–	–	–	–	29	16.3	1.8	(1.2–2.6)*
Corpus uteri (172)	–	–	–	–	8	13.2	0.6	(0.3–1.2)
Ovary (175)	–	–	–	–	16	13.8	1.2	(0.7–1.9)
Male genital organs (177–179)	170	133.6	1.3	(1.1–1.5)*	–	–	–	–
Prostate gland (177)	135	100.7	1.3	(1.1–1.6)**	–	–	–	–
Testis (178)	27	28.1	1.0	(0.6–1.4)	–	–	–	–

*$P < 0.05$.
**$P < 0.001$.

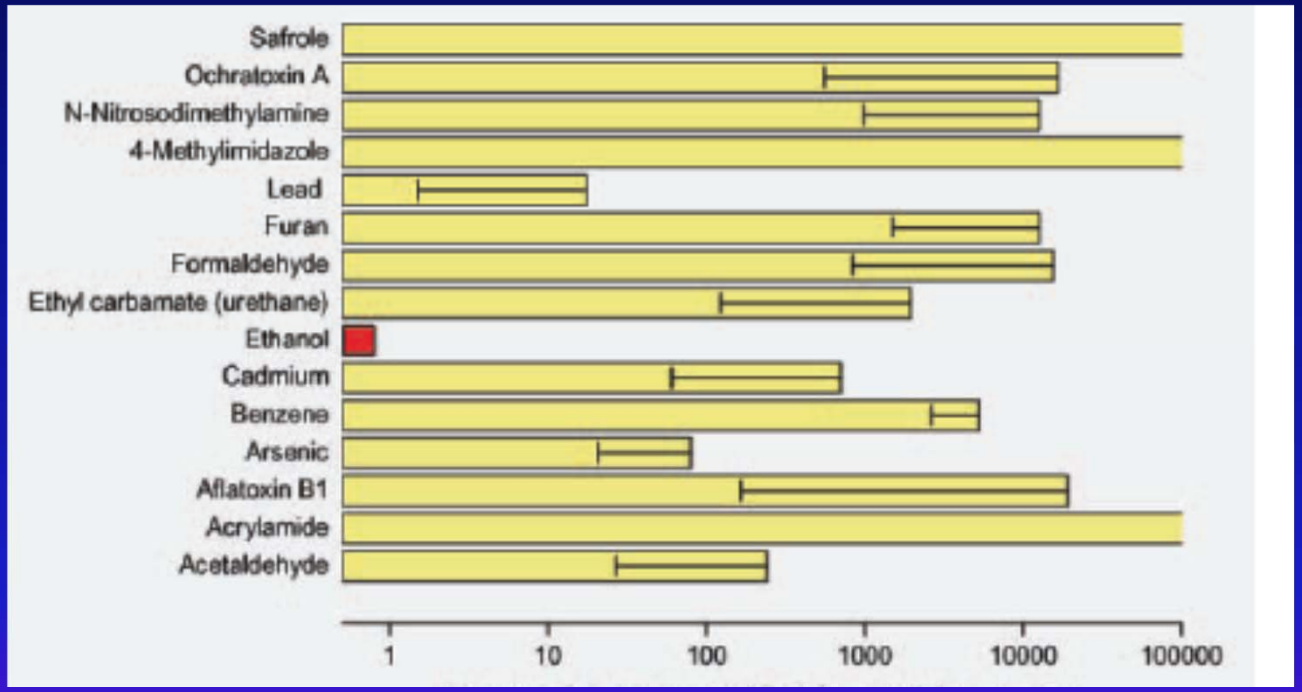
Thygesen et al, Alcohol and Alcoholism 2009

Table 1. Summary of WHO International Agency for Research on Cancer (IARC) evaluation of carcinogenicity of substances that may be present in alcoholic beverages (updated from IARC[2])

	IARC Monographs evaluation of Carcinogenicity			
Agent	**In animals**	**In humans**	**IARC group[1]**	***IARC Monographs* (Volume Number)**
Acetaldehyde associated with consumption of alcoholic beverages	Sufficient	Sufficient	1	36, Sup 7, 71, 100E
Acrylamide	Sufficient	Inadequate	2A	60
Aflatoxins	Sufficient	Sufficient	1	56, 82, 100F
Arsenic	Sufficient	Sufficient	1	23, Sup 7, 100C
Benzene	Sufficient	Sufficient	1	29, Sup 7, 100F
Cadmium	Sufficient	Sufficient	1	58, 100C
Ethanol in alcoholic beverages	Sufficient	Sufficient	1	44, 96, 100E
Ethyl carbamate (urethane)	Sufficient	Inadequate	2A	7, Sup 7, 96
Formaldehyde	Sufficient	Sufficient	1	88, 100F
Furan	Sufficient	Inadequate	2B	63
Lead compounds, inorganic	Sufficient	Limited	2A	87
4-Methylimidazole	Sufficient	Inadequate	2B	101
N-Nitrosodimethylamine	Sufficient	Inadequate	2A	17, Sup 7
Ochratoxin A	Sufficient	Inadequate	2B	56
Safrole	Sufficient	Inadequate	2B	10, Sup 7

[1]Group 1: Carcinogenic to humans; Group 2A: Probably carcinogenic to humans; Group 2B: Possibly carcinogenic to humans (for definitions of groups, see monographs.iarc.fr).

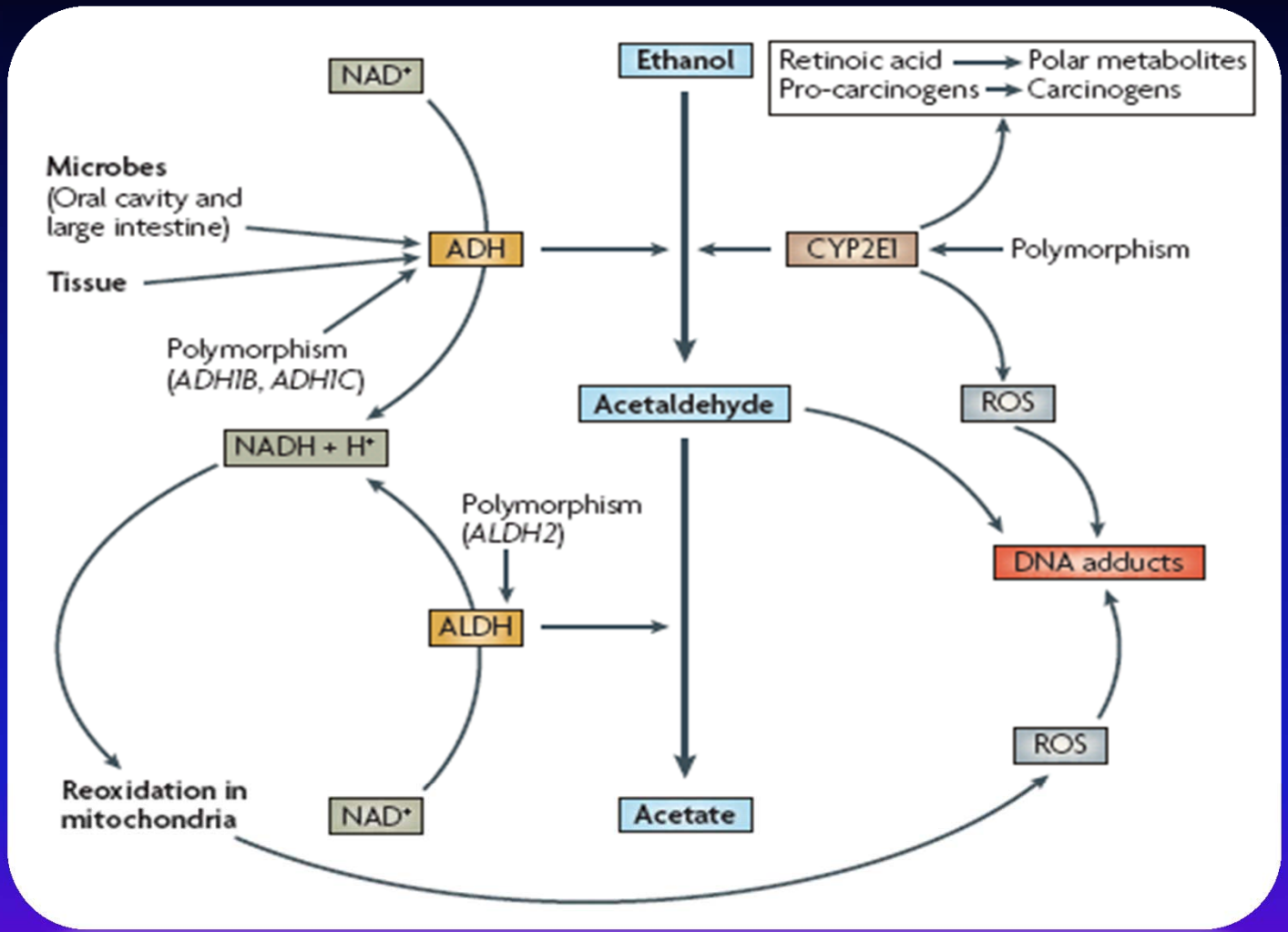
MARGIN OF EXPOSURE (MOE)



ALCOHOL AND CARCINOGENESIS

- ✓ Local Effect
- ✓ Acetaldehyde (ALDH isoenzymes polymorphism)
- ✓ Polymorphisms of ADH1B, ADH1C
- ✓ Induction of CYP2E1 (conversion of various xenobiotics)
- ✓ Nutritional Deficiencies
- ✓ Interaction with Retinoids
- ✓ Changes in the degree of Methylation
- ✓ Immune Surveillance

Testino G, Hepatogastroenterol 2008


NAD+
Ethanol
Retinoic acid → Polar metabolites
Pro-carcinogens → Carcinogens
Microbes
(Oral cavity and
large intestine)
Tissue
ADH
CYP2E1
Polymorphism
Polymorphism
(ADH1B, ADH1C)
Acetaldehyde
ROS
NADH + H+
Polymorphism
(ALDH2)
DNA adducts
ALDH
ROS
Reoxidation in
mitochondria
NAD+
Acetate

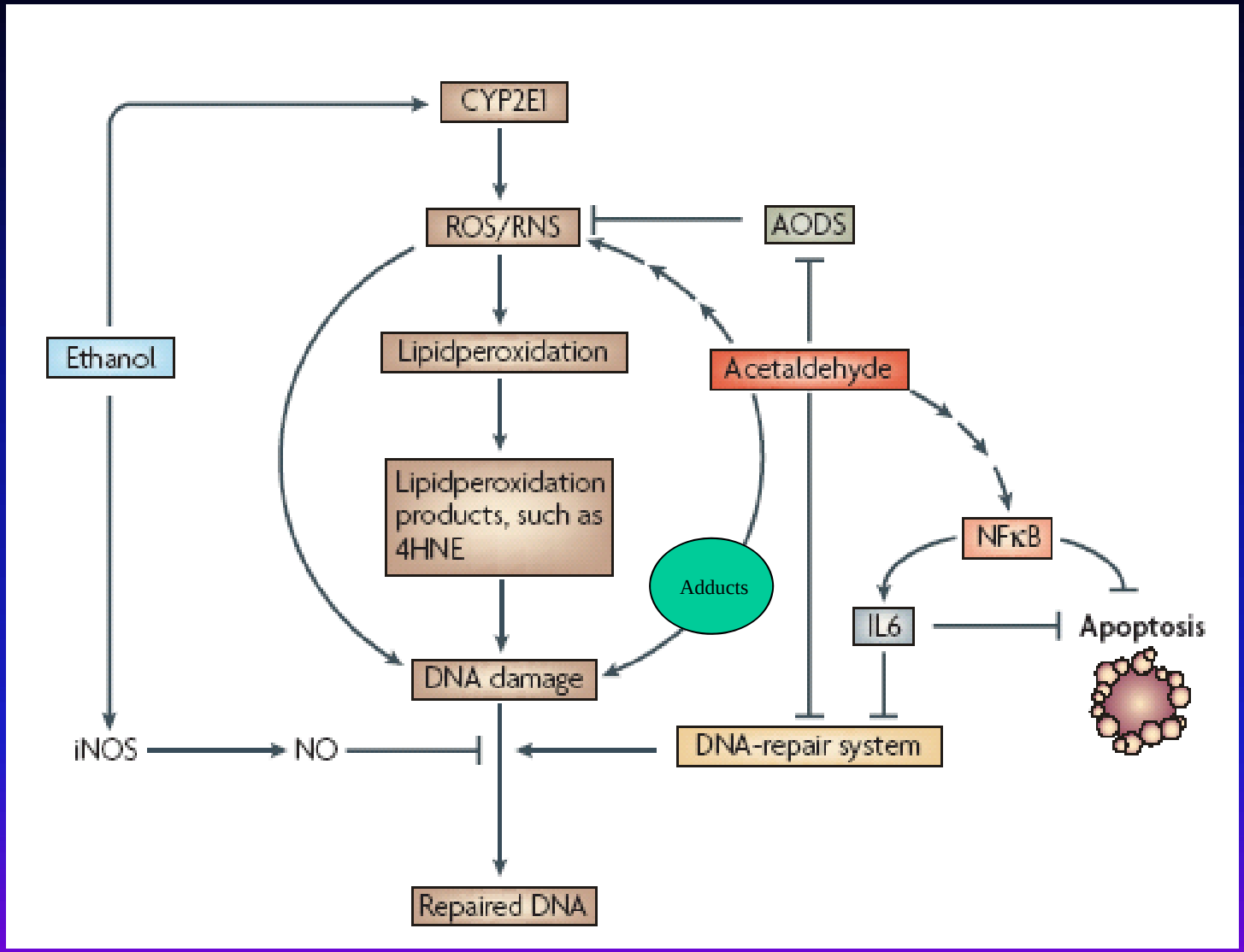

CYP2E1
ROS/RNS
AODS
Ethanol
Lipidperoxidation
Acetaldehyde
Lipidperoxidation products, such as 4HNE
NFκB
Adducts
IL6
Apoptosis
DNA damage
iNOS
NO
DNA-repair system
Repaired DNA

TABLEAU 1 : POLYMORPHISMES GÉNÉTIQUES ASSOCIÉS AUX ENZYMES QUI MÉTABOLISENT L'ALCOOL

Enzyme	Allèles humains	Ancienne nomenclature	Activité enzymatique	Fréquence par population	Référence
ADH1B	*ADH1B*1*	*ADH2*1*	Active		Bosron, 1986 ; Quertemont, 2004 ; Brennan, 2004b ; Coutelle, 1998
	ADH1B*2	***ADH2*2***	**Hyperactive** (x 43 / *ADH1B*1*)	Européenne 0-10 % Africaine 0-15 % Asiatique 10-90 %	
	*ADH1B*3*	*ADH2*3*	Hyperactive		
ADH1C	***ADH1C*1***	***ADH3*1***	**Hyperactive** (x 2,5 / *ADH1C*2*)	Européenne 45-70 % Africaine 75-90 % Asiatique 85-100 %	Bosron, 1986 ; Quertemont, 2004 ; Brennan, 2004b ; Coutelle, 1998
	*ADH1C*2*	*ADH3*2*	Active		
ALDH2	*ALDH2*1*		Active		Crabb, 1989 ; Brennan, 2004b
	ALDH2*2		**Inactive** (/ *ADLH2*1*)	Européenne 0-5 % Asiatique 0-35 %	
CYP2E1	*c1*		Active		Bouchardy, 2000 ; Hildesheim, 1997
	c2		**Hyperactive** (/ *CYP2E1 c1*)	Européenne 0-10 % Asiatique 20-25 %	

Institute National du Cancer, www.e-cancer.fr 2007

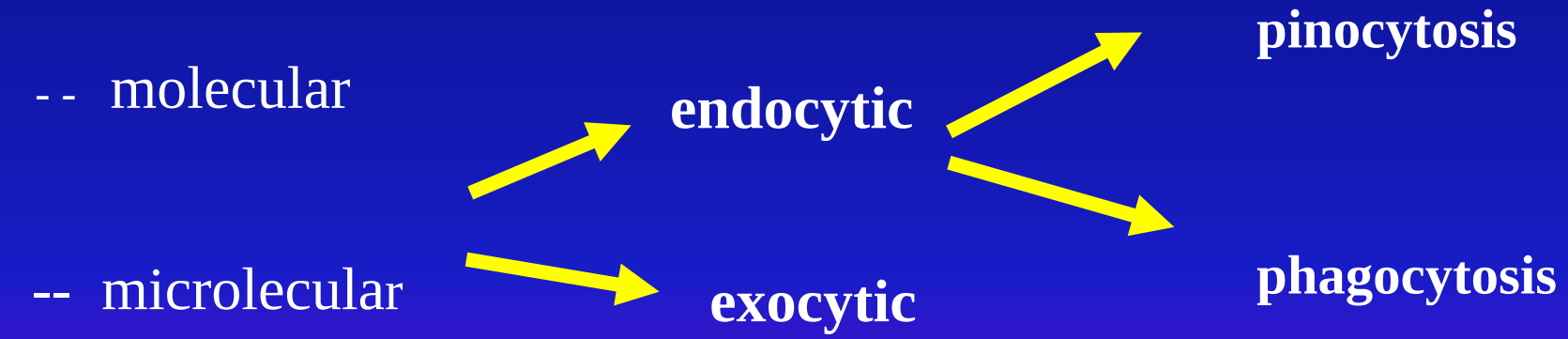
IMPACT OF ALDH2-DEFICIENCY GENES ON THE RISK FOR OESOPHAGEAL CANCER

Genes/polymorphisms	Alcohol 1-30 g/day	Alcohol > 30/ g/day
ALDH2-active	OR 7.2	
ALDH2-deficiency	OR 14.5	OR 102.5
Slow ADH1B + ALDH2-deficiency	OR 37.5	OR 382.3

Salaspuro M, Scand J Gastroenterol 2009

ALCOHOL AND ORAL CANCER

Cytological alterations (reduction cytoplasmic area,abnormal DNA profile...)
- mucosal transport : intercellular passage
- mucosal transport : intracellular mechanisms



Cowpe et al, 1988; Axford et al, 1999; Howie et al, 2001; Graham, 2005; Tramacere et al, Oral Oncology 2010

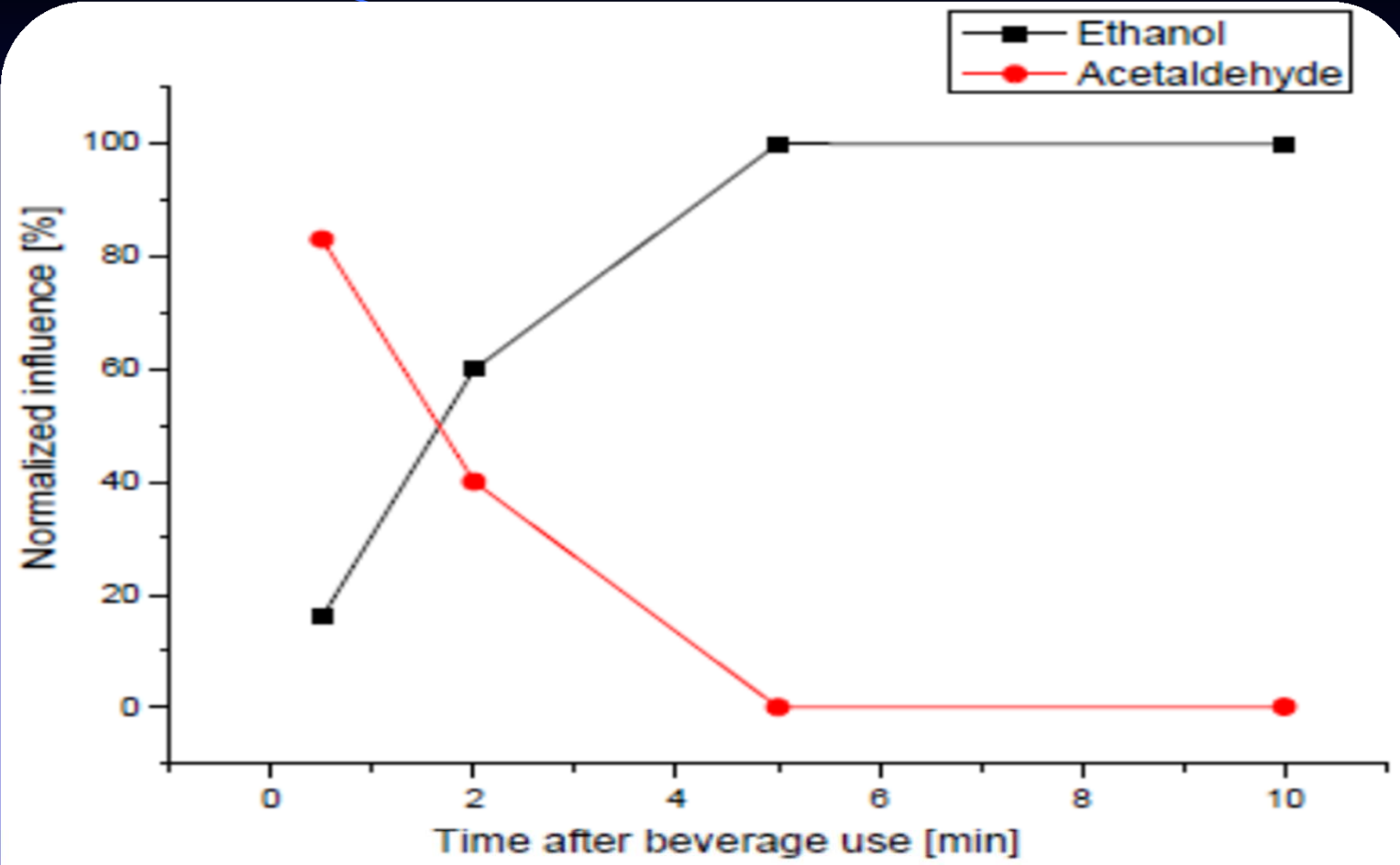


Figure 2 Influence of ethanol and acetaldehyde content of the beverages on the salivary acetaldehyde concentration.

Lachenmeier and Monakhova, J Exp Cin Cancer Res 2011

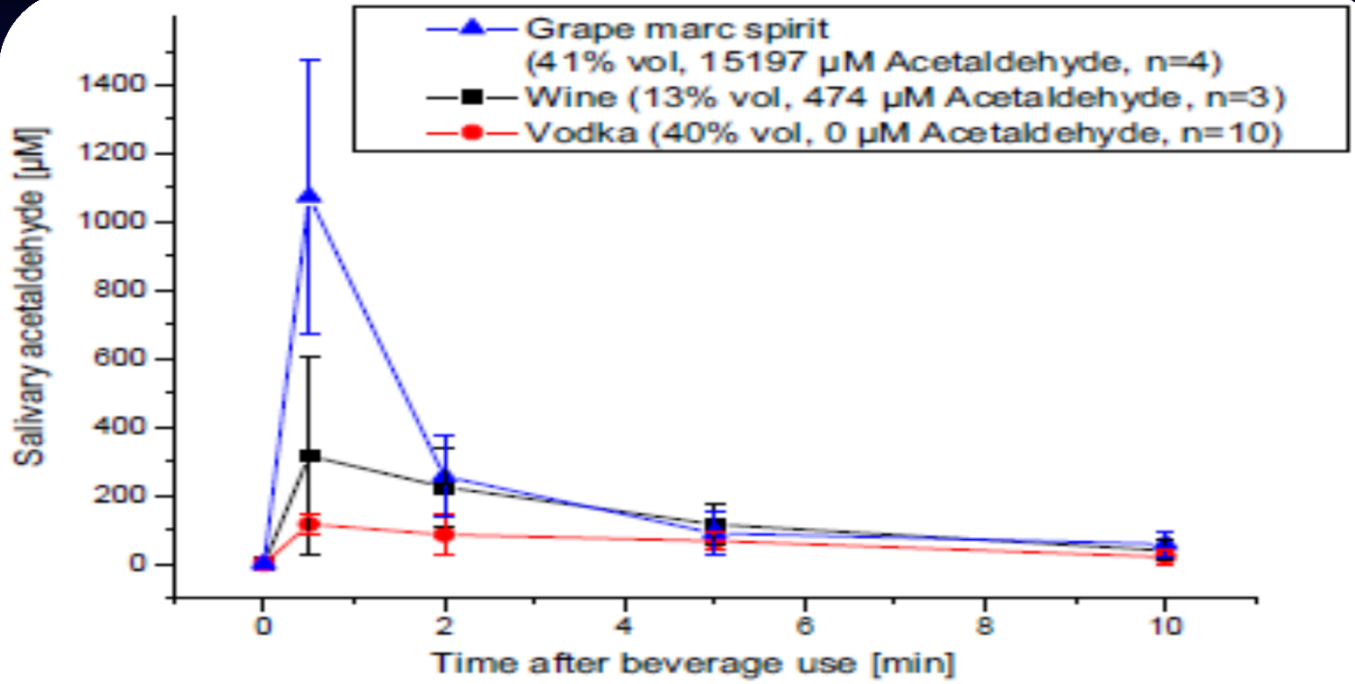
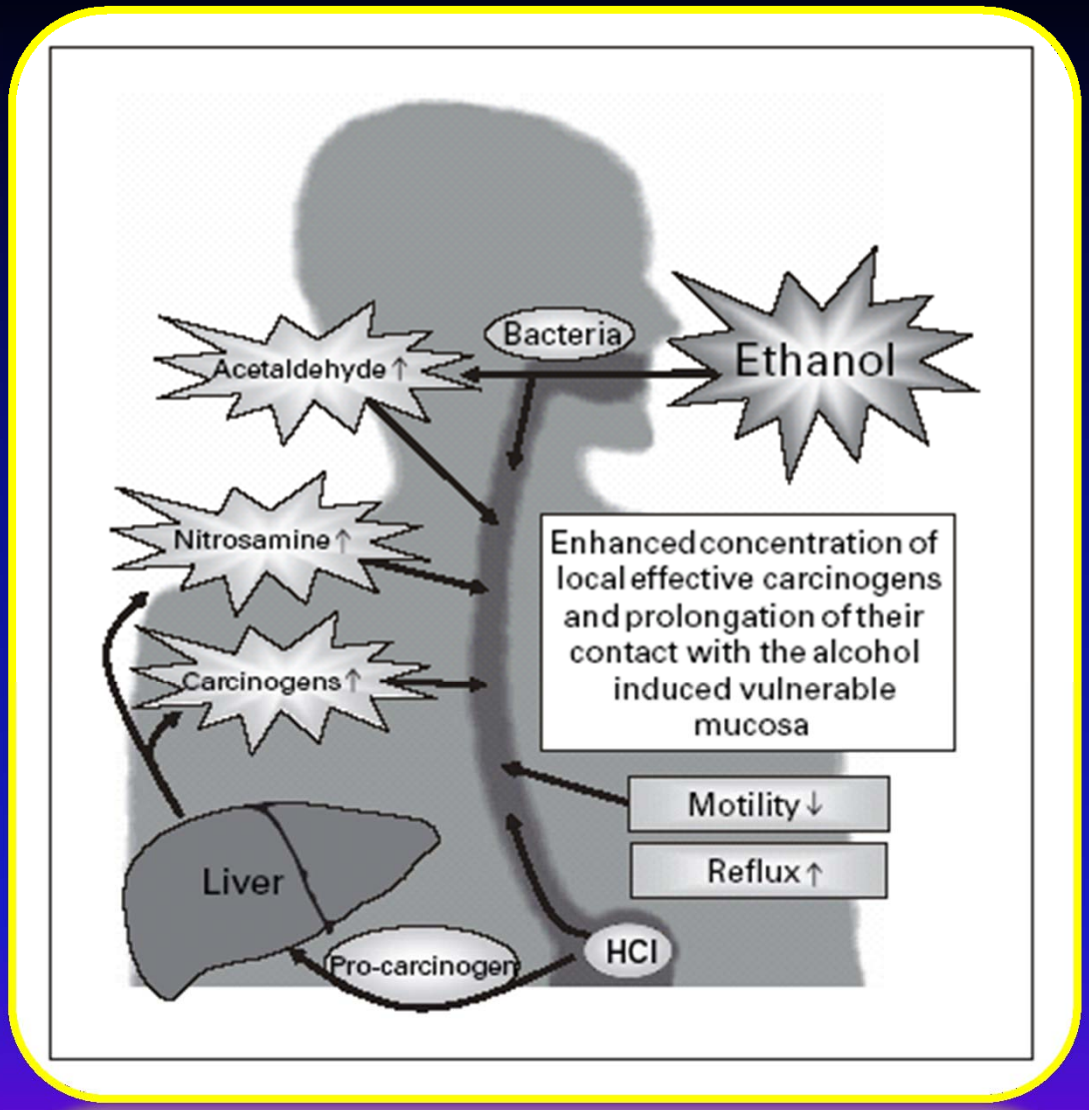


Figure 1 Salivary acetaldehyde concentrations after alcoholic beverage use in three different samples. The values are average and standard deviation of all assessors. The figure legend states the alcoholic strength (in % vol) and the acetaldehyde content (in µM) in the beverages, as well as the number of assessors used for each beverage.

Lachenmeier and Monakhova, J Exp Clin Cancer Res 2011



Franke et al, Dig Dis 2005

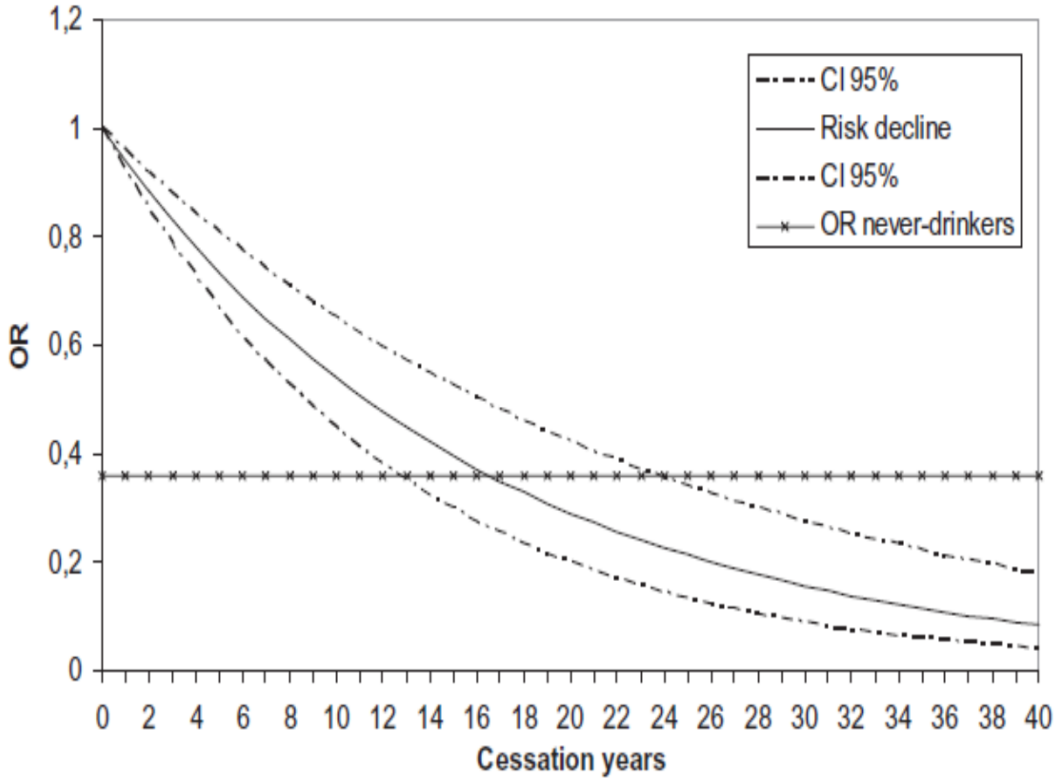


Figure 3 Estimated temporal characteristics of decline in risk of oesophageal cancer after drinking cessation; OR: odds ratio; CI: confidence interval

Jarl and Gerdtham, Addiction 2011

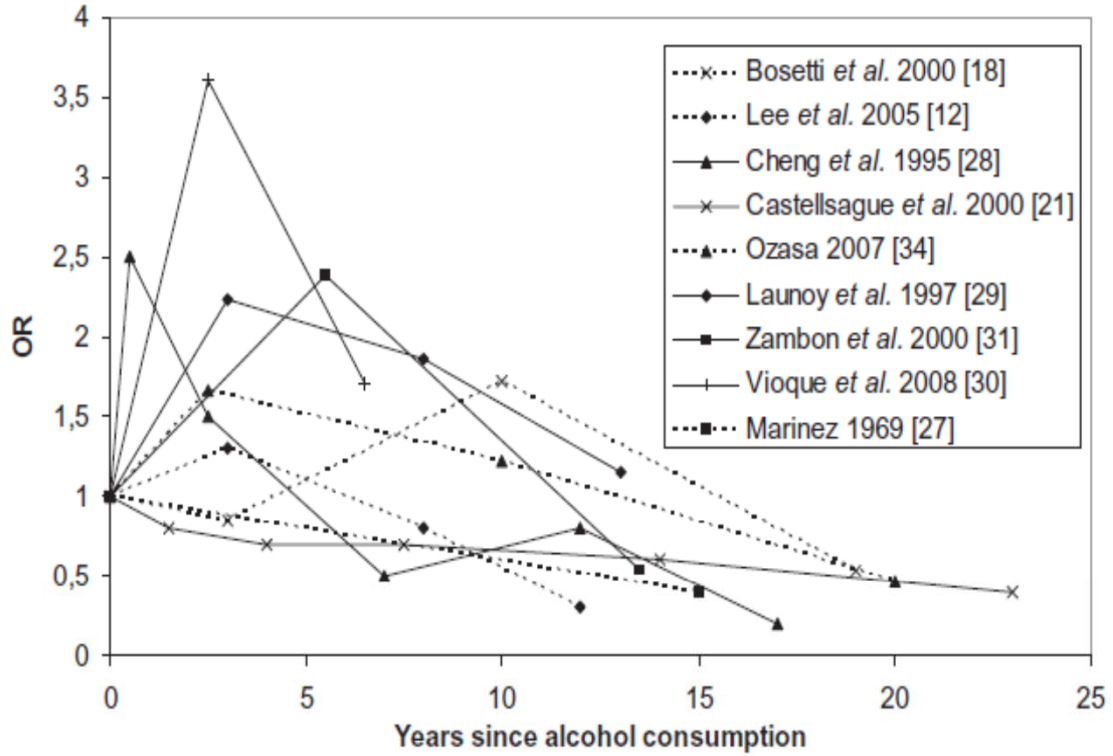


Figure 1 Risk of oesophageal cancer following drinking cessation, studies included in the meta-analysis; OR: odds ratio

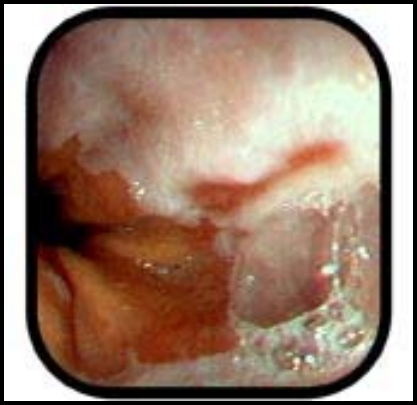
Jarl and Gerdtham, Addiction 2011

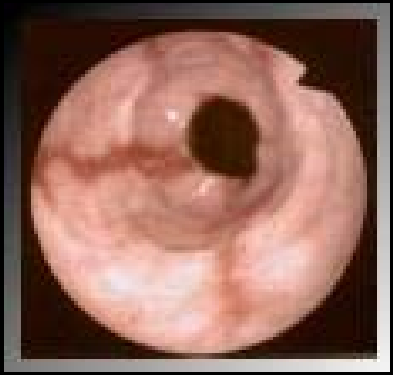
acido (Hcl)

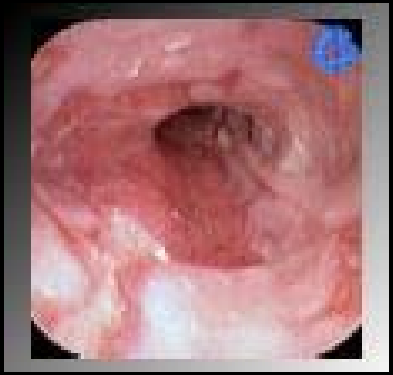
pepsina

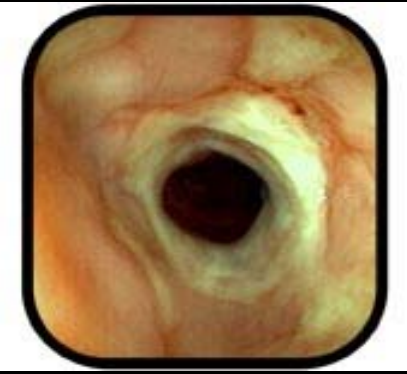
bile

esofagite

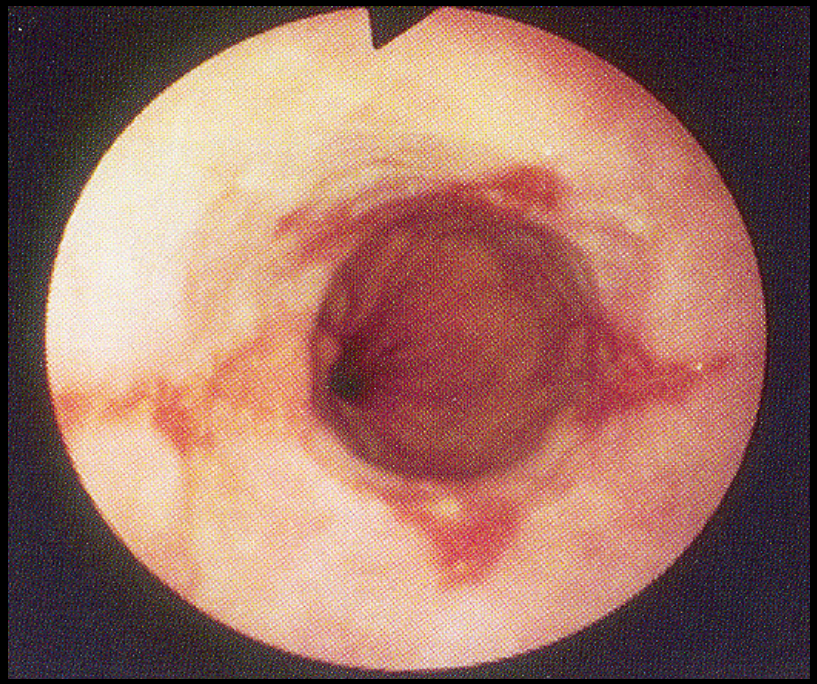






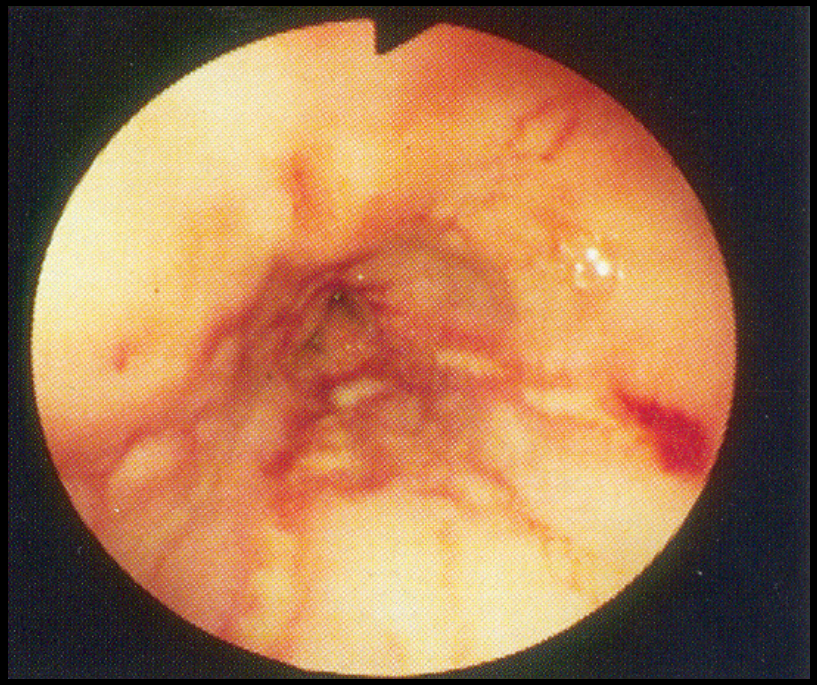


Stadiazione endoscopica delle esofagiti mediante classificazione di Los Angeles



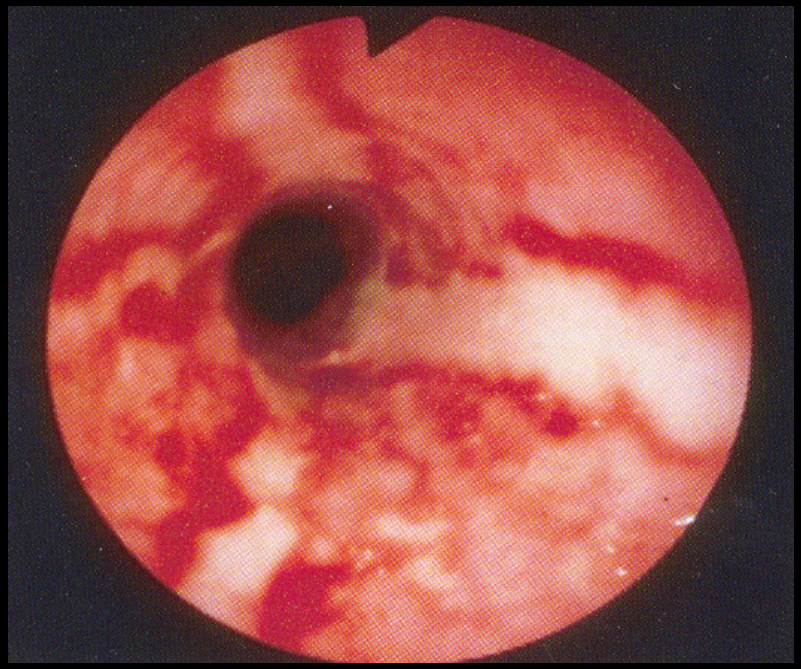
Grado A: Una o più erosioni nessuna superiore a 5 mm

Classificazione di Los Angeles



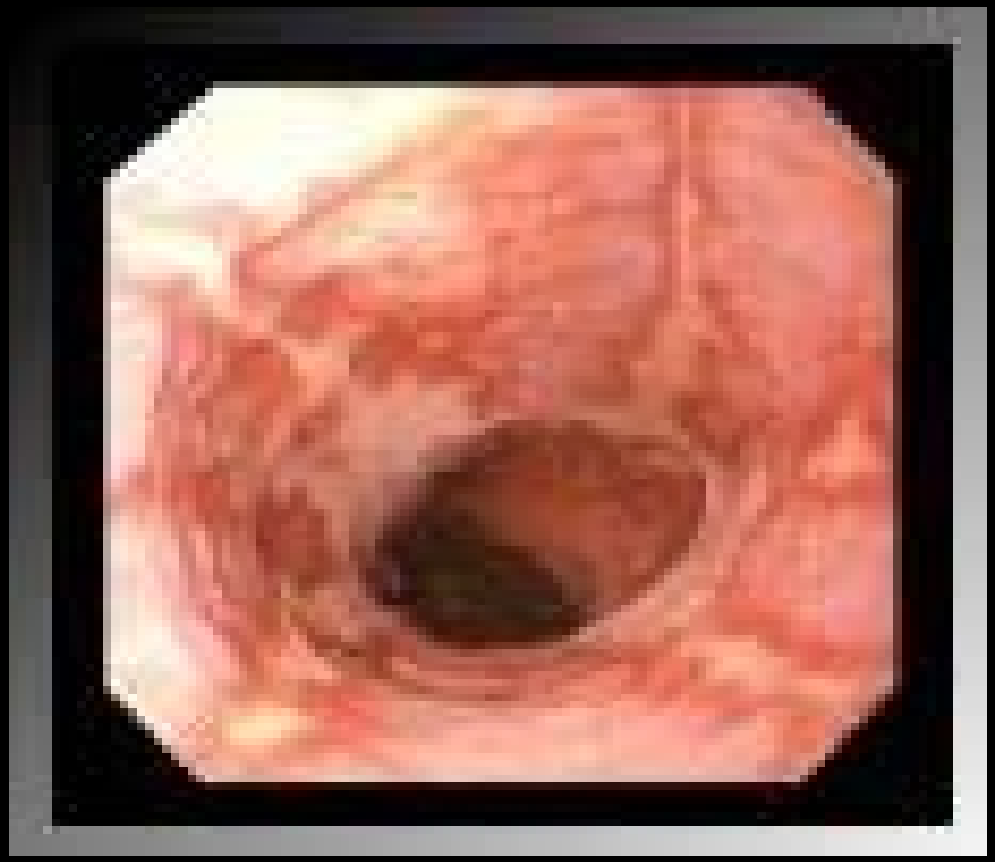
Grado B: presenza di erosioni, superiori a 5 mm, senza confluenza tra due pliche esofagee

Classificazione di Los Angeles



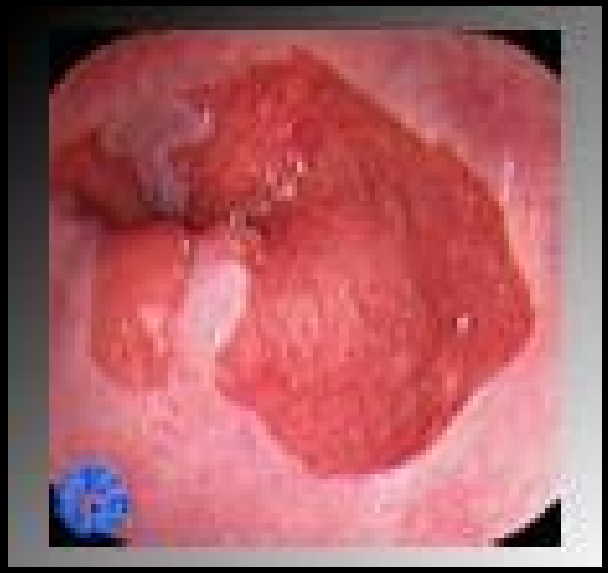
Grado C: almeno un erosione continua tra due pliche ma non circonferenziale

Classificazione di Los Angeles



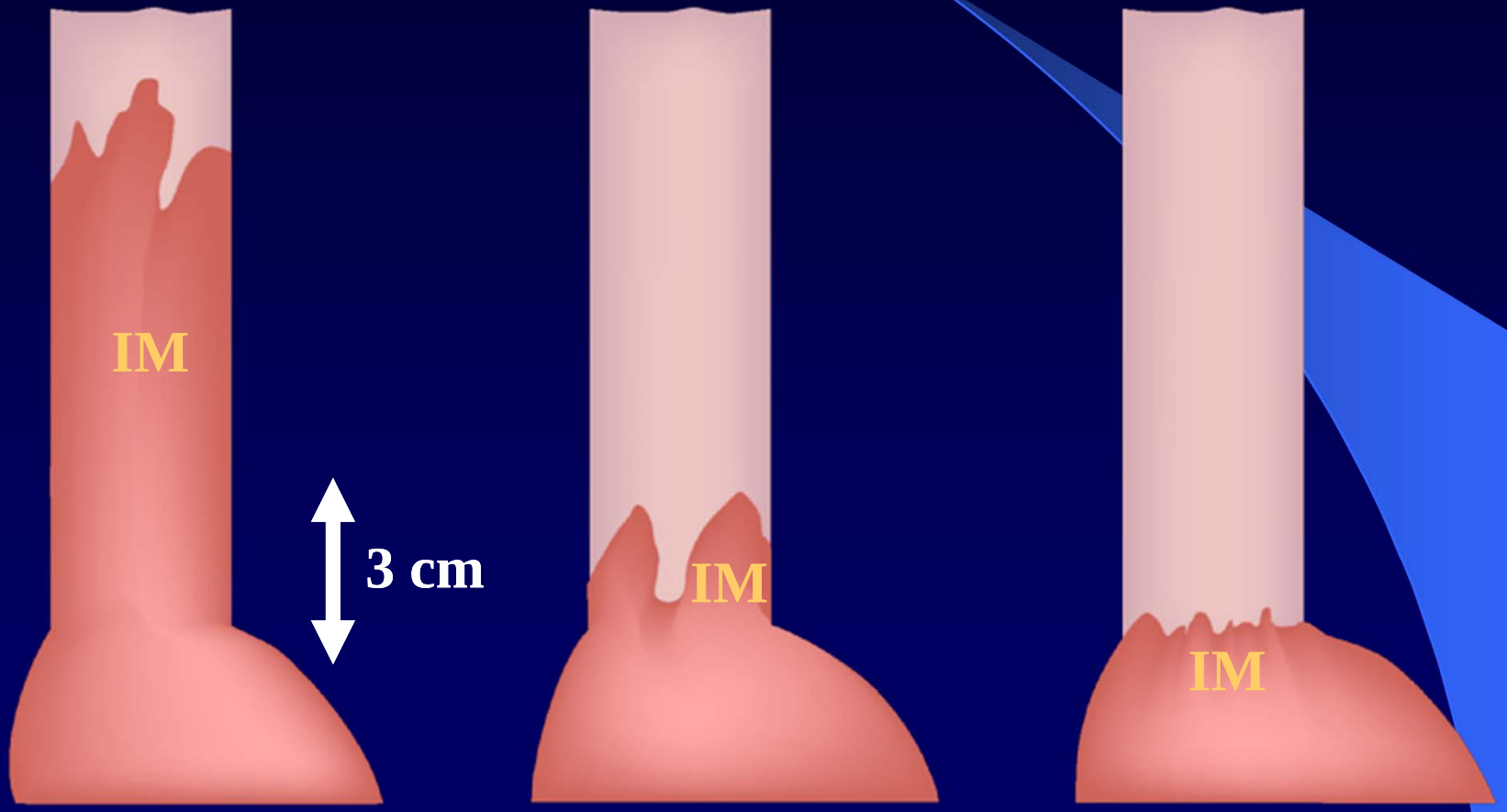
Grado D : Erosioni circonferenziali

Esofago di Barrett



Sostituzione dell'epitelio squamoso dell'esofago da parte di un epitelio colonnare specializzato caratterizzato da "globet cells" e strutture villose (metaplasia intestinale)

Long and Short Barrett's Esophagus and Intestinal Metaplasia of the Cardia



Prof. Massimo Conio, Osp. Sanremo

ALCOL/ ESOFAGO: PREVENZIONE SECONDARIA

Mucosa Normale (III Inferiore)

↓

Esofagite Istologica/ endoscopica (non sempre)

↓

Metaplasia Intestinale (Esofago di Barrett)

↓

Displasia a basso grado

↓

Displasia ad alto grado

↓

adenocarcinoma

Biopsie multiple anche al III medio e superiore per prevenzione

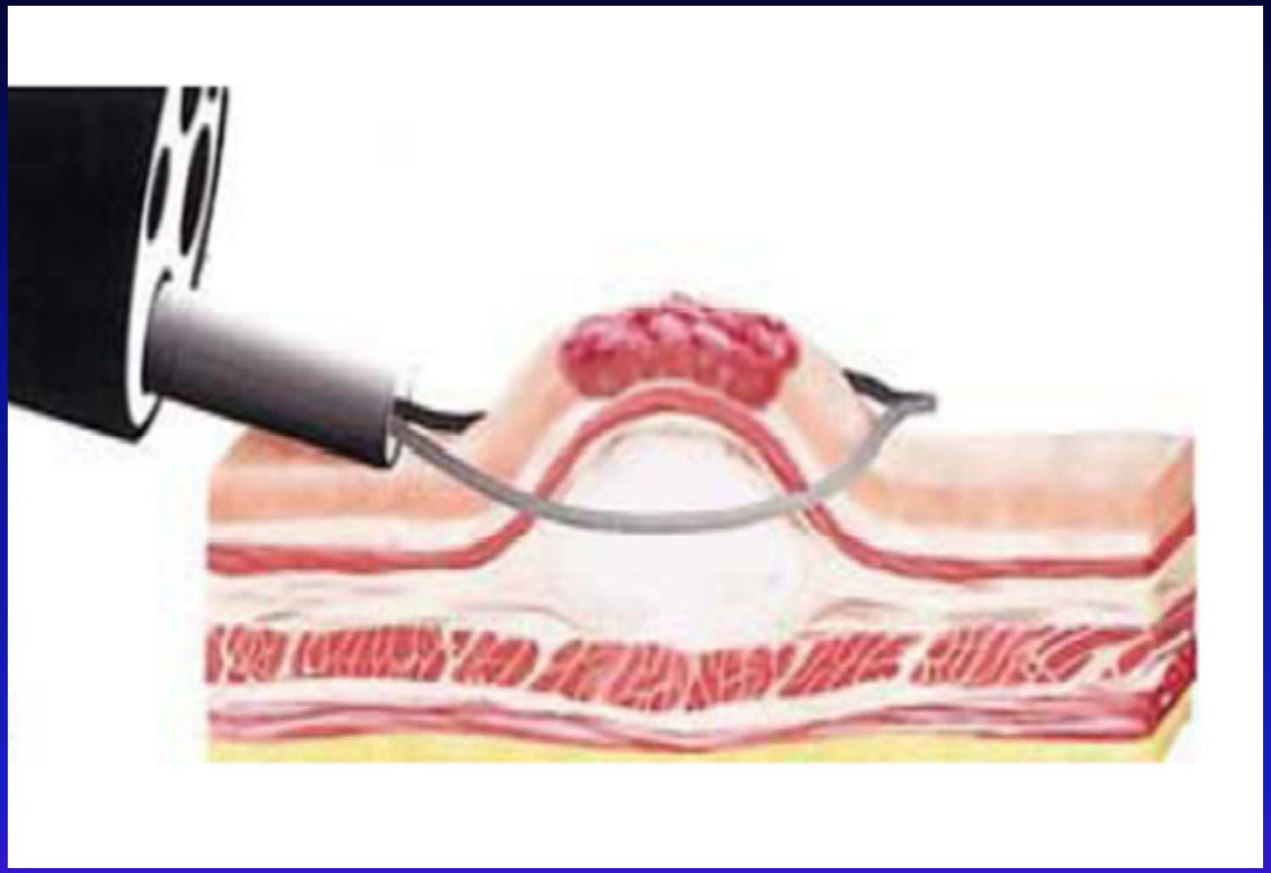
Carcinoma Squamo-Cellulare (il piu' frequente) !!!

ALCOL/ ESOFAGO: PREVENZIONE SECONDARIA (II)

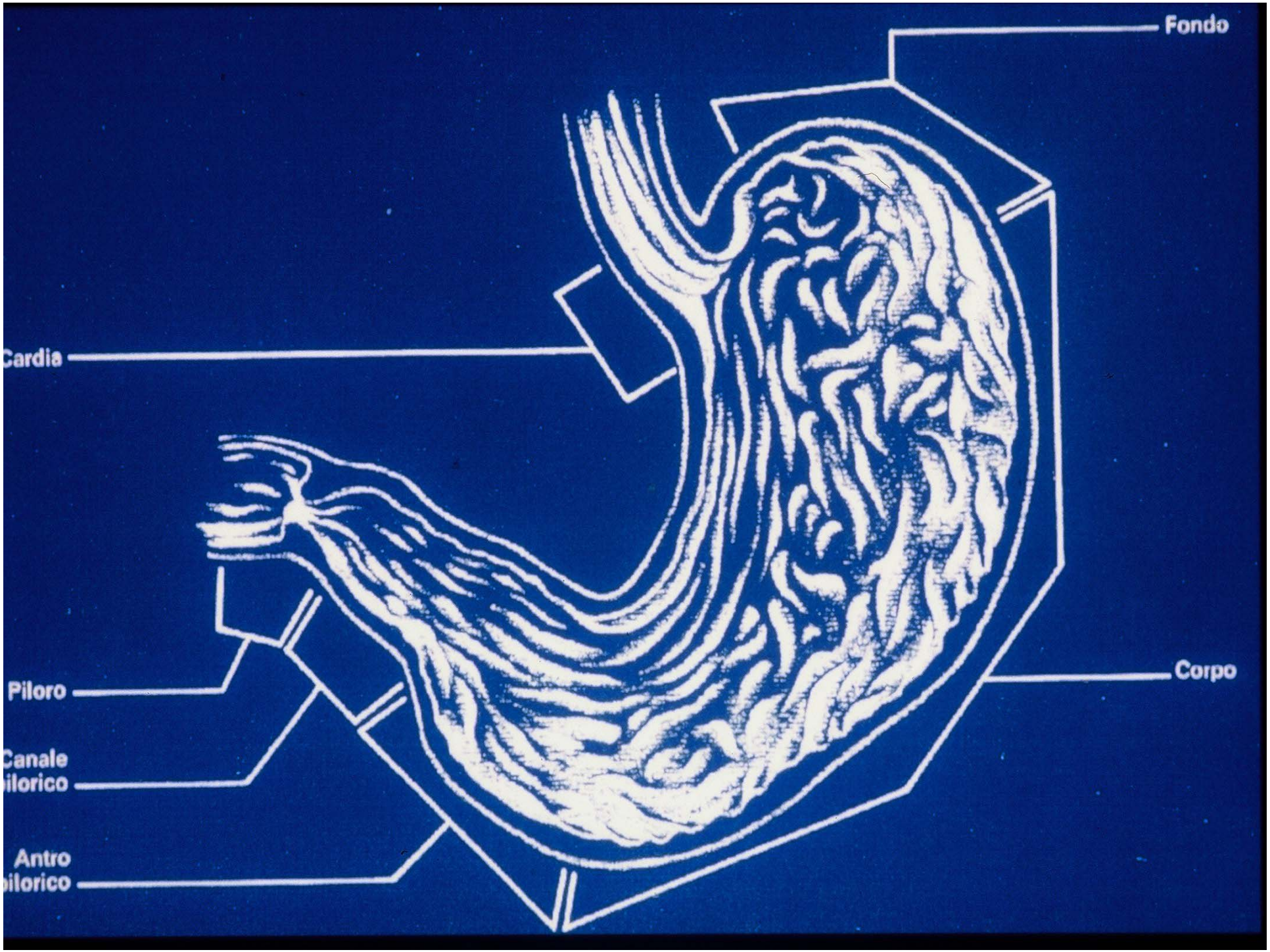
endoscopia + mappatura istologica

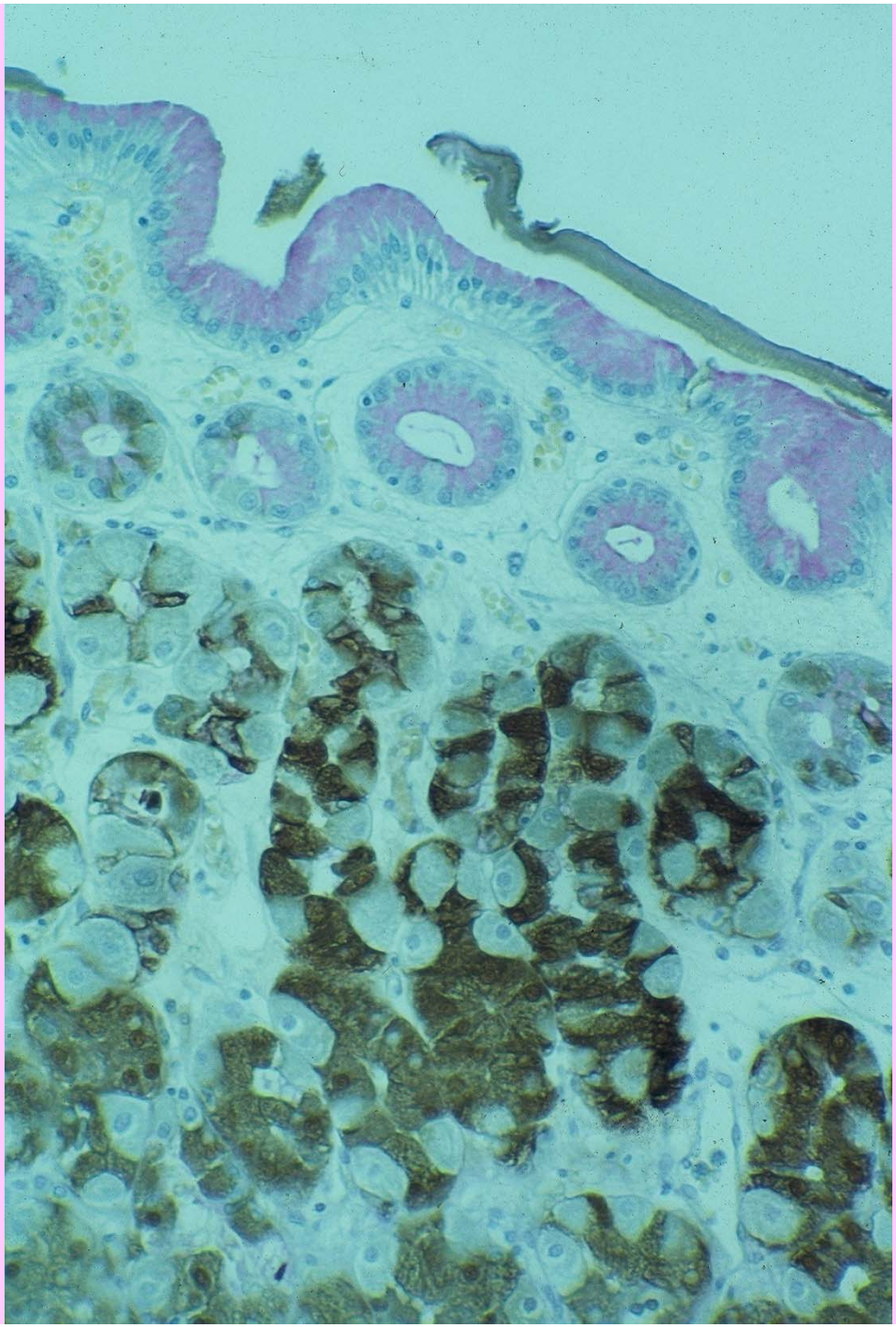
Se negativita':	proseguire controlli secondo le indicazioni della clinica
Se esofago di Barrett:	endoscopia con biopsie entro un anno e dopo ogni 3 anni
Se displasia a basso grado:	contollo entro 6 mesi e successivamente ogni anno
Se displasia ad alto grado:	controllo entro 3 mesi se conferma: mucosectomia endoscopica o intervento chir.

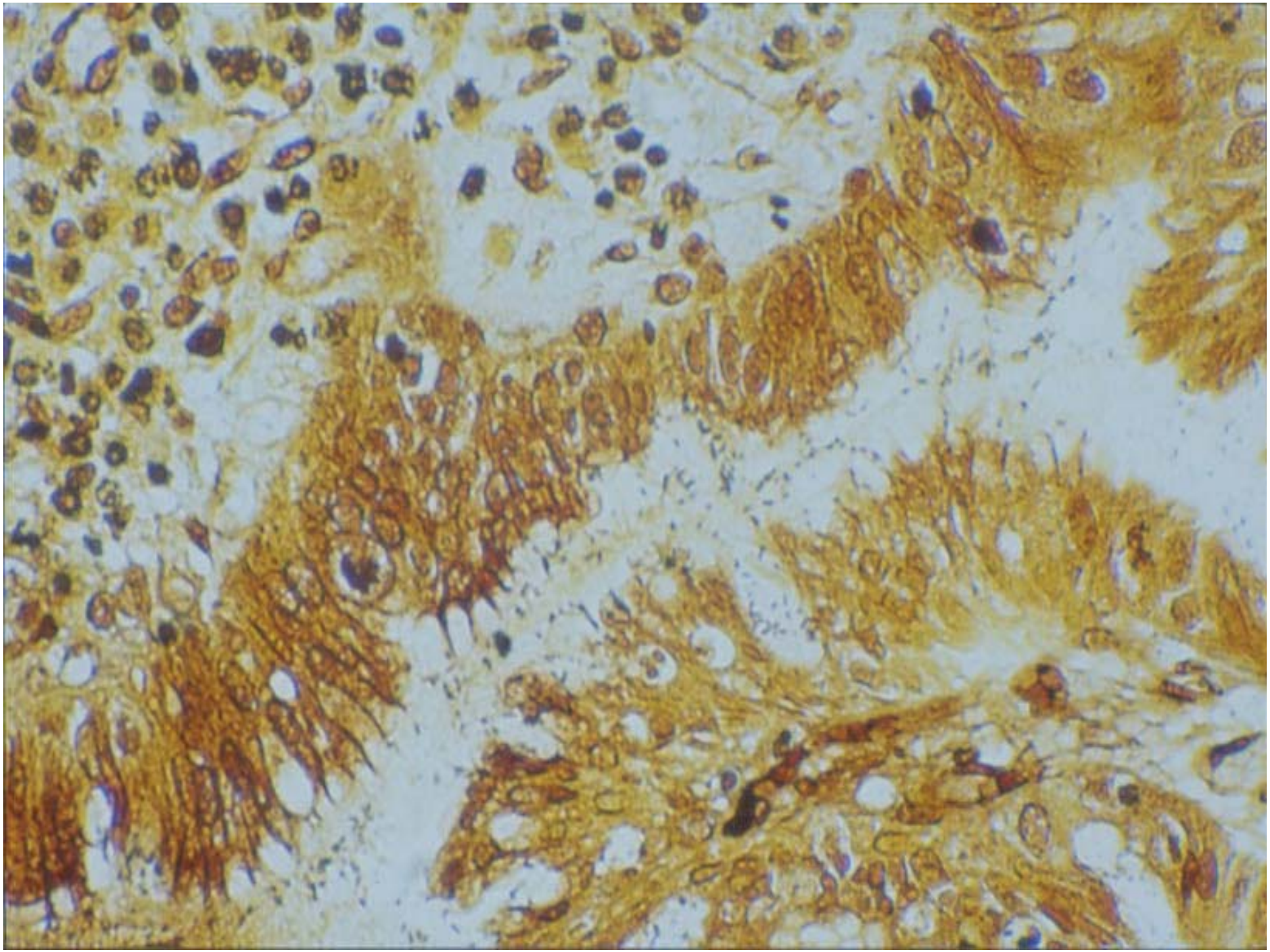
MUCOSECTOMIA ENDOSCOPICA

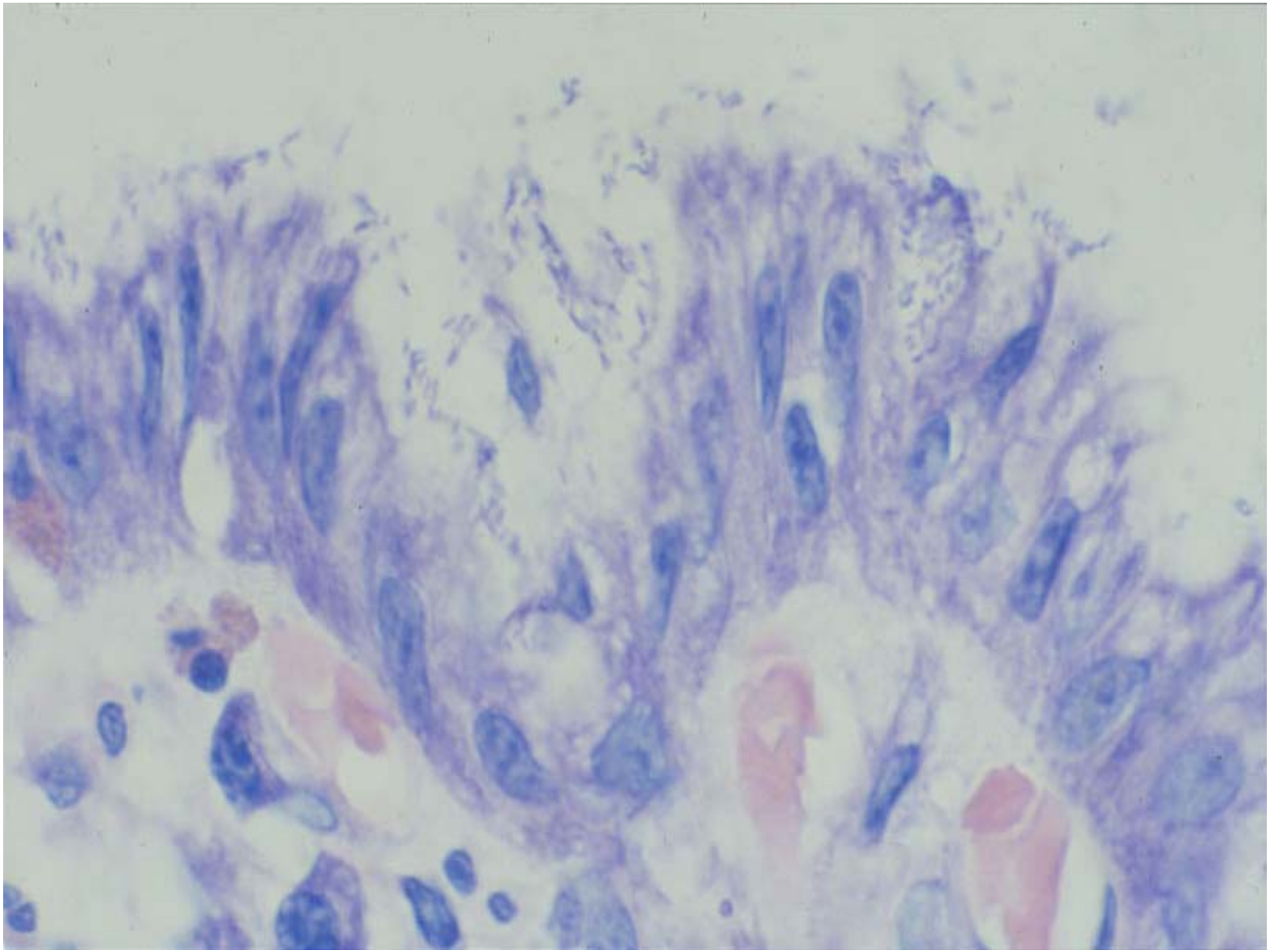


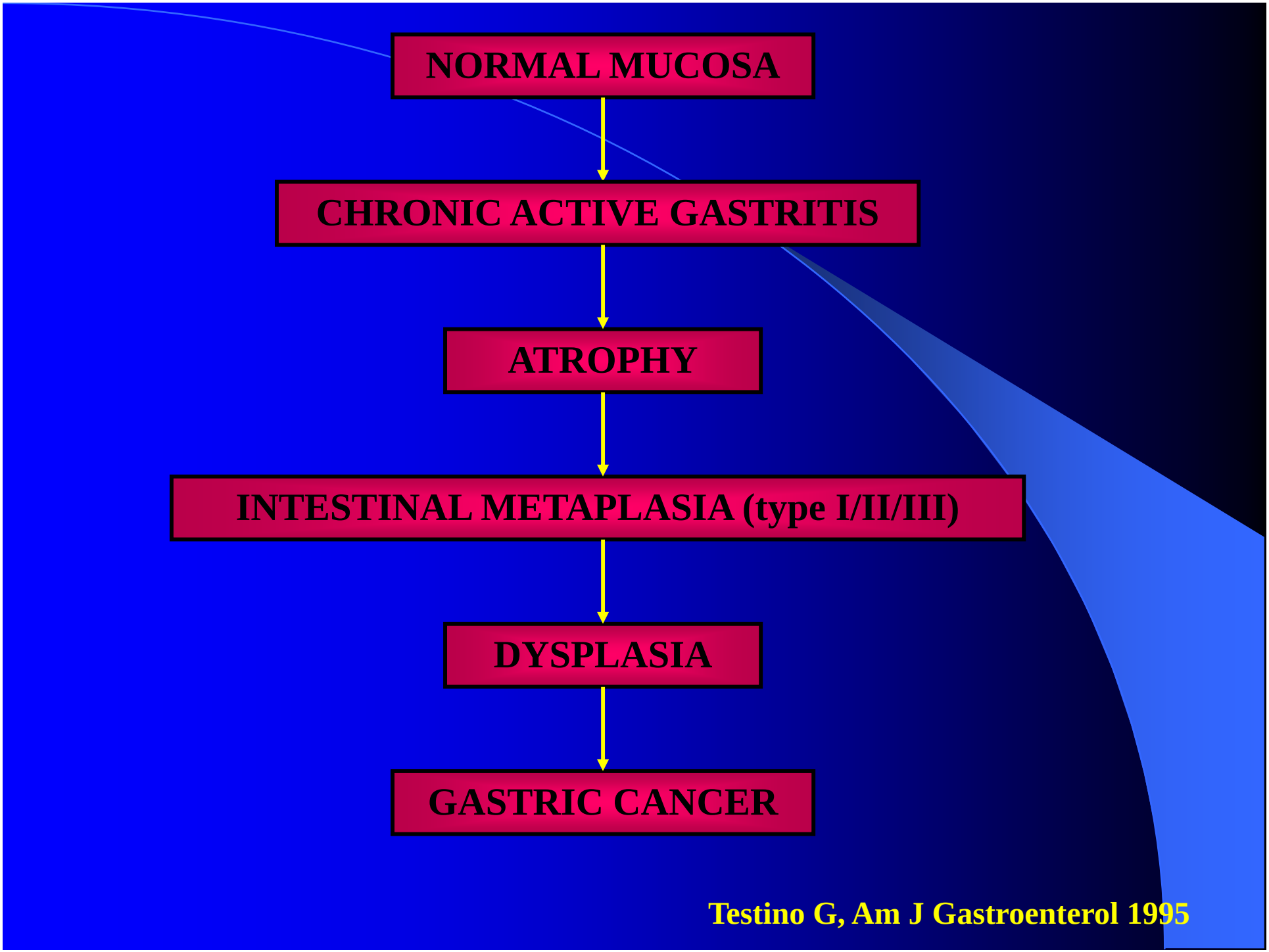
PDTA, IRCCS San Martino-IST, Genova


Fondo
Cardia
Piloro
Corpo
Canale
ilorico
Antro
ilorico








NORMAL MUCOSA
CHRONIC ACTIVE GASTRITIS
ATROPHY
INTESTINAL METAPLASIA (type I/II/III)
DYSPLASIA
GASTRIC CANCER
Testino G, Am J Gastroenterol 1995

SORVEGLIANZA ENDOSCOPICA

Polipi Gastrici Adenomatosi

Dopo asportazione follow-up endoscopico ad un anno per valutare eventuale recidiva e/o insorgenza di neoplasia anche in altra sede.
Successivo controllo a 3-5 anni

Polipi Gastrici in corso di FAP

Sorveglianza endoscopica ogni 12-24 mesi (ogni 3-5 anni in corso di FAP senza lesioni gastriche)

Ulcera Gastrica

Prelievi bioptici (almeno 8) e valutazione citologica al momento della diagnosi.
Ripetizione endoscopico/ bioetica dopo 4-8 settimane.
Successivamente un controllo dopo 3, 6 e 12 mesi.
Negli anni successivi secondo alcuni Autori un controllo all'anno da proseguire nel tempo a seconda delle variazioni cliniche

SORVEGLIANZA ENDOSCOPICA

Gastrite Cronica con Metaplasia Intestinale Completa (multifocale o diffusa)

Eradicazione dell'Hp con controllo endoscopico/ bioptico dopo circa 5 anni

Gastrite Cronica con Metaplasia Intestinale Incompleta (multifocale o diffusa)

Eradicazione dell'Hp con controllo endoscopico/ bioptico dopo circa 1-2 anni

Familiarita'

Eradicazione dell'Hp con controlli periodici dell'avvenuta eradicazione.

Non definiti i periodici controlli endoscopici

SORVEGLIANZA ENDOSCOPICA

Displasia Epiteliale

- **Se suddivisione in Lieve, Moderata e Severa**

  Lieve: controllo dopo 12 mesi

  Moderata: controllo dopo 6 mesi

  Severa: secondo controllo entro un mese

  - se riconferma: terapia chirurgica

- **Se suddivisione a basso e ad alto grado**

Basso Grado: controllo endoscopico/ bioptico in associazione alla citologia se la lesione e' ulcerosa ogni 3-6 mesi in associazione alla eradicazione dell'Hp

Alto Grado: secondo controllo entro un mese

- in caso di negativita' o regressione: controllo endoscopico/ bioptico ogni 3 mesi per un anno
- in caso di conferma: mucosectomia per endoscopica o intervento chirurgico

CARCINOGENESIS
NUTRITIONAL FACTORS

Ethanol and Retinoid Metabolism

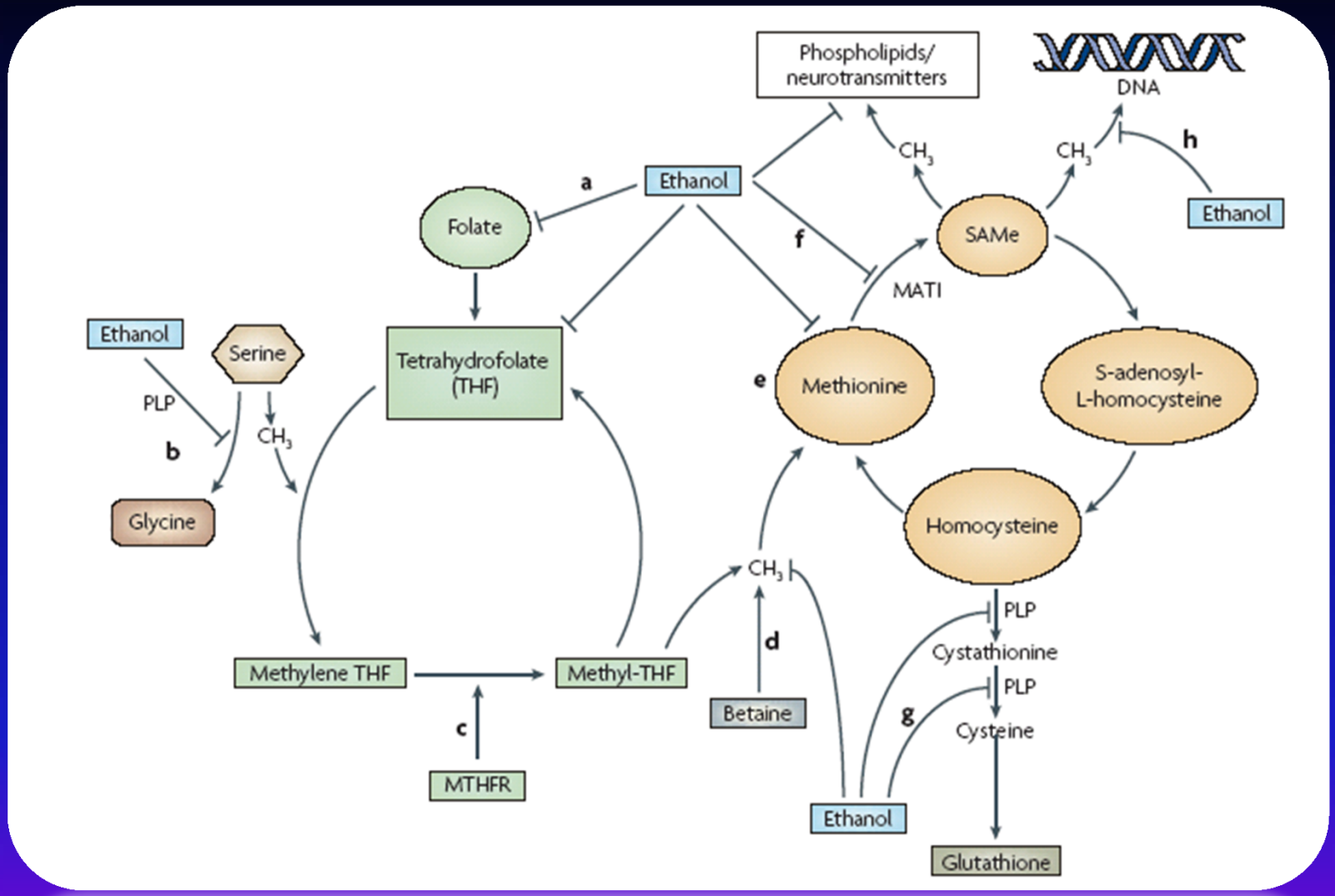
vitamin A and Retinoic Acid in the liver
(> catabolism by rthanol – induced CYP2E1)

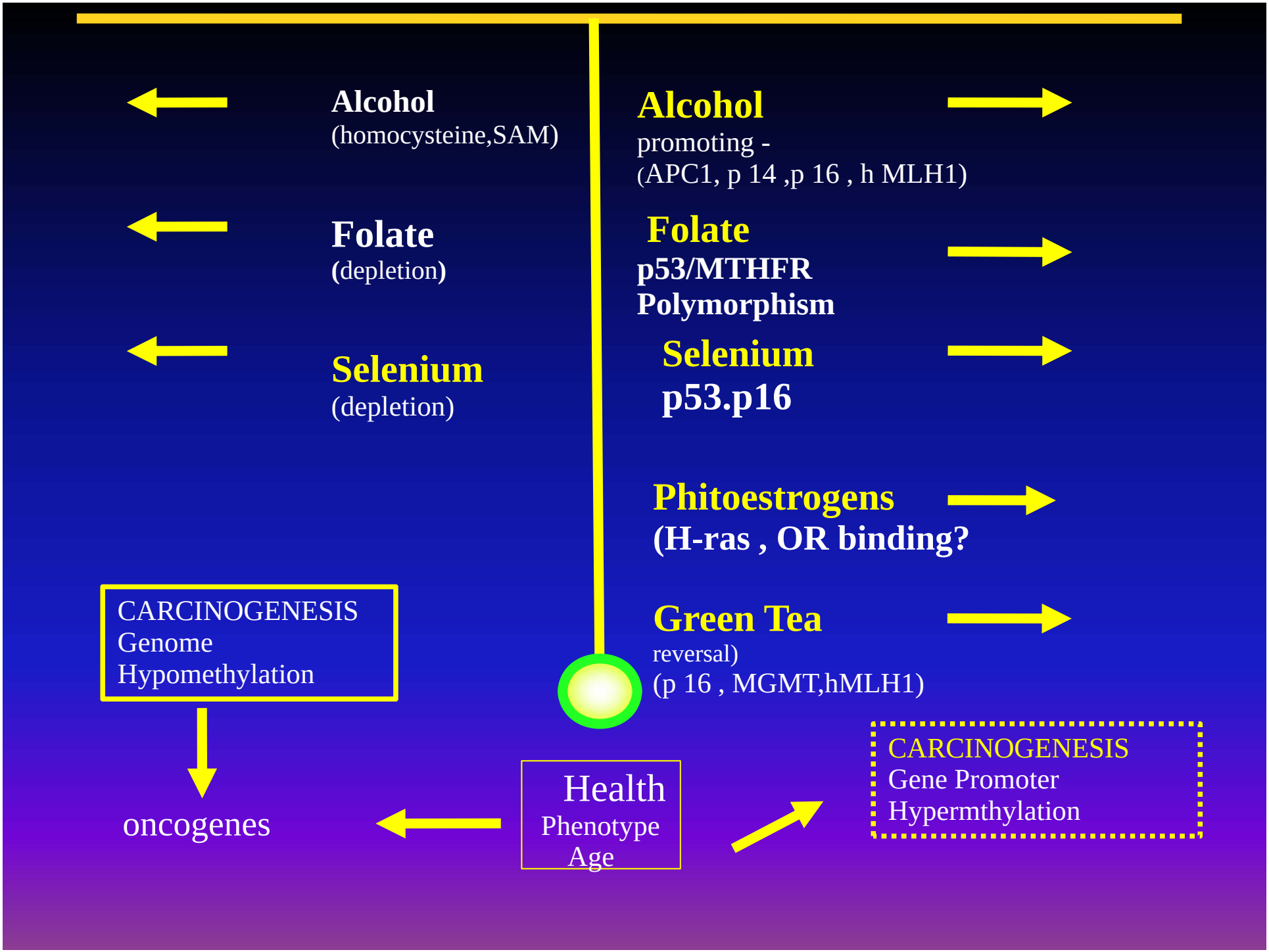
< in mitogen -activaded protein kinase (MAPK)
> in levels of phosphorylated JNK

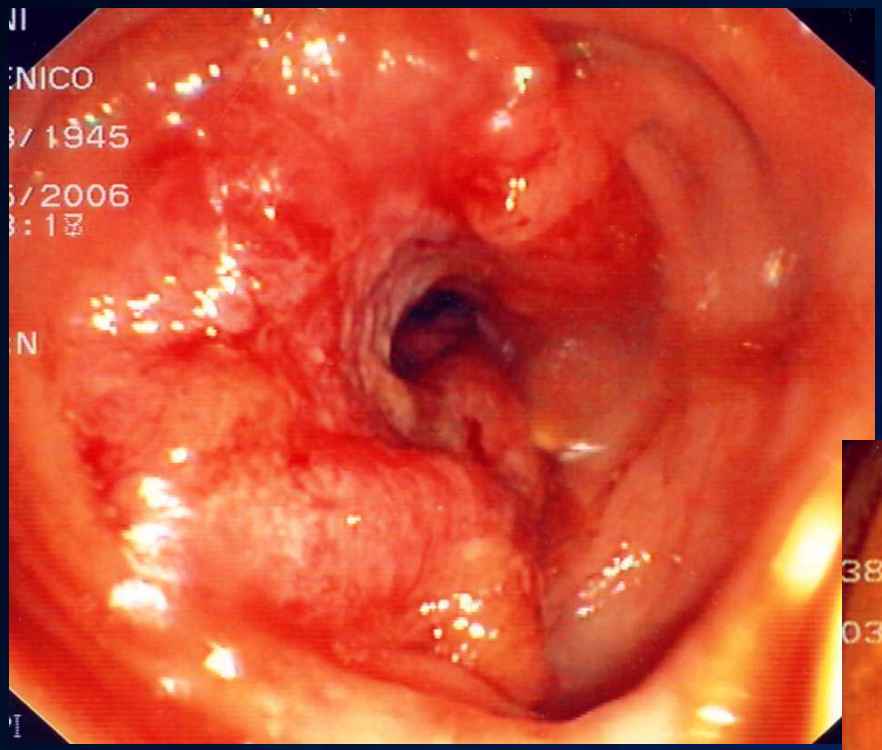
expression AP1 (JUN and FOS) transcripttional complex

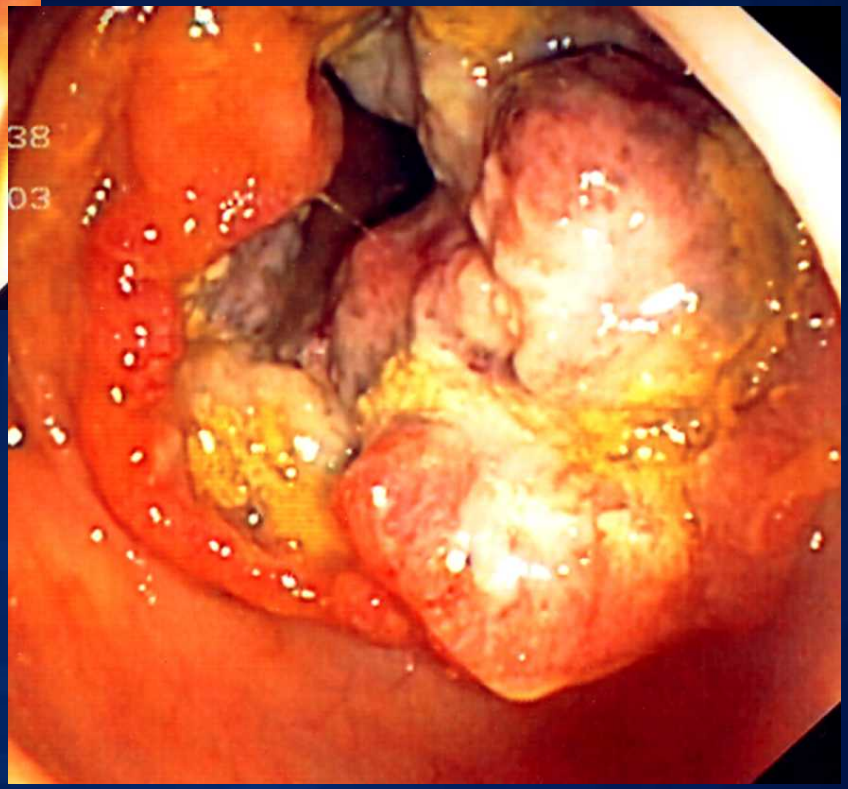
> cell hyperproliferation/ < apoptosis
Liu et al, Gastroenterology 2001; Chung et al Carcinogenesis 2001;
Liu et al , Alcoholism Clin Exp Res 2002; Napoli JL 2011

Ethanol and Altered Methyl Group Transfer (Thompson et al, Liver Int 2011)

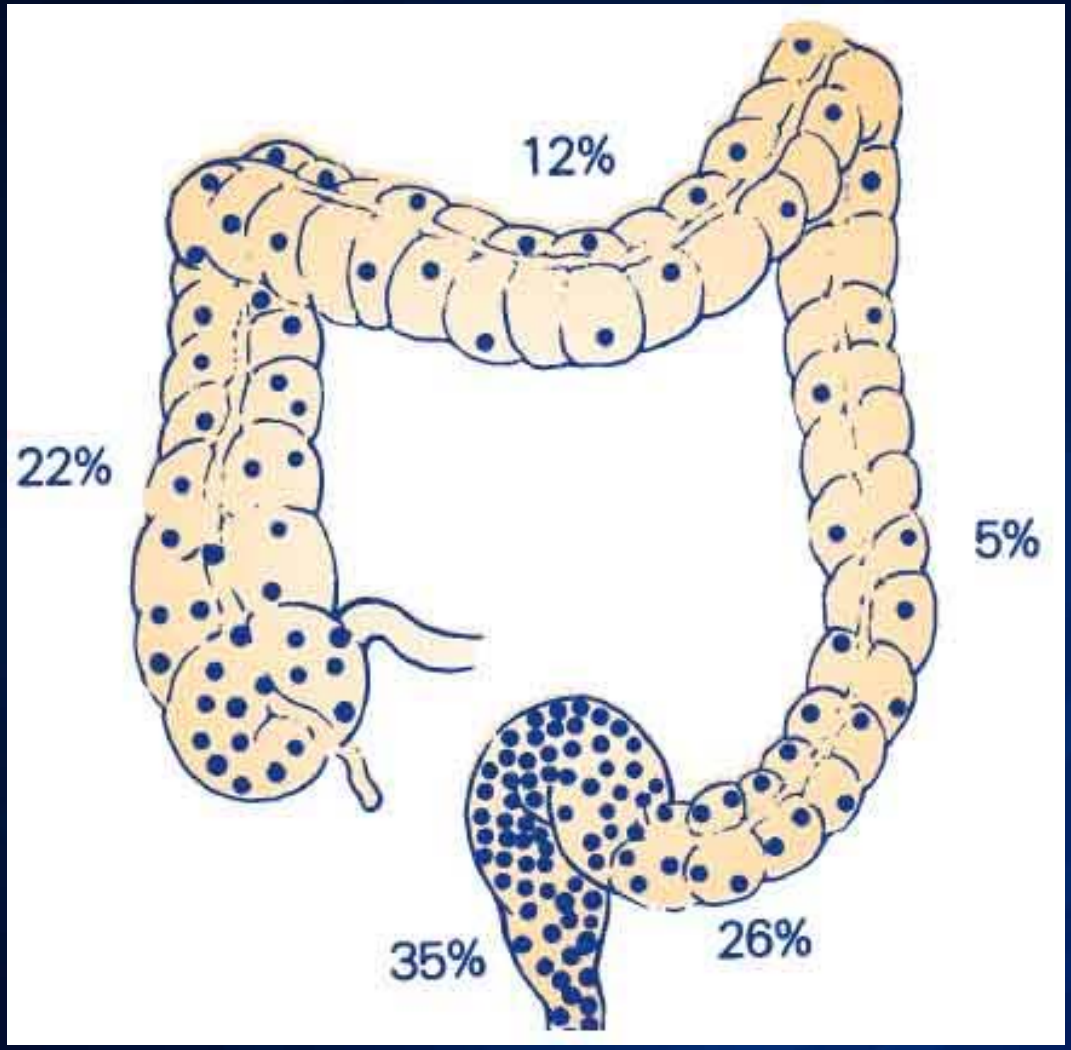

Phospholipids/
neurotransmitters
DNA
CH3
CH3
h
Ethanol
a
Ethanol
Folate
f
SAMe
MATI
Ethanol
Serine
Tetrahydrofolate
(THF)
e
Methionine
S-adenosyl-
L-homocysteine
PLP
b
CH3
Glycine
Homocysteine
CH3
PLP
Cystathionine
d
PLP
Methylene THF
Methyl-THF
Betaine
g
Cysteine
c
MTHFR
Ethanol
Glutathione


Alcohol
(homocysteine,SAM)
Folate
(depletion)
Selenium
(depletion)
Alcohol
promoting -
(APC1, p 14 ,p 16 , h MLH1)
Folate
p53/MTHFR
Polymorphism
Selenium
p53.p16
Phitoestrogens
(H-ras , OR binding?
Green Tea
reversal)
(p 16 , MGMT,hMLH1)
CARCINOGENESIS
Genome
Hypomethylation
oncogenes
Health
Phenotype
Age
CARCINOGENESIS
Gene Promoter
Hypermthylation

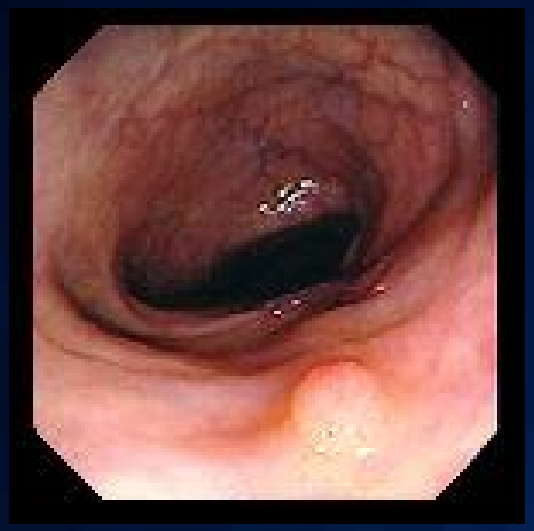

NICO
/1945
/2006

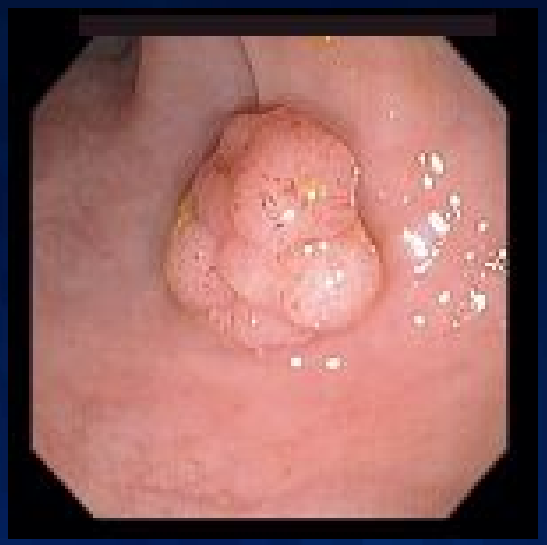

38
03

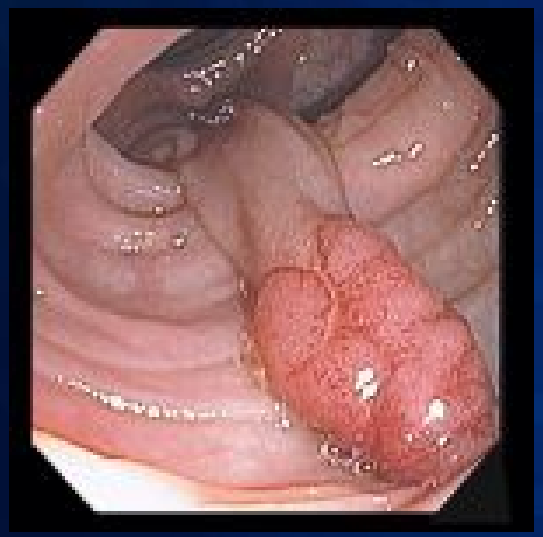
Localizzazione del cancro colorettale

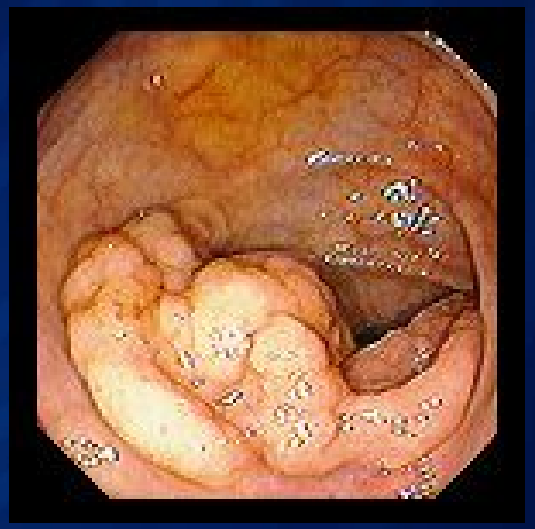


Polipi adenomatosi

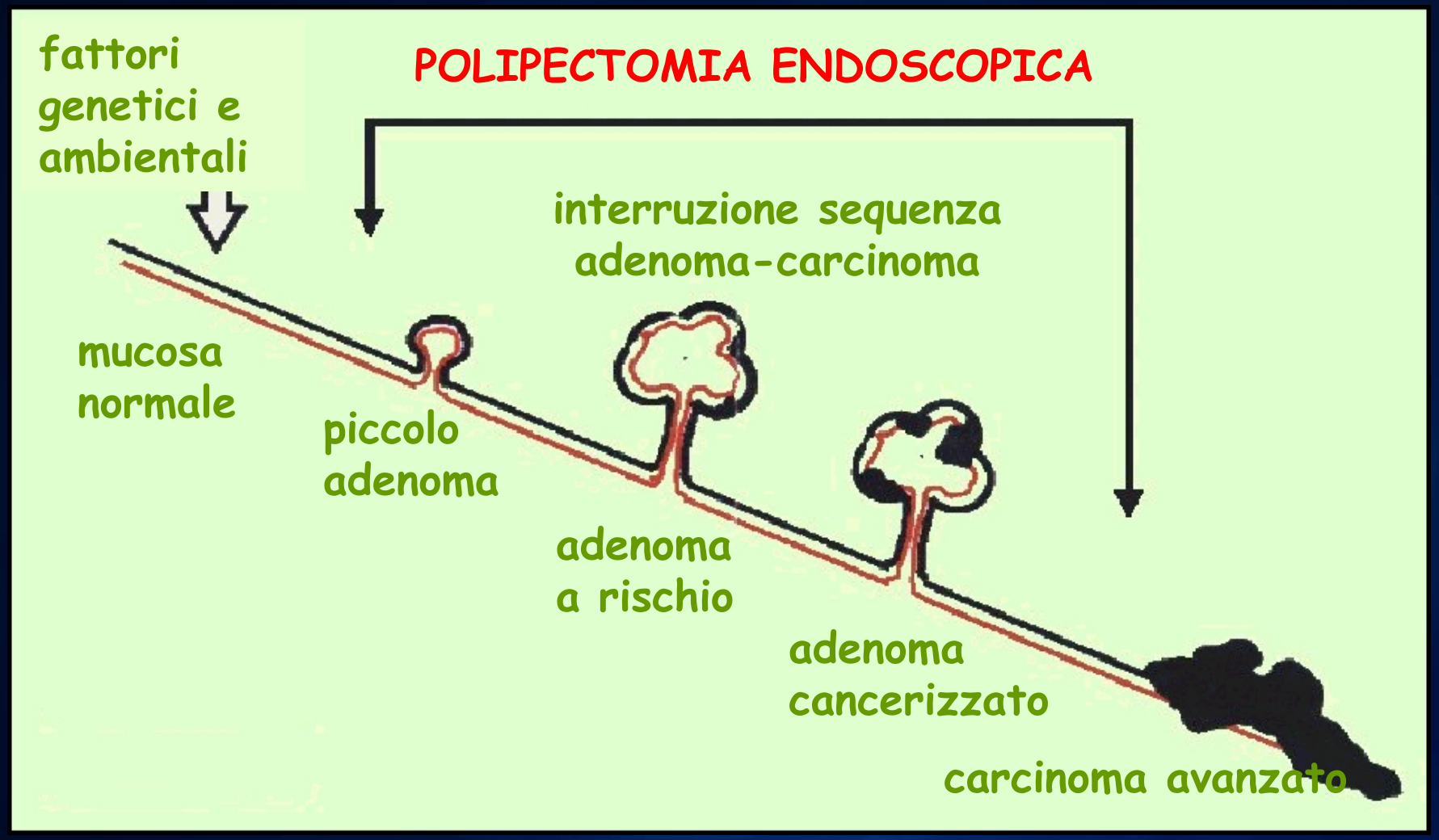




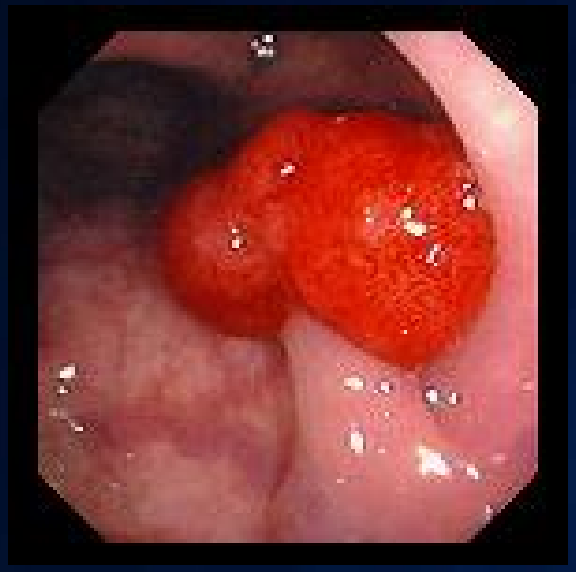


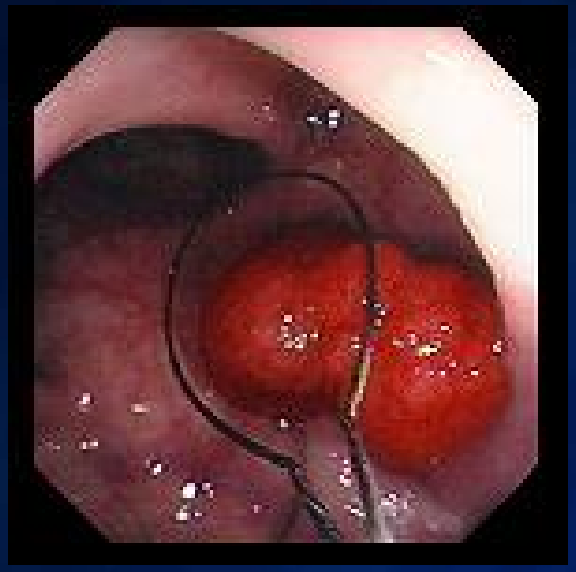


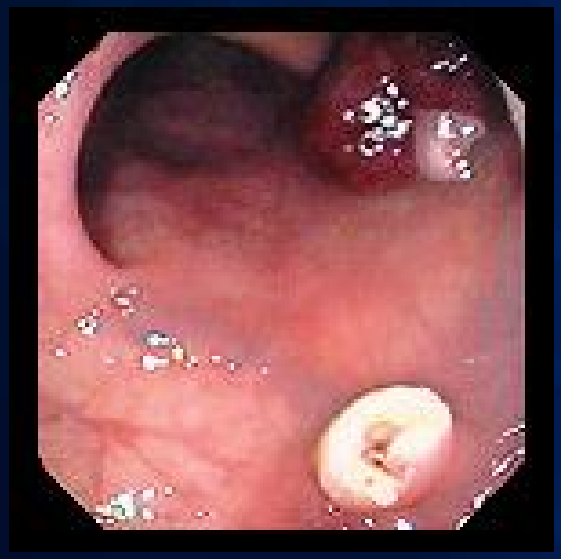
Storia naturale del cancro colorettale

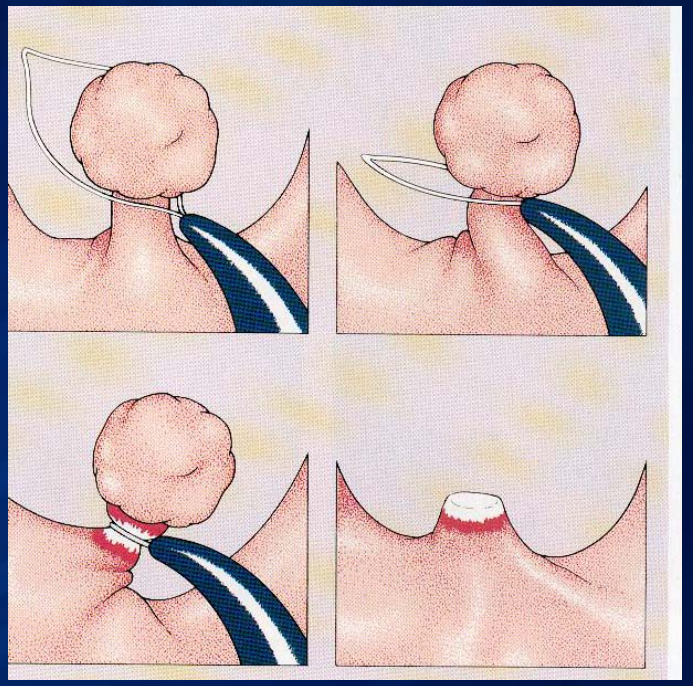


Polipectomia endoscopica







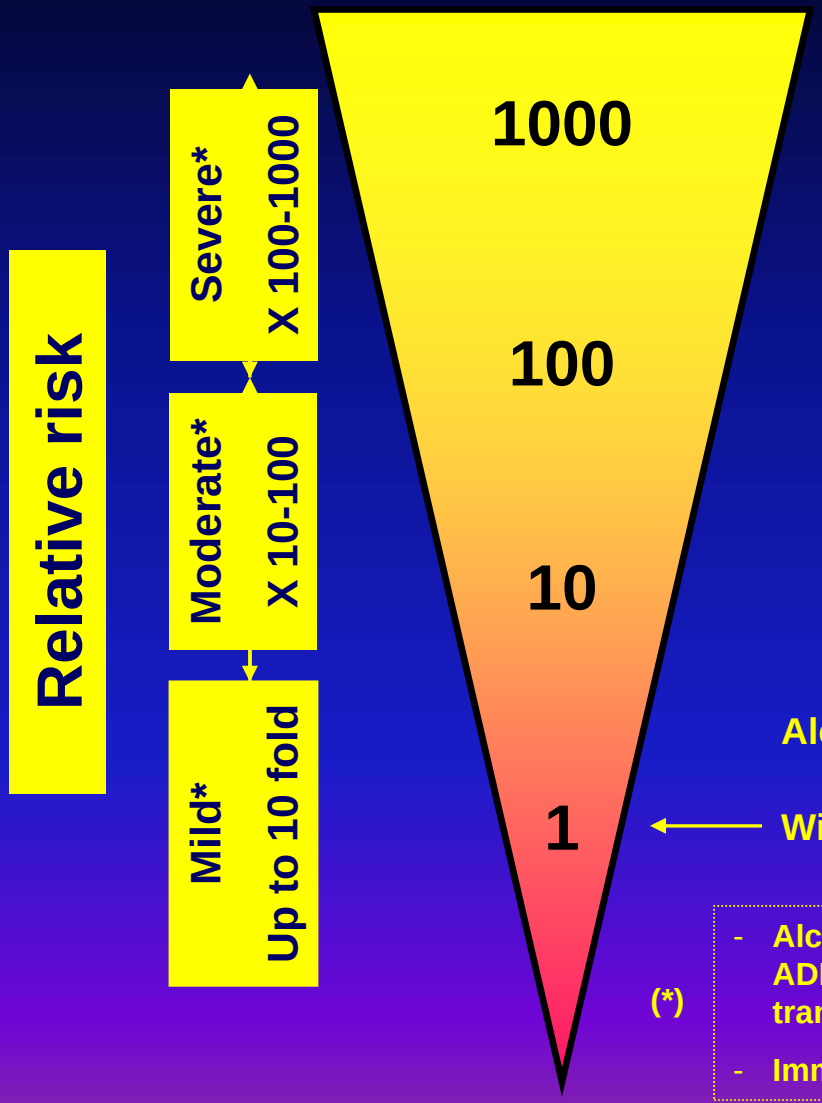


N° e TIPO POLIPO/I	1° CONTROLLO	CONTROLLI SUCCESSIVI
Polipo iperplastico	FOBT a 5 aa	
Poliposi iperplastica	Colonscopia a 5 aa	Se negativa FOBT a 5 aa
Adenoma a basso rischio: ▪ </= 2 polipi ▪ < 1 cm ▪ tubulare	Colonscopia dopo 5 aa	Se negativa FOBT a 5 aa
Adenoma ad alto rischio. ▪ Displasia di alto grado ▪ >/= 1 cm ▪ Componente villosa > 25% **Adenomi multipli:** ▪ tra 3 e 10 polipi	Colonscopia a 3 aa	Se negativa ripetere dopo 3 aa, se negativa FOBT a 5 aa
▪ **Polipo sessile >/= 2 cm** ▪ **Polipectomia incompleta o "piecemeal"**	Colonscopia a 3-6 mesi e sino a clearance della lesione e verifica di clean colon	Se negativa ripetere dopo 3 aa; se ancora negativa FOBT a 5 aa
Più di 10 adenomi	▪ Considerare ipotesi di sindrome poliposica ▪ Management individuale	
Adenoma con ca intramucoso	Come adenoma ad alto rischio	

Note:

MC Parodi et al, PDTA IRCCS San Martino-IST, Genova

Strenght of genetic and environmental risk factors of chronic pancreatitis



N291/R122H + smoking

N291/R122H

SPINK1/N34S (homozygous)/alcohol

PRSS1/Smoking/Alcohol

N34S + alcohol

N34S/CFTR

Alcohol 80 g/d

← Without detectable risk

(*)

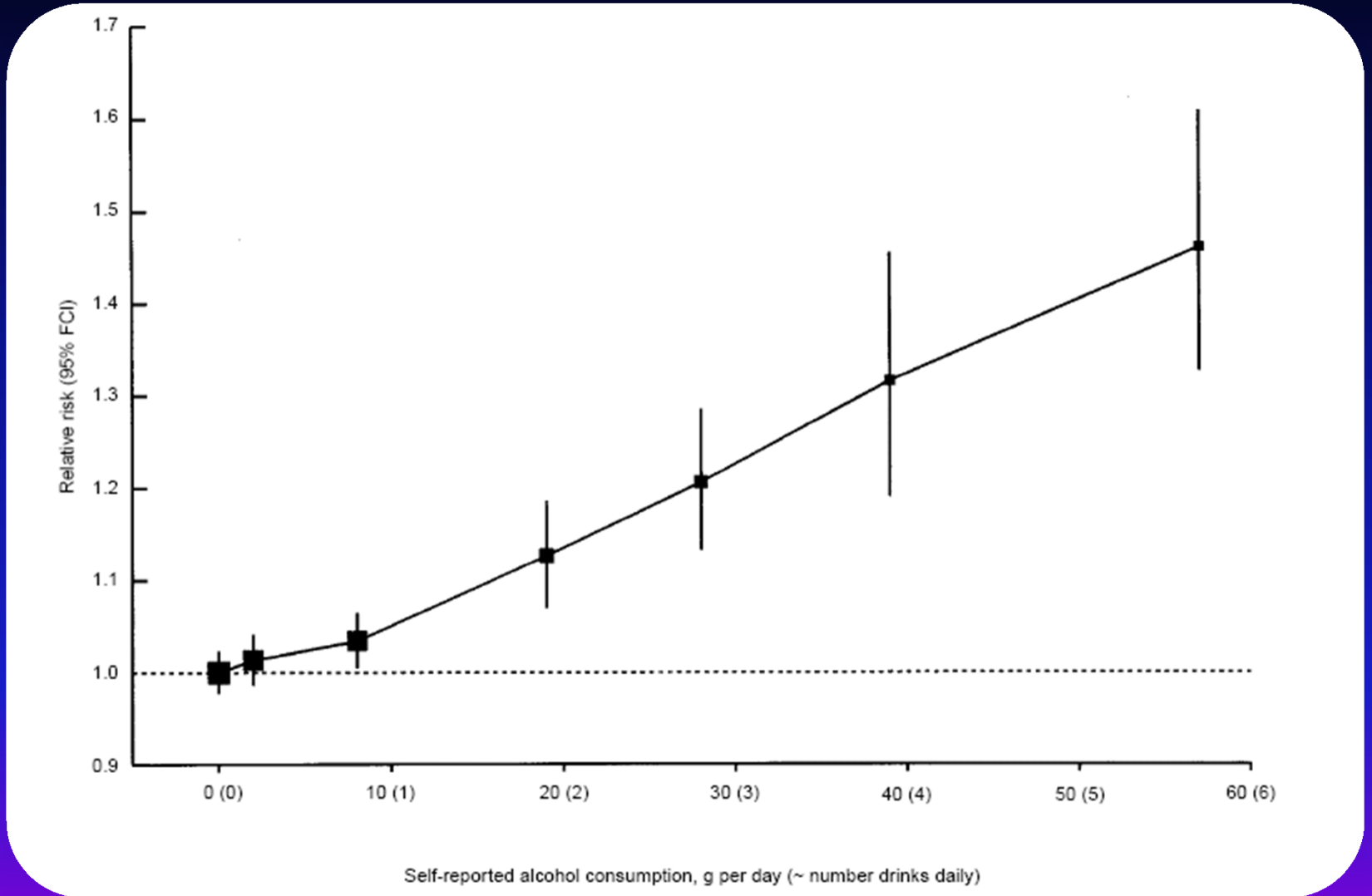
- Alcohol-Metabolizing/Detoxifying Genes (ADH2, ADH3, CYP2E1 polimorphisms, Glutathione S-transferase, ALDH2)
- Immune Response Genes (HLA patterns)

Dufour, Pancreas 2003; Teich, Med Sci Monit 2004; Keim, Scand J Surg 2005; Conwell 2008

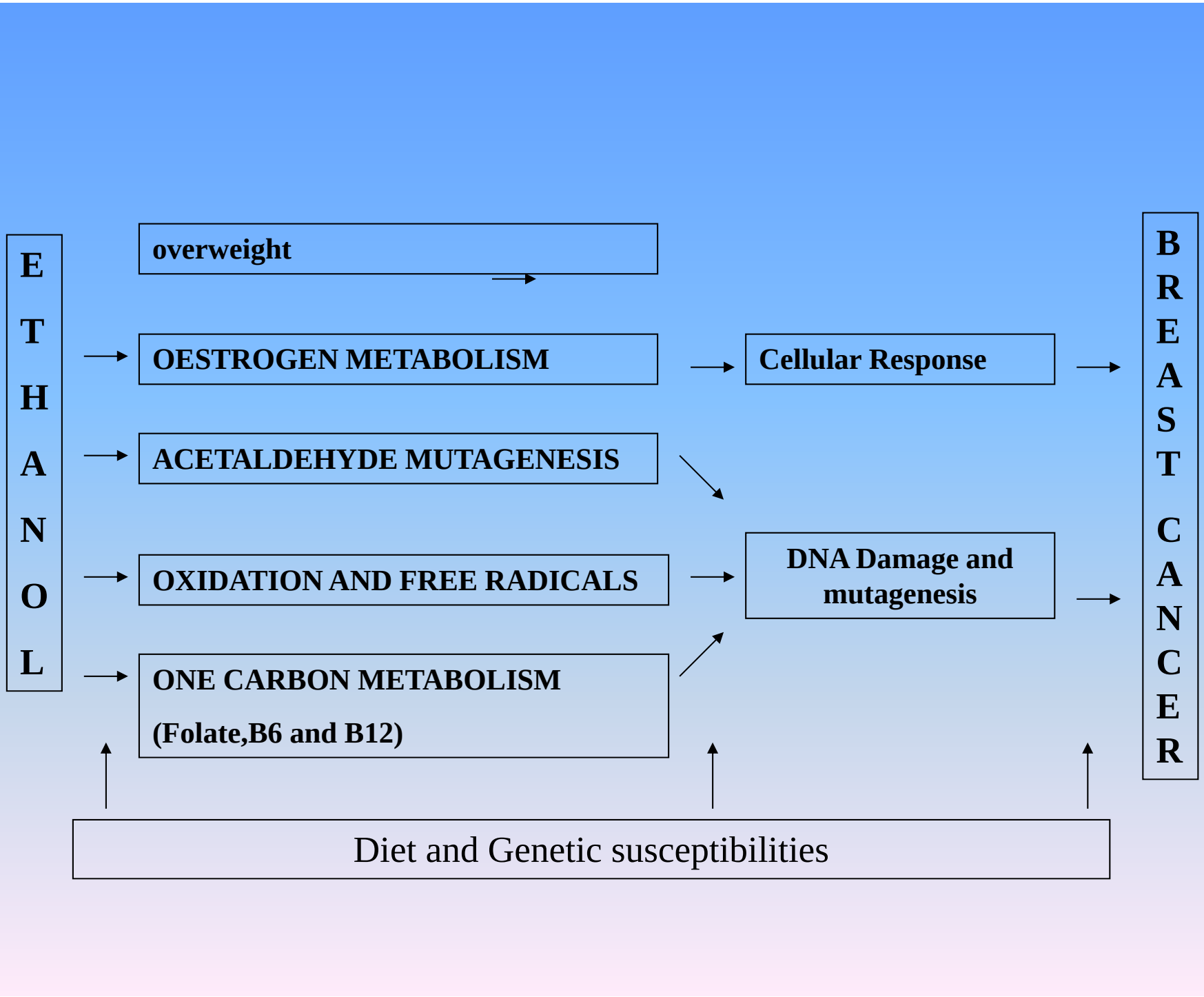
ASSOCIATION OF ALCOHOL INTAKE WITH PANCREATIC CANCER MORTALITY

Alcohol Intake, Drinks per Day	No. of Deaths	Relative Risk (95% CI)
Nondrinker	1792	1.00
Occasional	469	1.08
1	141	1.06
2	92	1.02
> 3	131	1.36

Gapstur et al, Arch Intern Med 2011



Br J of Cancer, 2002


ETHANOL
overweight
OESTROGEN METABOLISM
ACETALDEHYDE MUTAGENESIS
OXIDATION AND FREE RADICALS
ONE CARBON METABOLISM
(Folate,B6 and B12)
Cellular Response
DNA Damage and mutagenesis
BREAST CANCER
Diet and Genetic susceptibilities

ALCOHOL PROMOTES MAMMARY TUMOR DEVELOPMENT

Increased expression of aromatase (converts androgens to estrogens)

Increased systemic estrogen levels

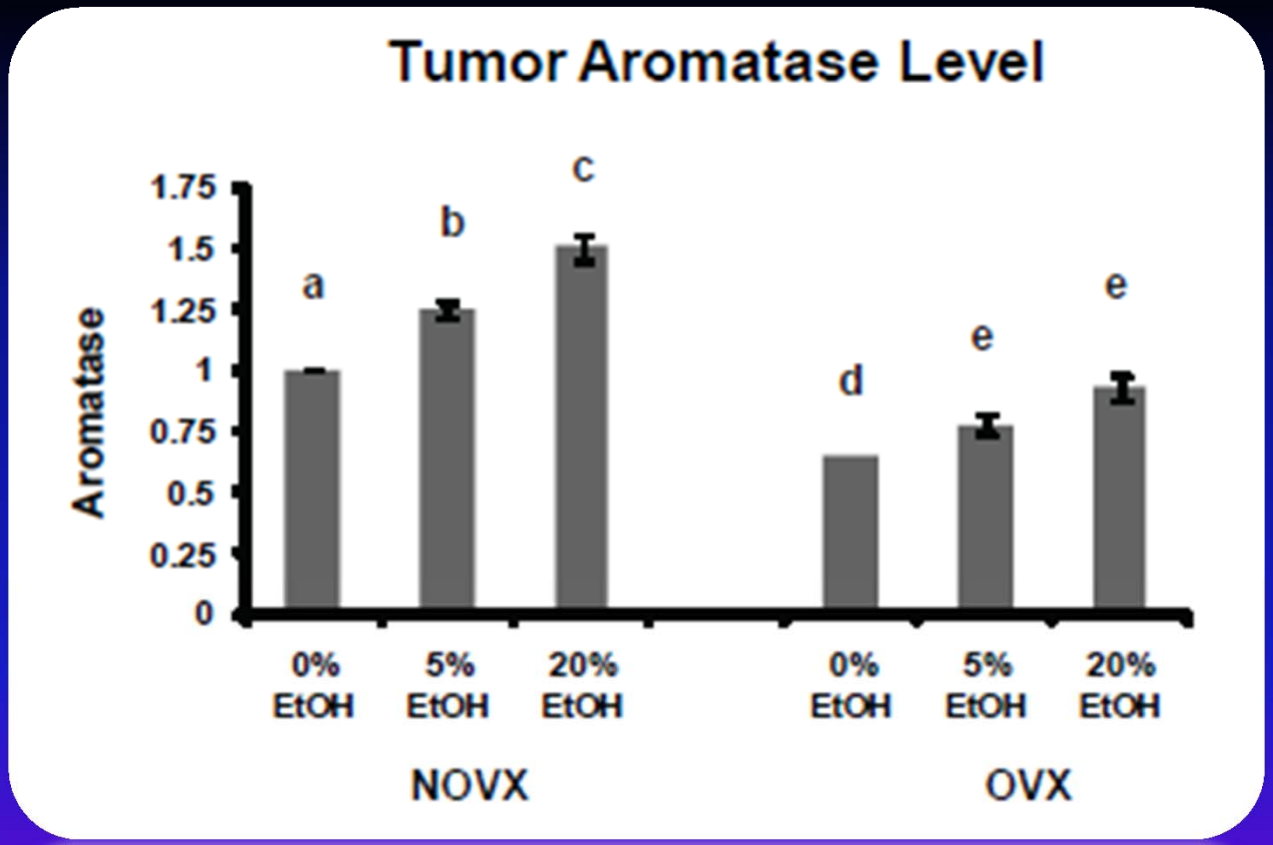
Increased expression Estrogen Receptor alpha

Wong et al., Alcoholism: Clinical and Experimental Research 2011

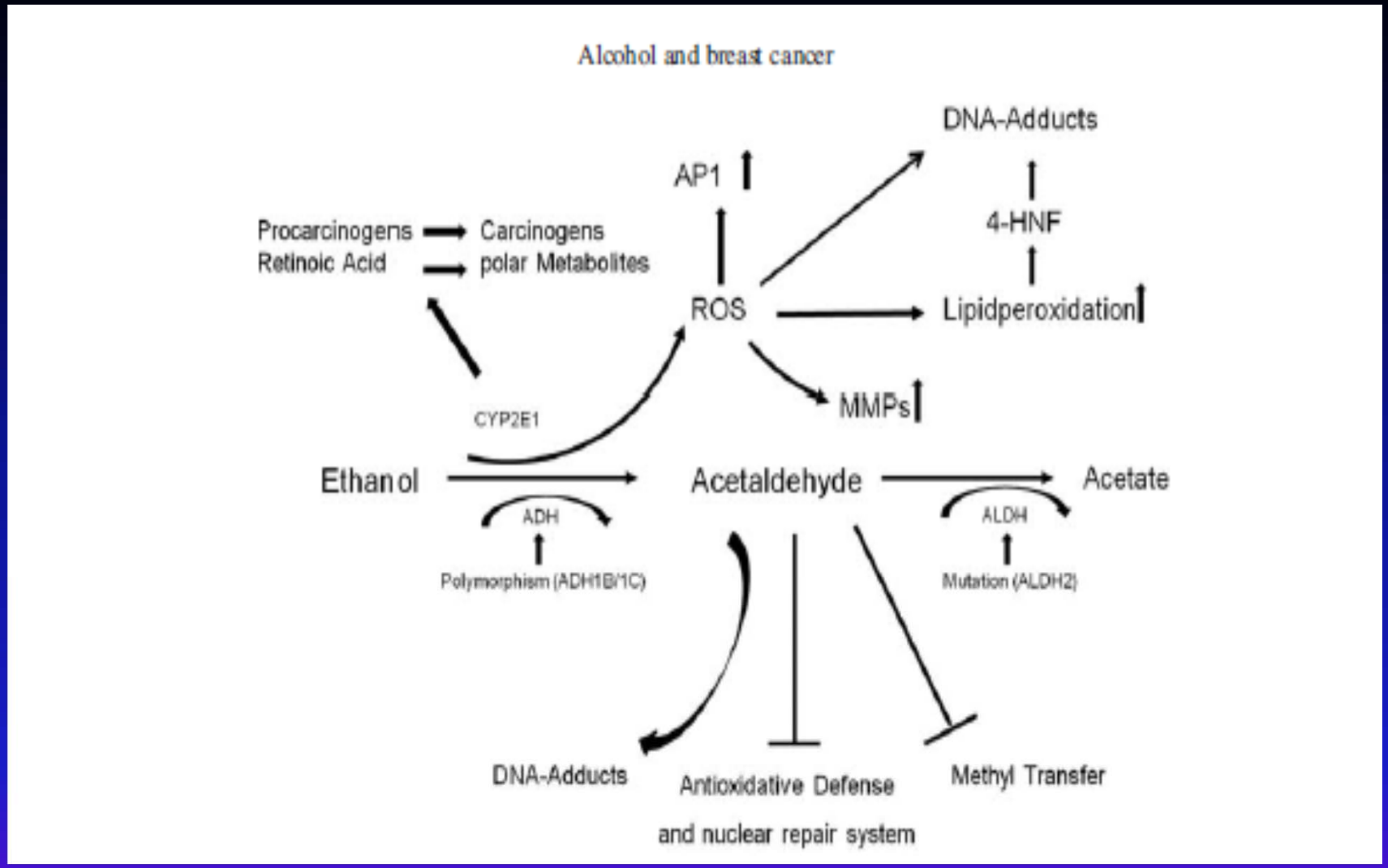
Alcohol increases insulin sensitivity

and promotes mammary tumorigenesis

Hong et al, Cancer Letters 2010


Tumor Aromatase Level
Aromatase
1.75
1.5
1.25
1
0.75
0.5
0.25
0
a
b
c
d
e
e
0% EtOH
5% EtOH
20% EtOH
0% EtOH
5% EtOH
20% EtOH
NOVX
OVX

Wong AW, 2011



Seitz HK et al, Alcohol and Alcoholism 2012

Low doses of alcohol are associated with the risk of breast cancer

- **up to one drink per day***
- **3-6 drinks/ week****

*** Giacosa et al, Eur J Cancer Prev 2011**

**** Pelucchi et al, Nutr Cancer 2011**

Prospective Study of Adolescent Alcohol Consumption and Risk of Benign Breast Disease in Young Women

Drinking Frequency	OR
Never to less than weekly	1.00 (referent)
1-2 U/ wk	1.72
3-5 U/ wk	3.34
6-7 U/ wk	5.94

Berkey CS et al, Pediatrics 2010

Printz C, Cancer 2010

Table 3. Risk of Biopsy-Confirmed BBD in Young Females With Family History of BC, Family History of Maternal BBD, Family History

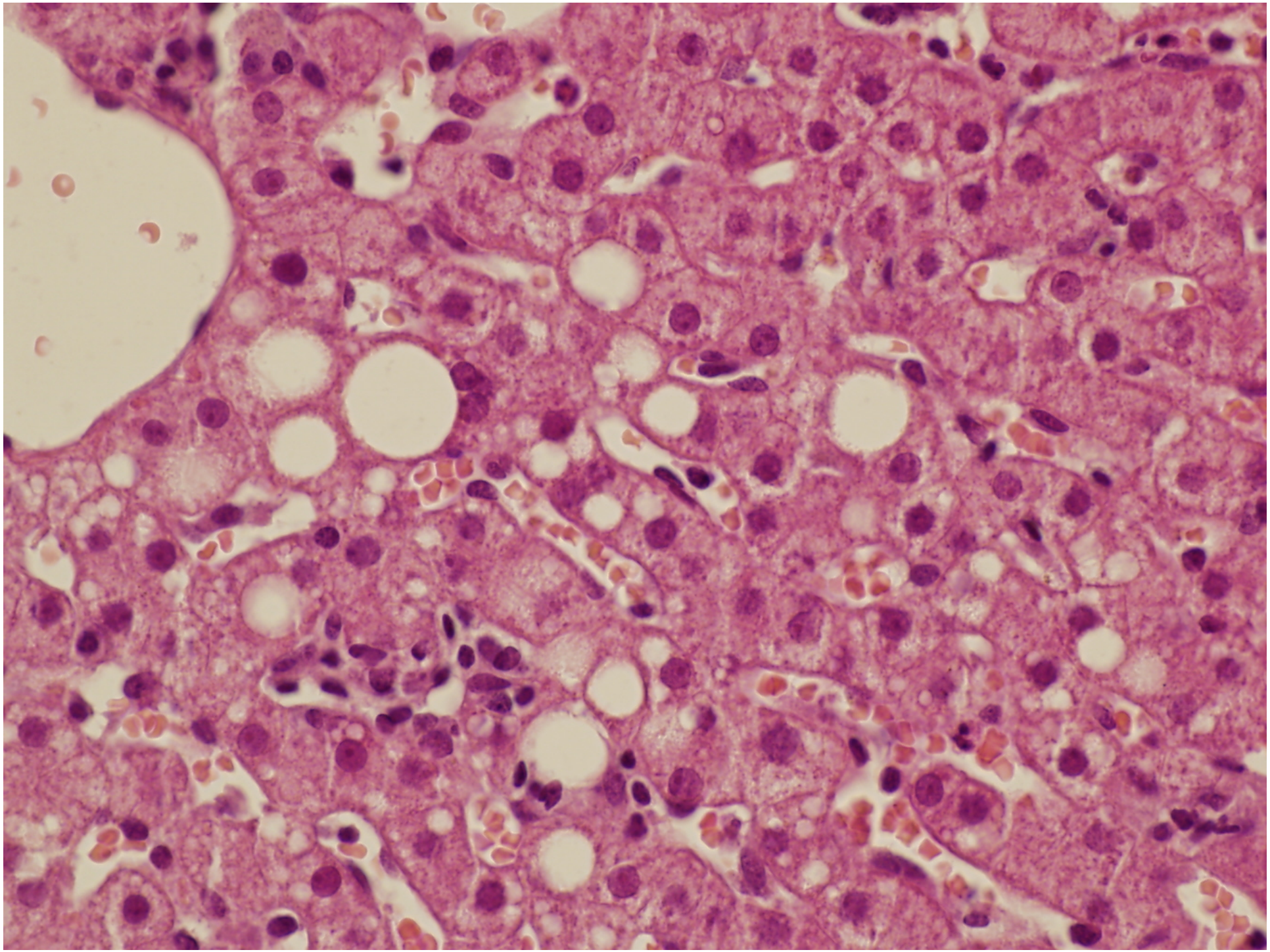
	BC in Affected Family Member			BDD in Mother
	Mother or Aunt	Grandmother	Any Family Member (Mother, Aunt, Grandmother)	
GUTS girls, No.	477	749	1157	1264
GUTS BBD cases, No.	10	10	19	18
Risk factor, OR (*P*)				
Adolescent alcohol, daily drink	3.80 (.02)	2.29 (.04)	2.28 (.01)	1.96 (.02)
PHV, in./y	1.82 (.05)	0.71 (.51)	1.21 (.49)	1.31 (.44)
Menarche age, y	1.21 (.47)	1.08 (.77)	1.05 (.78)	1.00 (.99)
Young adult height, in.	0.95 (.67)	0.93 (.54)	0.96 (.64)	1.07 (.44)
Childhood BMI, kg/m^2	1.00 (.97)	0.83 (.16)	0.93 (.37)	0.99 (.90)
BMI change, kg/m^2	1.03 (.72)	1.06 (.59)	1.04 (.58)	1.05 (.44)
Young adult BMI, kg/m^2	1.02 (.81)	0.94 (.51)	0.99 (.80)	1.02 (.63)
Adolescent waist circumference, in.	0.92 (.51)	0.90 (.37)	0.91 (.27)	1.08 (.30)

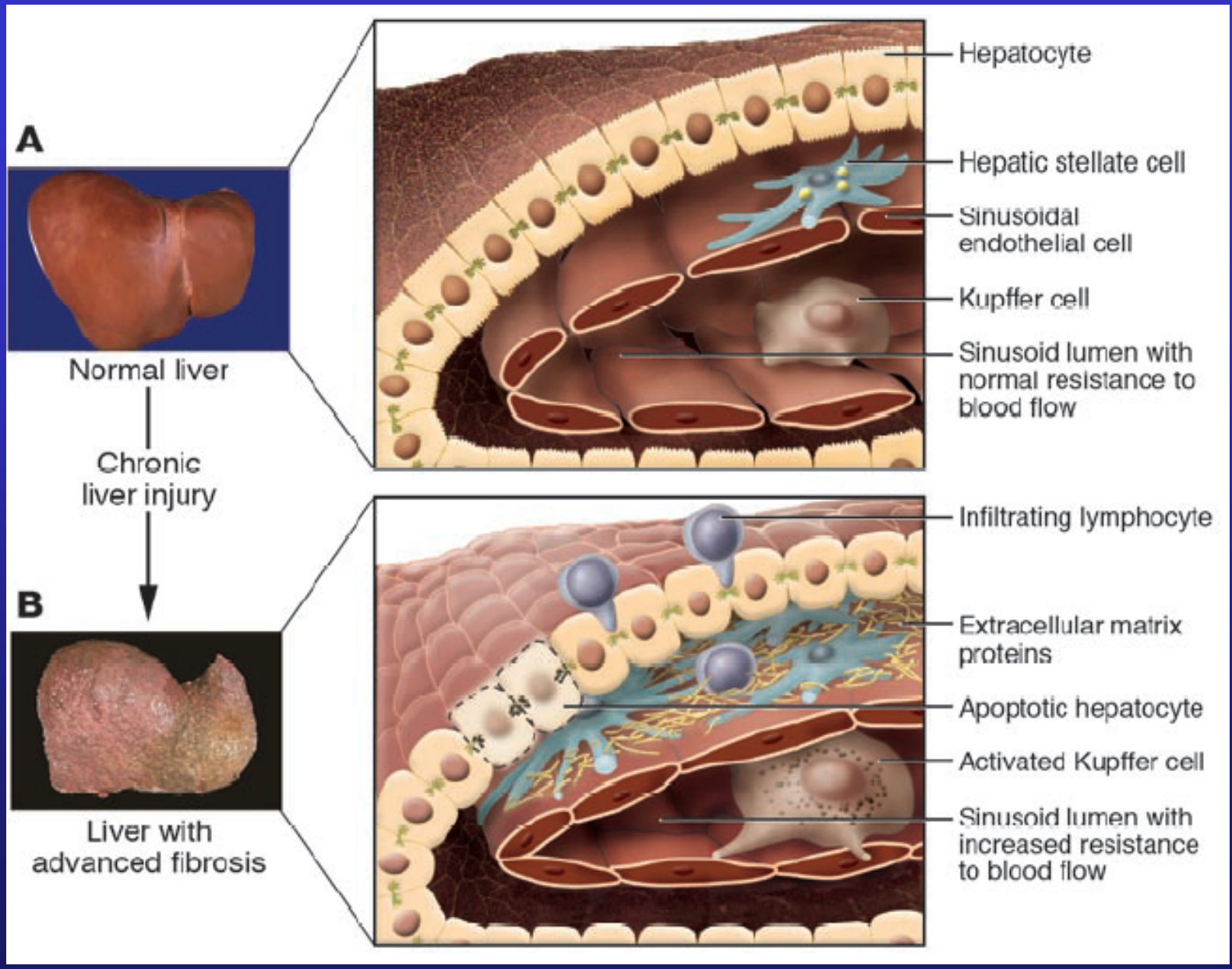
6888

18-27 years

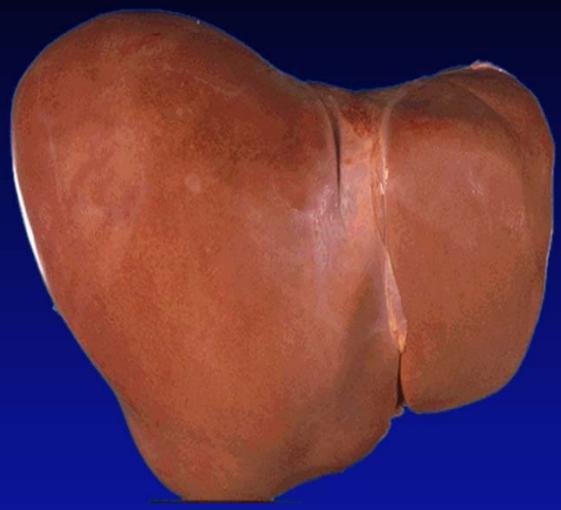
< 7 drinks/wk

Berkey CS et al, Cancer 2012




A
Normal liver
Chronic liver injury
B
Liver with advanced fibrosis
Hepatocyte
Hepatic stellate cell
Sinusoidal endothelial cell
Kupffer cell
Sinusoid lumen with normal resistance to blood flow
Infiltrating lymphocyte
Extracellular matrix proteins
Apoptotic hepatocyte
Activated Kupffer cell
Sinusoid lumen with increased resistance to blood flow

gr/die ⟶



12-20 women, 25-80 men

O'Shea, 2010

Daily Alcohol Intake > 30 g/day

Odds of developing cirrhosis or lesser degrees of liver disease

cirrhosis: 13.7; lesser degrees: 23.6

Bellentani et al, 1997

THE SEARCH FOR GENETIC RISK FACTORS FOR ALCOHOLIC LIVER DISEASE

Genetic variation modulating addiction to alcohol

Genetic variation of alcohol-metabolising enzymes

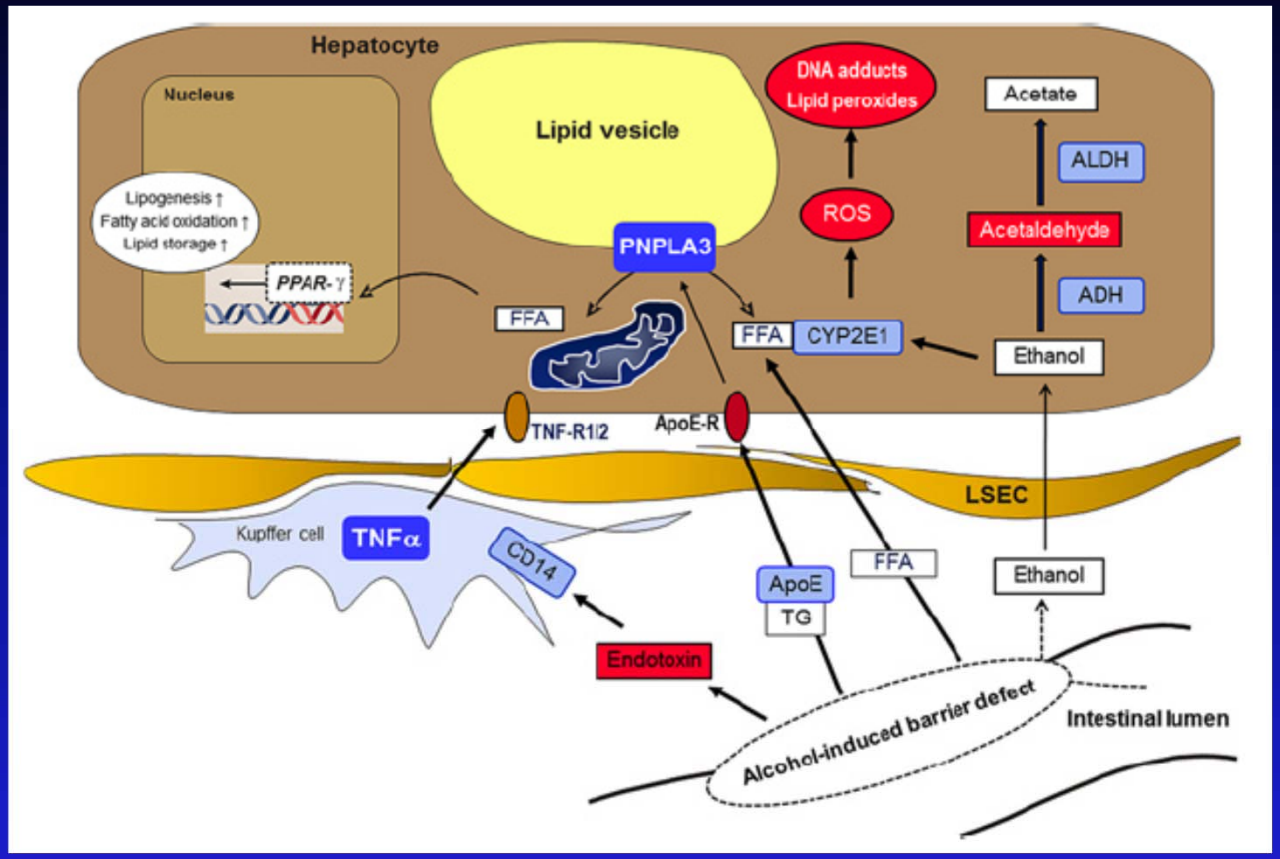
Genetic variations involved in oxidative stress

Genetic variations controlling hepatic lipid storage

Genetic polymorphisms modulating endotoxin inflammation

Polymorphic variants of fibrosis-associated genes

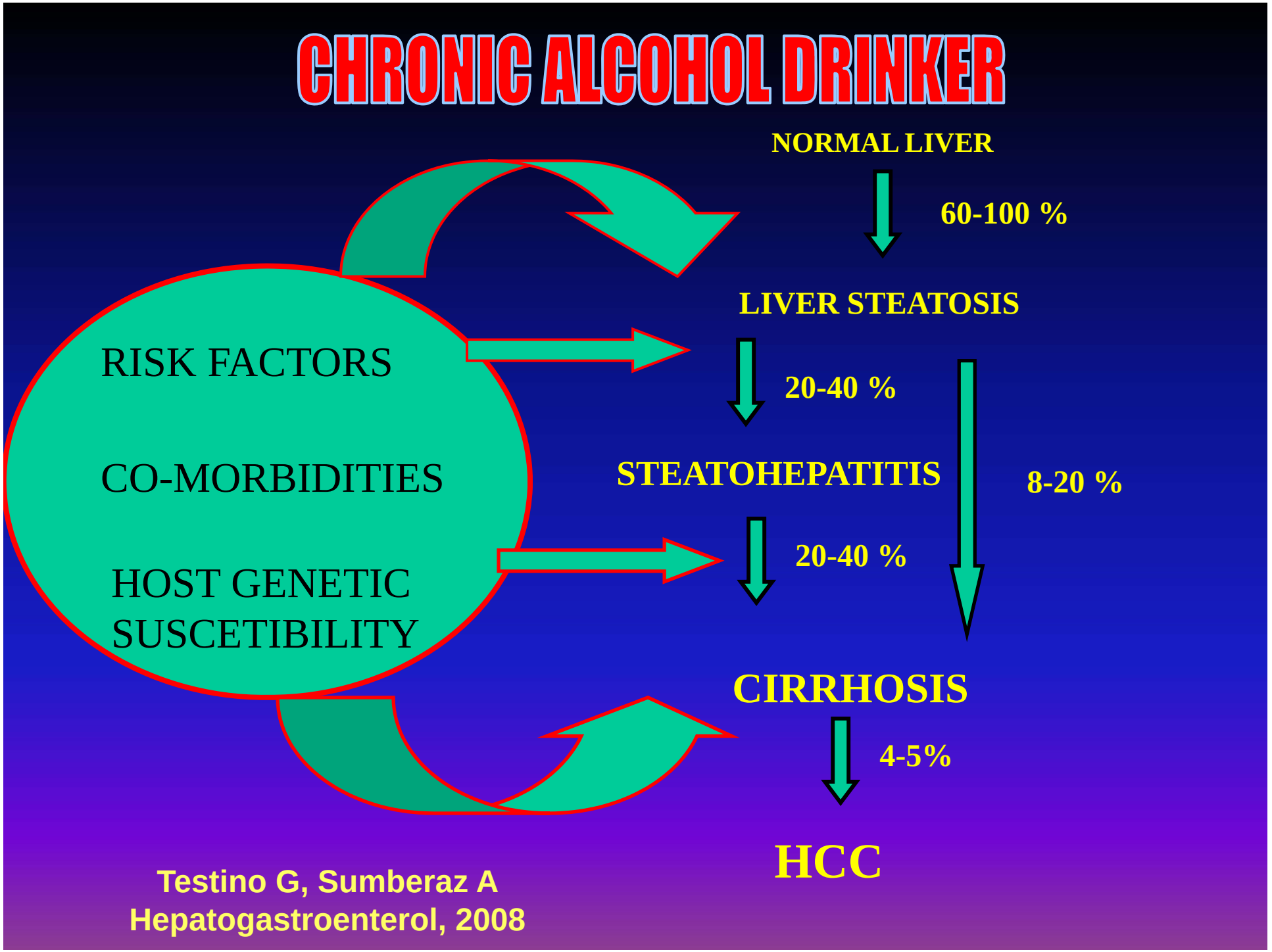
Stickel and Hampe, Gut 2011

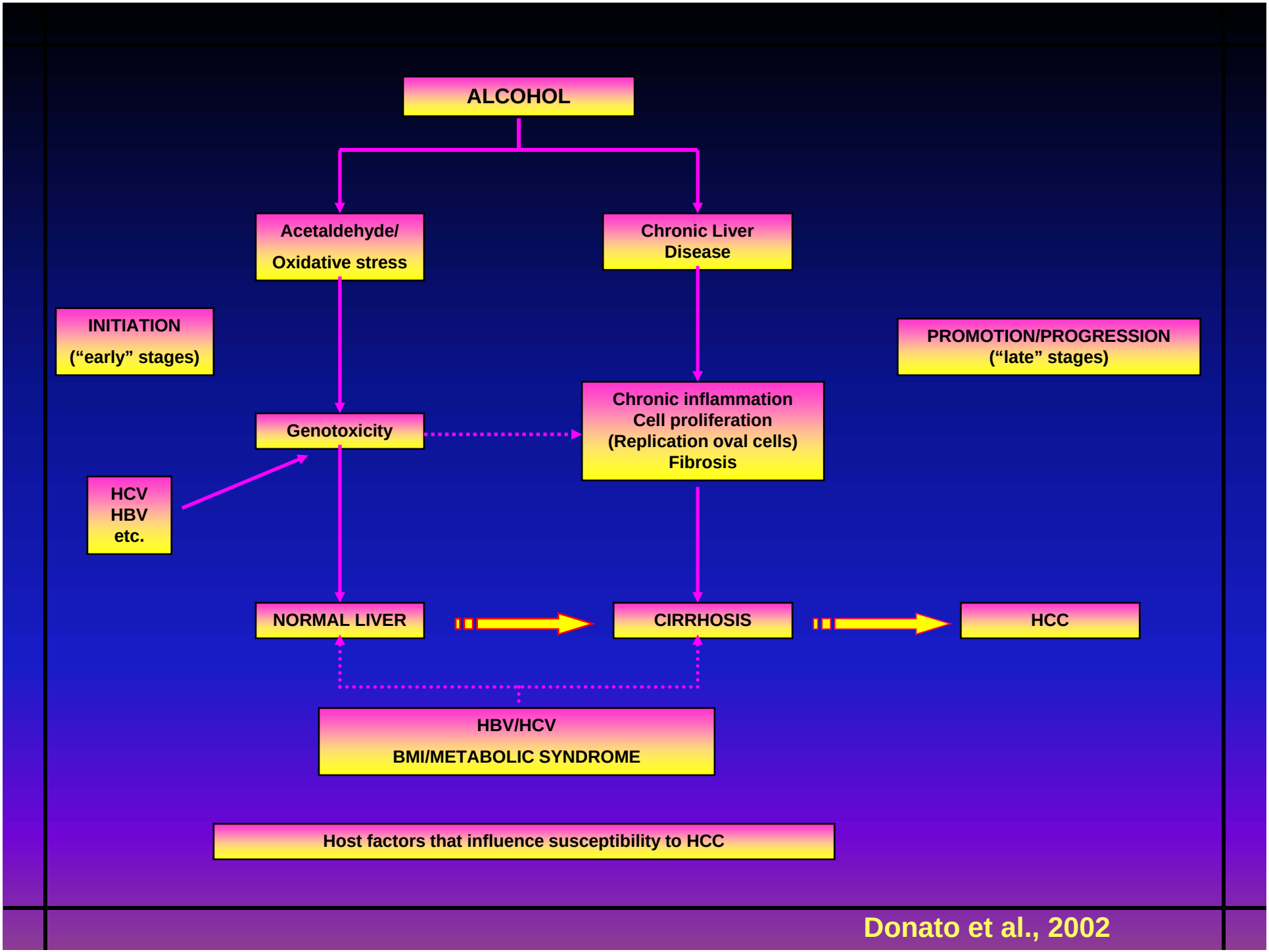


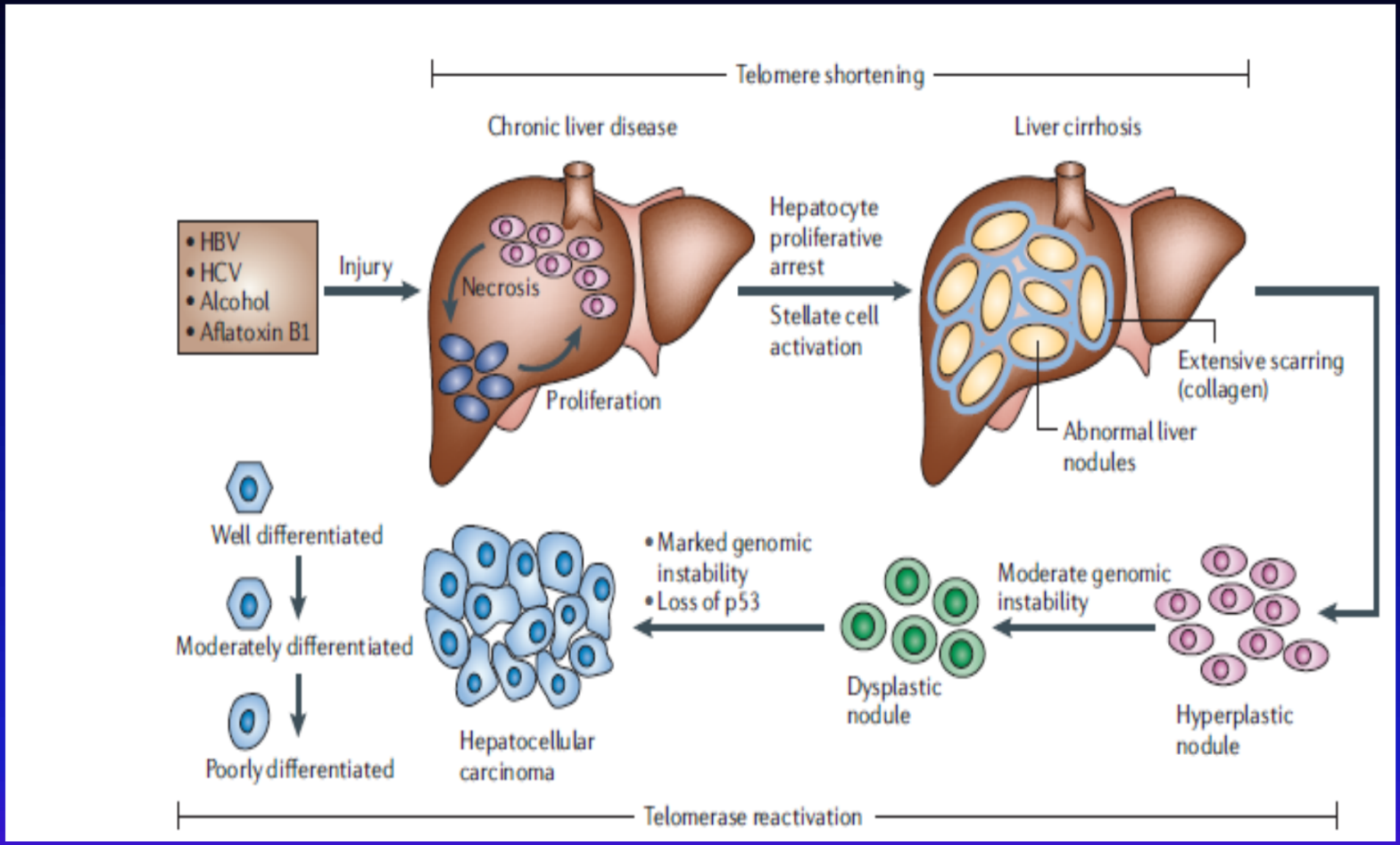
Tumor Necrosis Factor alpha – 238A

PNPLA3 rs738409 G: patatin-like phospholipase domain-containing 3

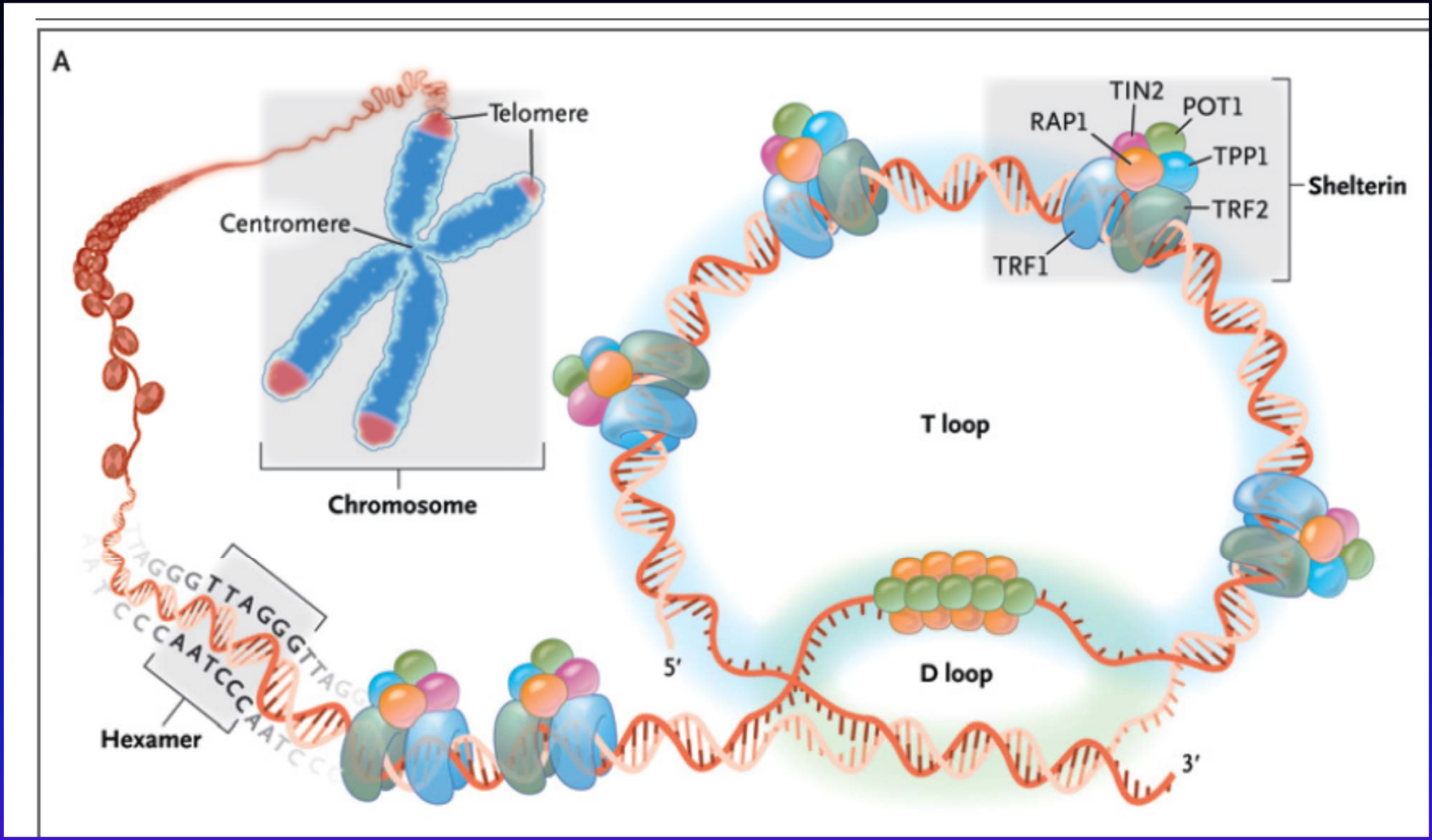
Sookoian S et al, Hepatology 2011


CHRONIC ALCOHOL DRINKER
NORMAL LIVER
60-100 %
LIVER STEATOSIS
20-40 %
STEATOHEPATITIS
20-40 %
8-20 %
CIRRHOSIS
4-5%
HCC
RISK FACTORS
CO-MORBIDITIES
HOST GENETIC SUSCETIBILITY
Testino G, Sumberaz A
Hepatogastroenterol, 2008

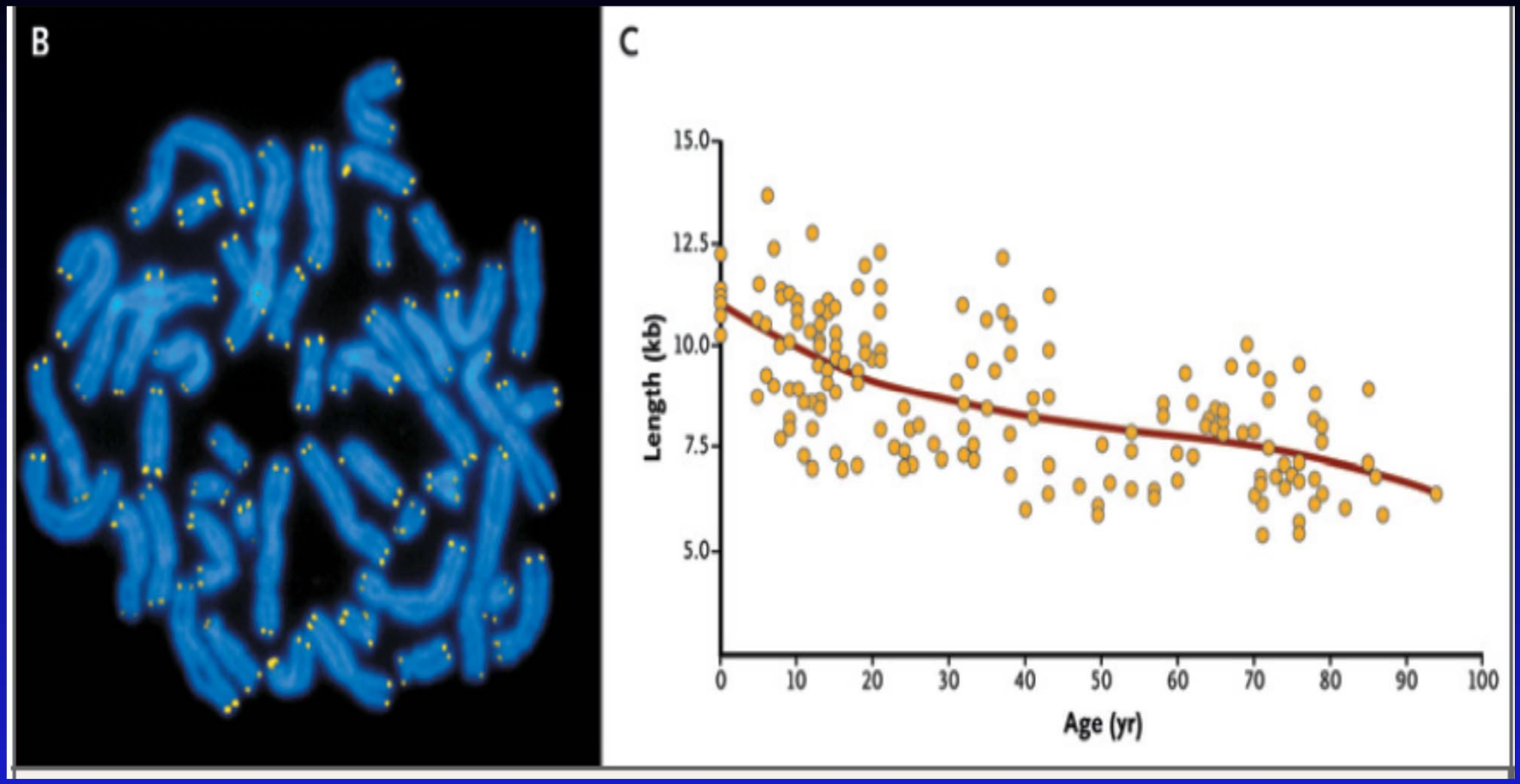

ALCOHOL
Acetaldehyde/
Oxidative stress
Chronic Liver
Disease
INITIATION
("early" stages)
PROMOTION/PROGRESSION
("late" stages)
Chronic inflammation
Cell proliferation
(Replication oval cells)
Fibrosis
Genotoxicity
HCV
HBV
etc.
NORMAL LIVER
CIRRHOSIS
HCC
HBV/HCV
BMI/METABOLIC SYNDROME
Host factors that influence susceptibility to HCC
Donato et al., 2002



Farazi et al, Nature 2006



Calado and Young, N Engl J Med 2009



Calado and Young, N Engl J Med 2009

TELOMERE LENGHT ACCORDING TO USUAL DRINKING CATEGORIES

	Geometric mean	95% CI	P-value	P-trend
0-1 drink-units/day	0.67	(0.63-0.72)	Ref.	
2-4 drink-units/day	0.61	(0.56-0.68)	0.14	
>4 drink-units/day	0.48	(0.39-0.59)	0.002	0.003

Pavanello et al, International Journal of Cancer 2011

FREQUENCY OF DNA HYPERMETHYLATION IN HCC AND THEIR ASSOCIATION WITH ALCOHOL

Gene	Percentage of hypermethylated tumor samples
RASSF1A	67%
GSTP1	44%
P14 ARF	0%
GNMT	30%
DOK1	60%
MGMT	22%
CHRNA3	33%

RASSF1A: Ras signalling

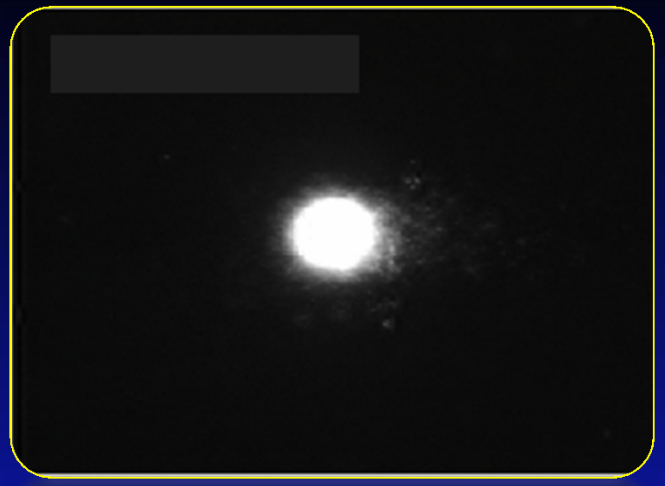
GSTP1: detoxification of carcinogens

DOK1: response to interferon

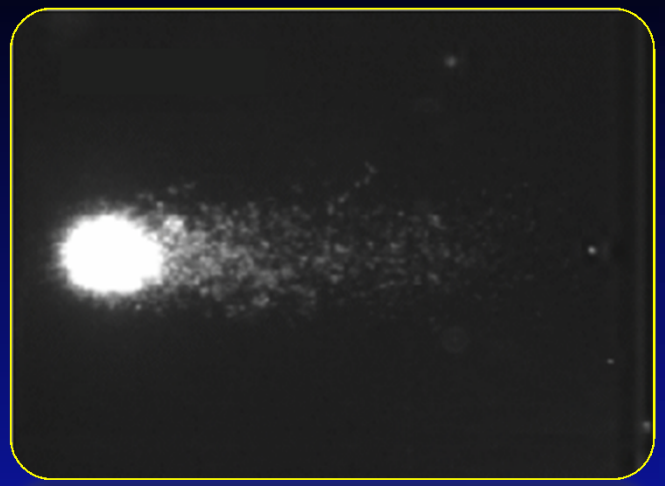
CHRNA3: angiogenic growth

MGMT: DNA repair

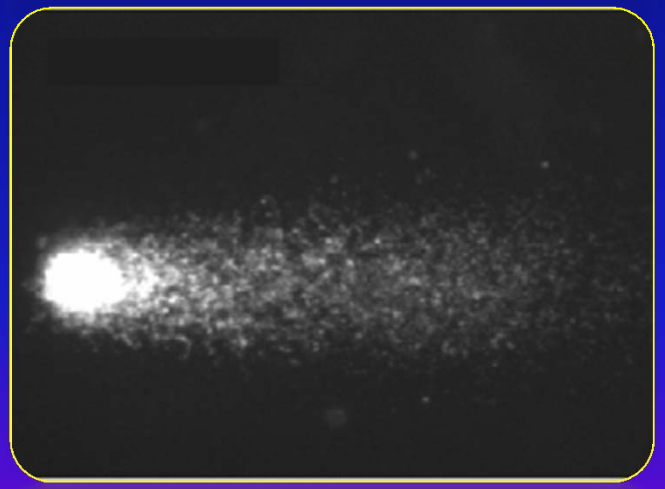
LAMBERT et al, J HEPATOL 2010



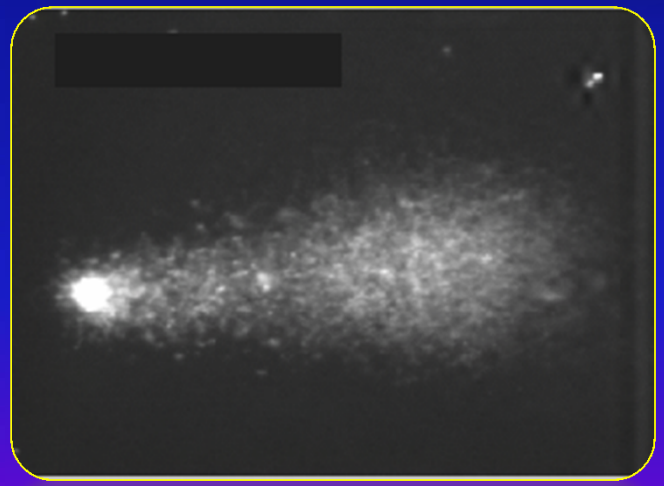
controllo



1



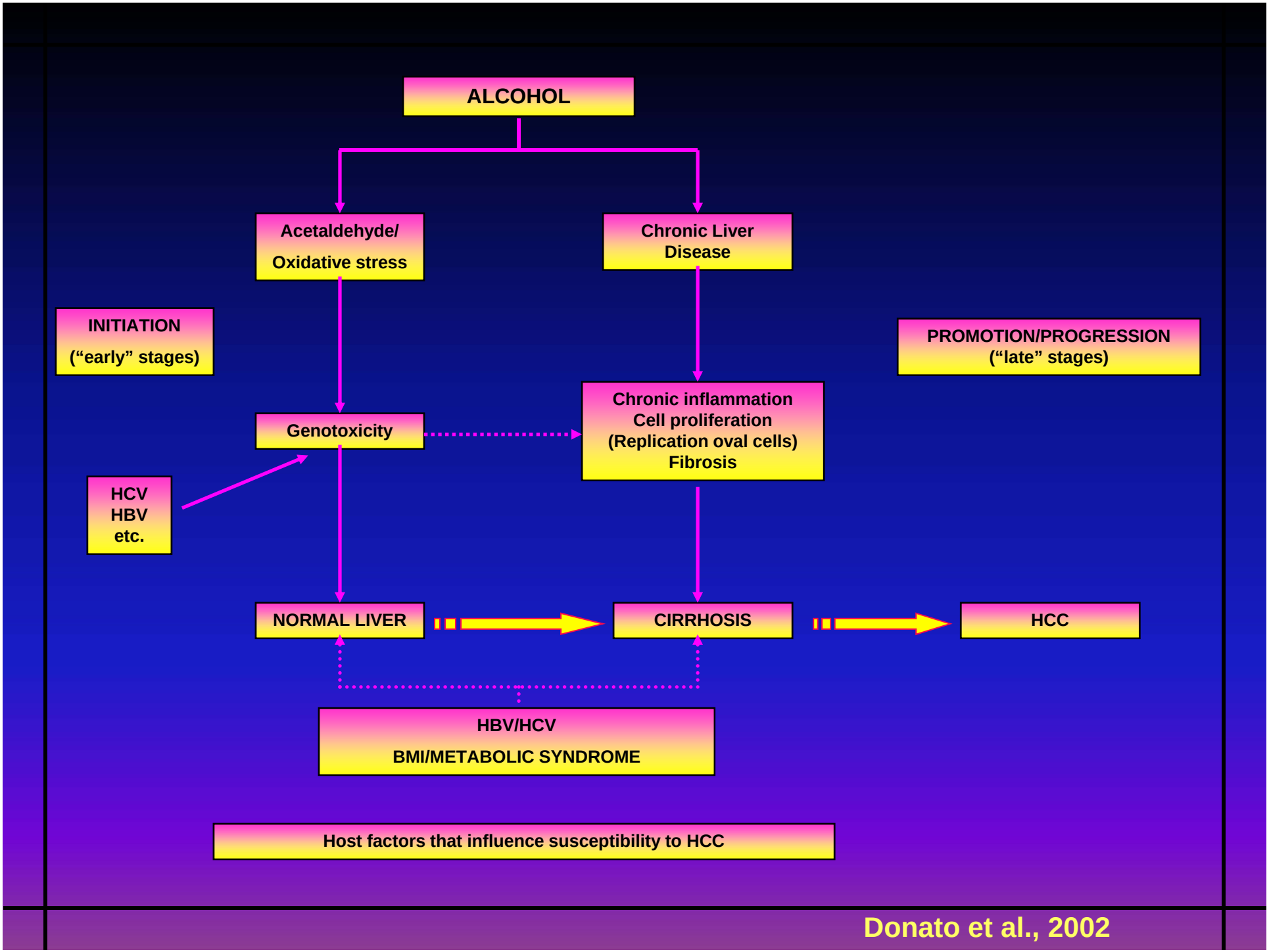
2

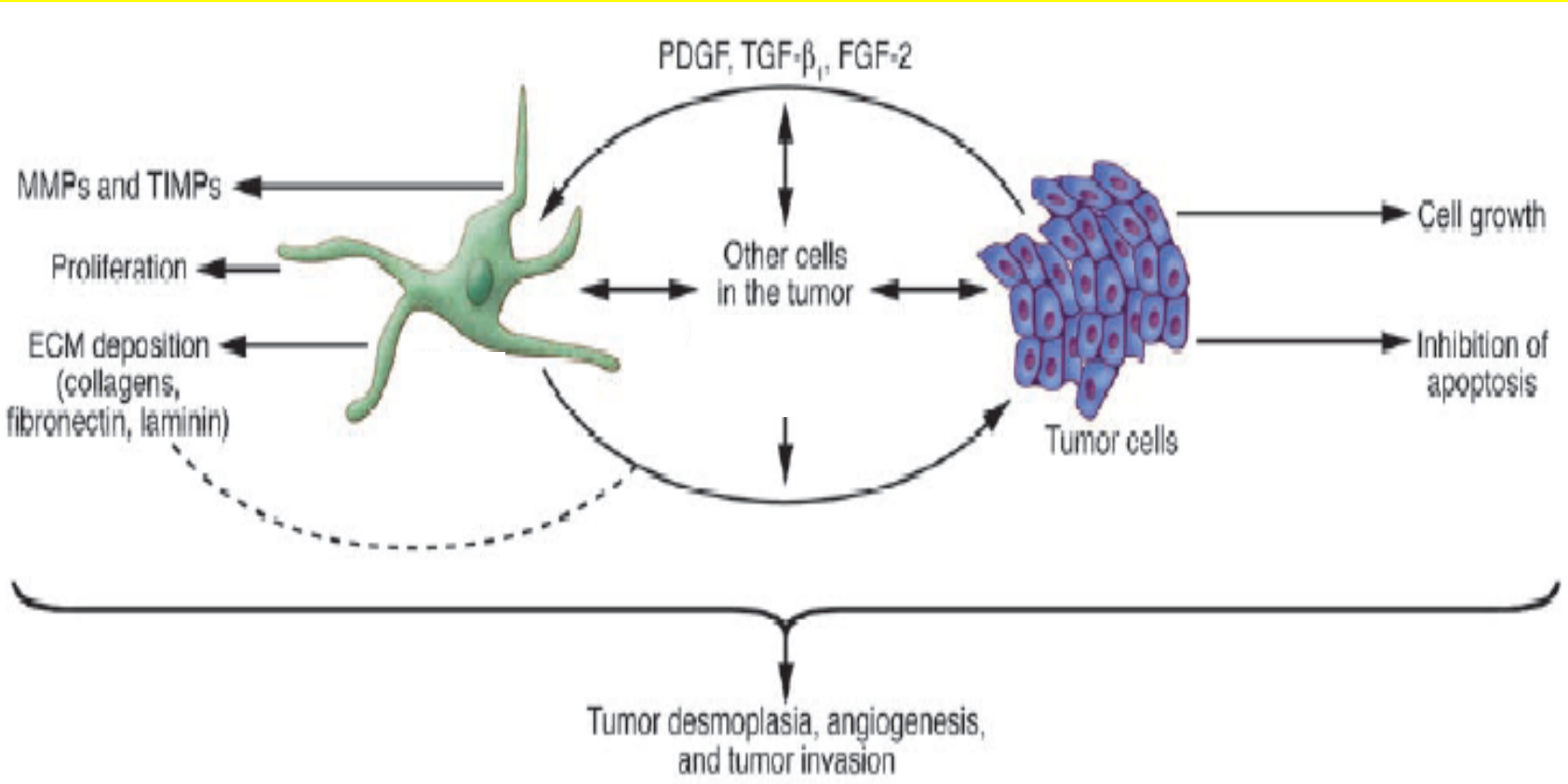


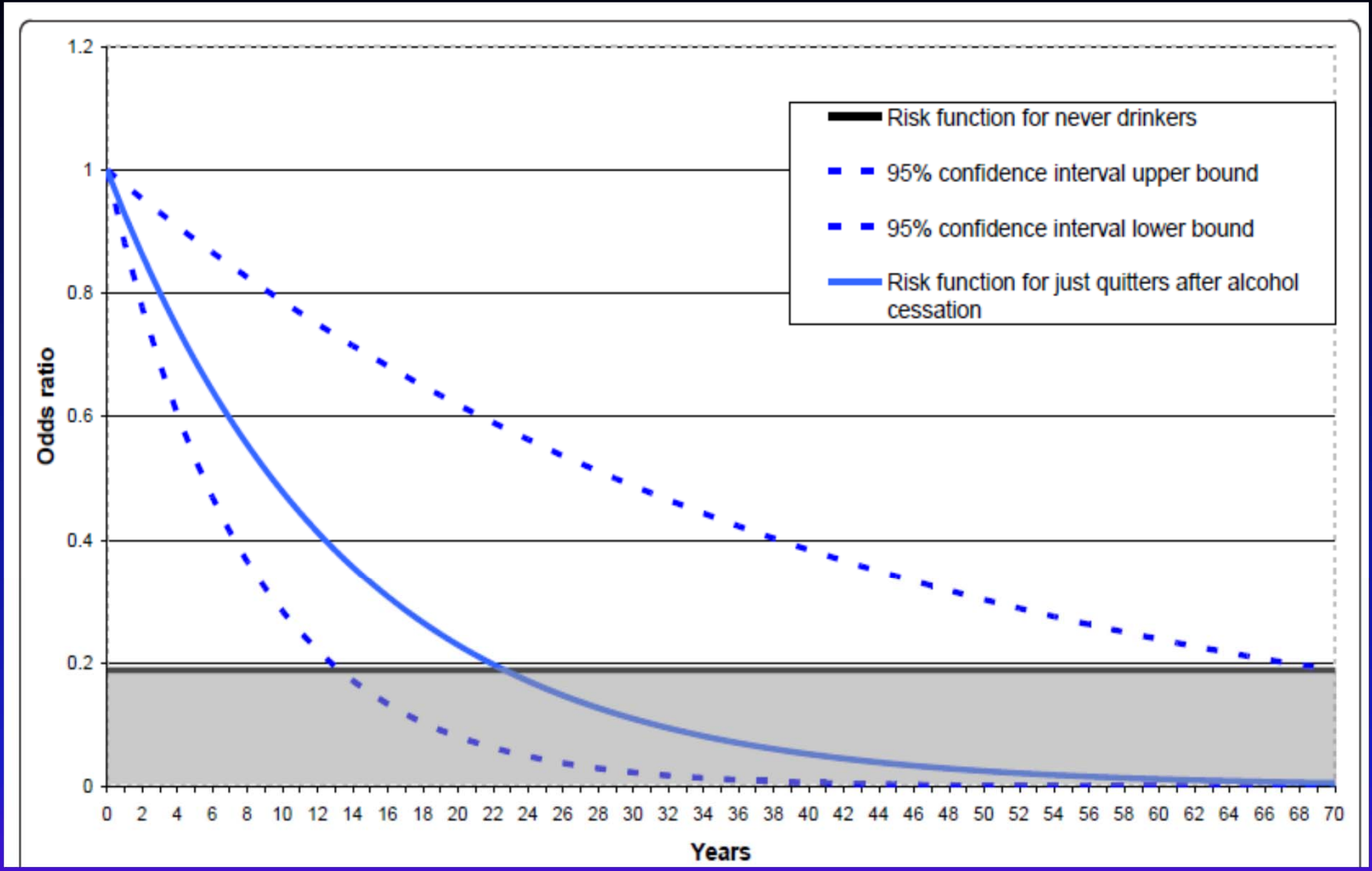
3

1,2,3 = diversi gradi di danno

Martelli, Sumberaz, Testino – European J Gastroenterol Hepatol 2008


ALCOHOL
Acetaldehyde/
Oxidative stress
Chronic Liver
Disease
INITIATION
("early" stages)
PROMOTION/PROGRESSION
("late" stages)
Chronic inflammation
Cell proliferation
(Replication oval cells)
Fibrosis
Genotoxicity
HCV
HBV
etc.
NORMAL LIVER
CIRRHOSIS
HCC
HBV/HCV
BMI/METABOLIC SYNDROME
Host factors that influence susceptibility to HCC
Donato et al., 2002


PDGF, TGF-β1, FGF-2
MMPs and TIMPs
Proliferation
ECM deposition
(collagens,
fibronectin, laminin)
Other cells
in the tumor
Cell growth
Inhibition of
apoptosis
Tumor cells
Tumor desmoplasia, angiogenesis,
and tumor invasion



Heckley GA et al, BMC Cancer 2011

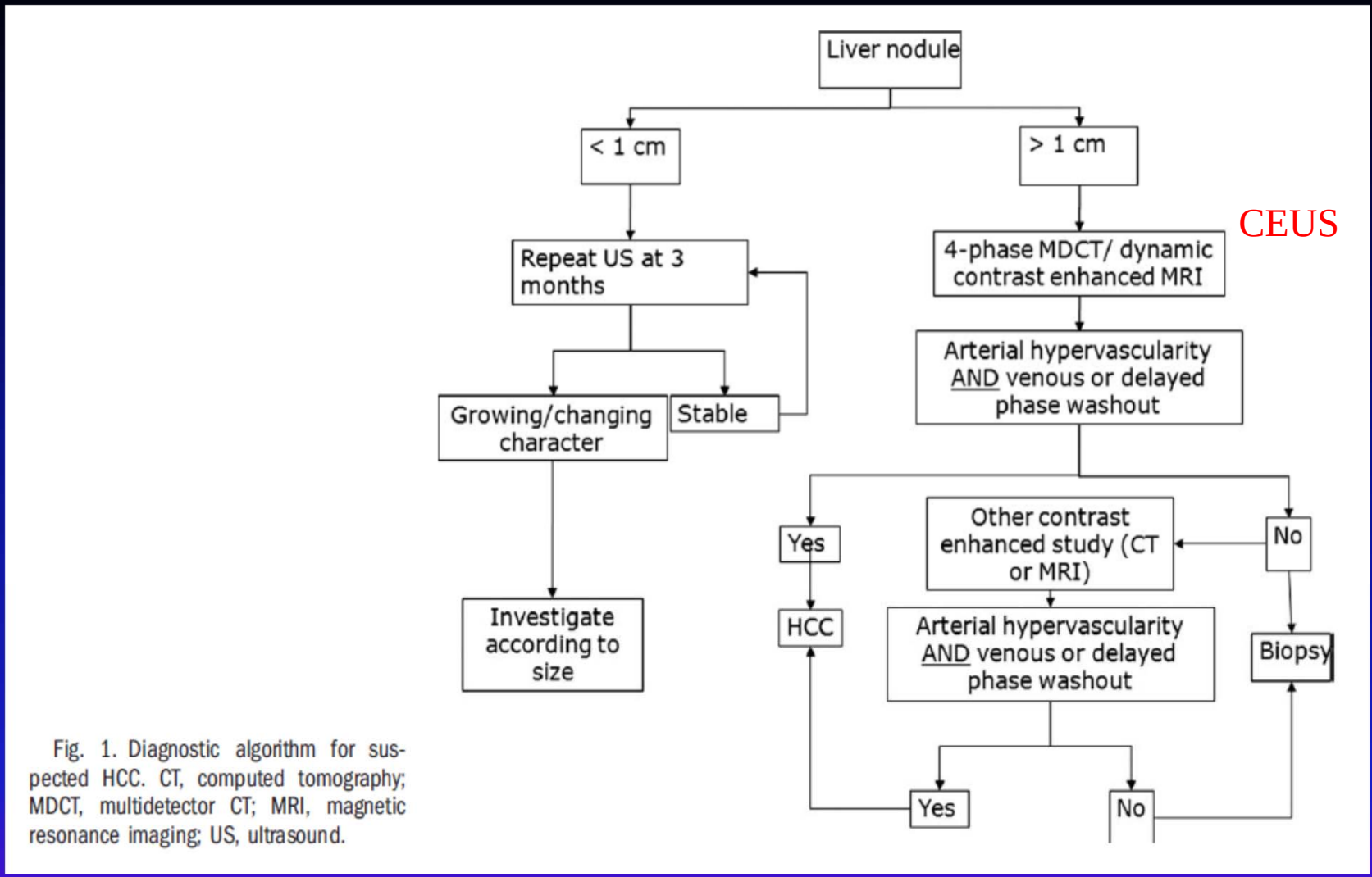


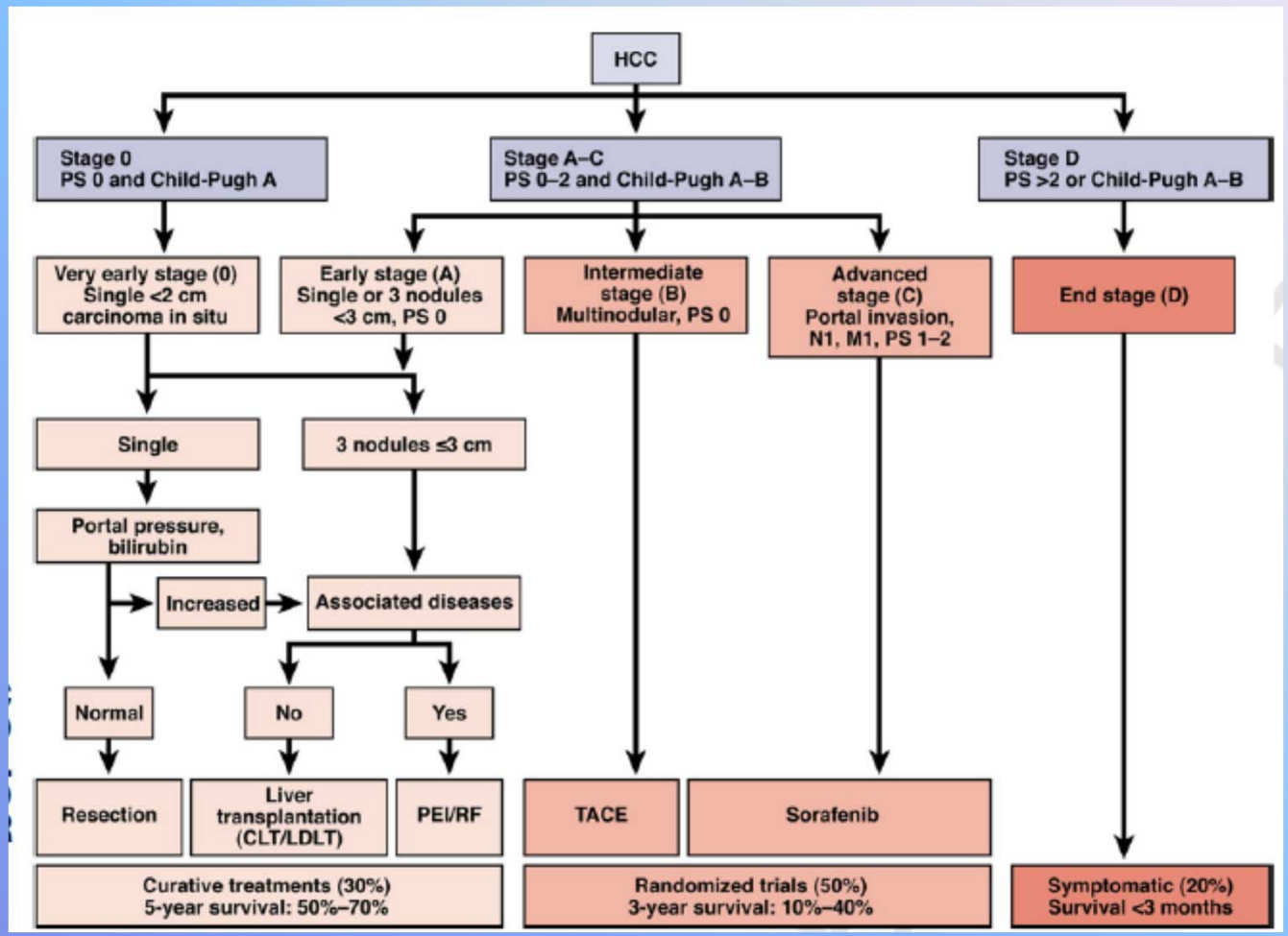
Fig. 1. Diagnostic algorithm for suspected HCC. CT, computed tomography; MDCT, multidetector CT; MRI, magnetic resonance imaging; US, ultrasound.

CEUS

AASLD, Hepatology 2010

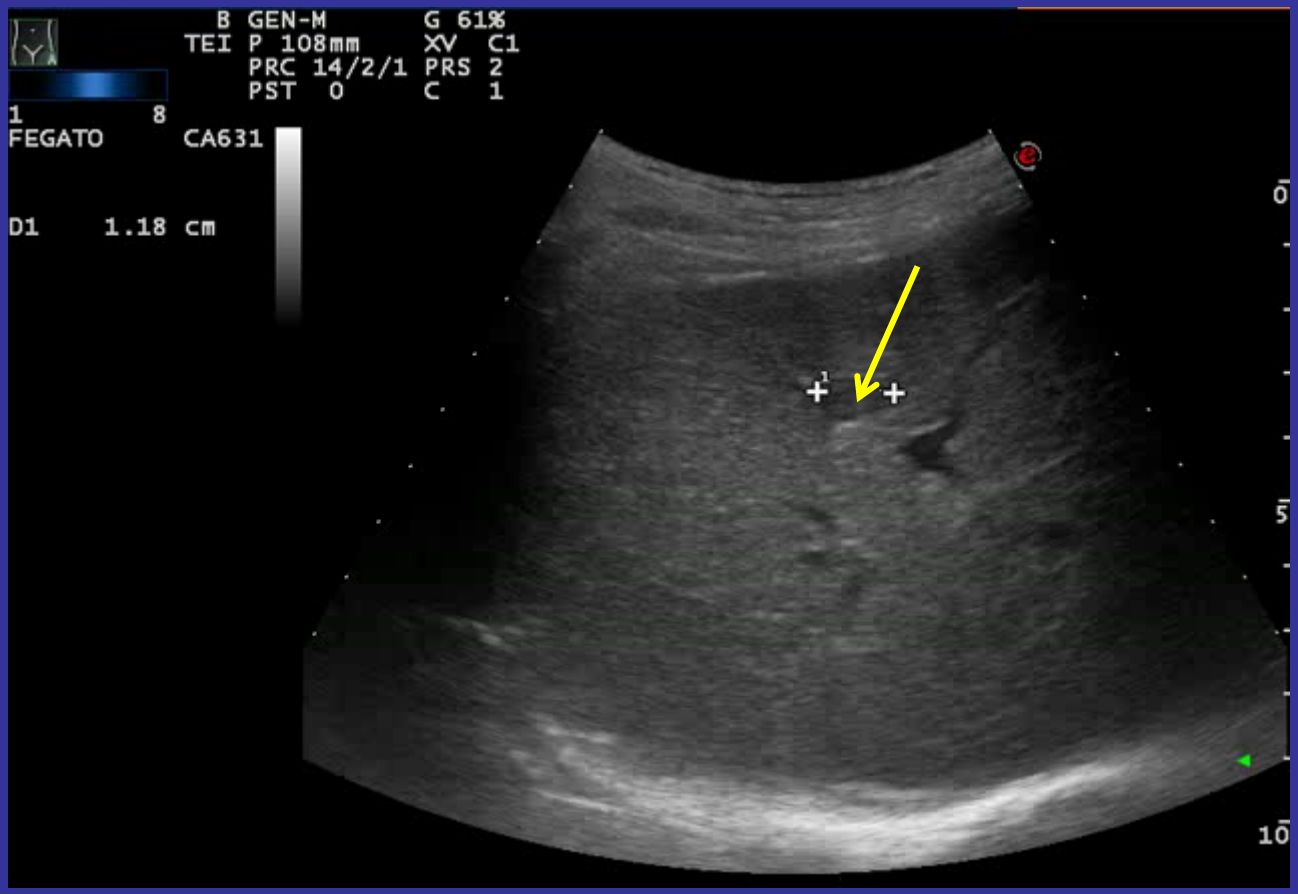
CEUS: Contrast-Enhanced Ultrasound

Minami et al, World J Radiol 2009; Omata et al, Hepatol Int 2010; Minami and Kudo, World J Gastroenterol 2010; Giorgio et al, Anticancer Res 2011

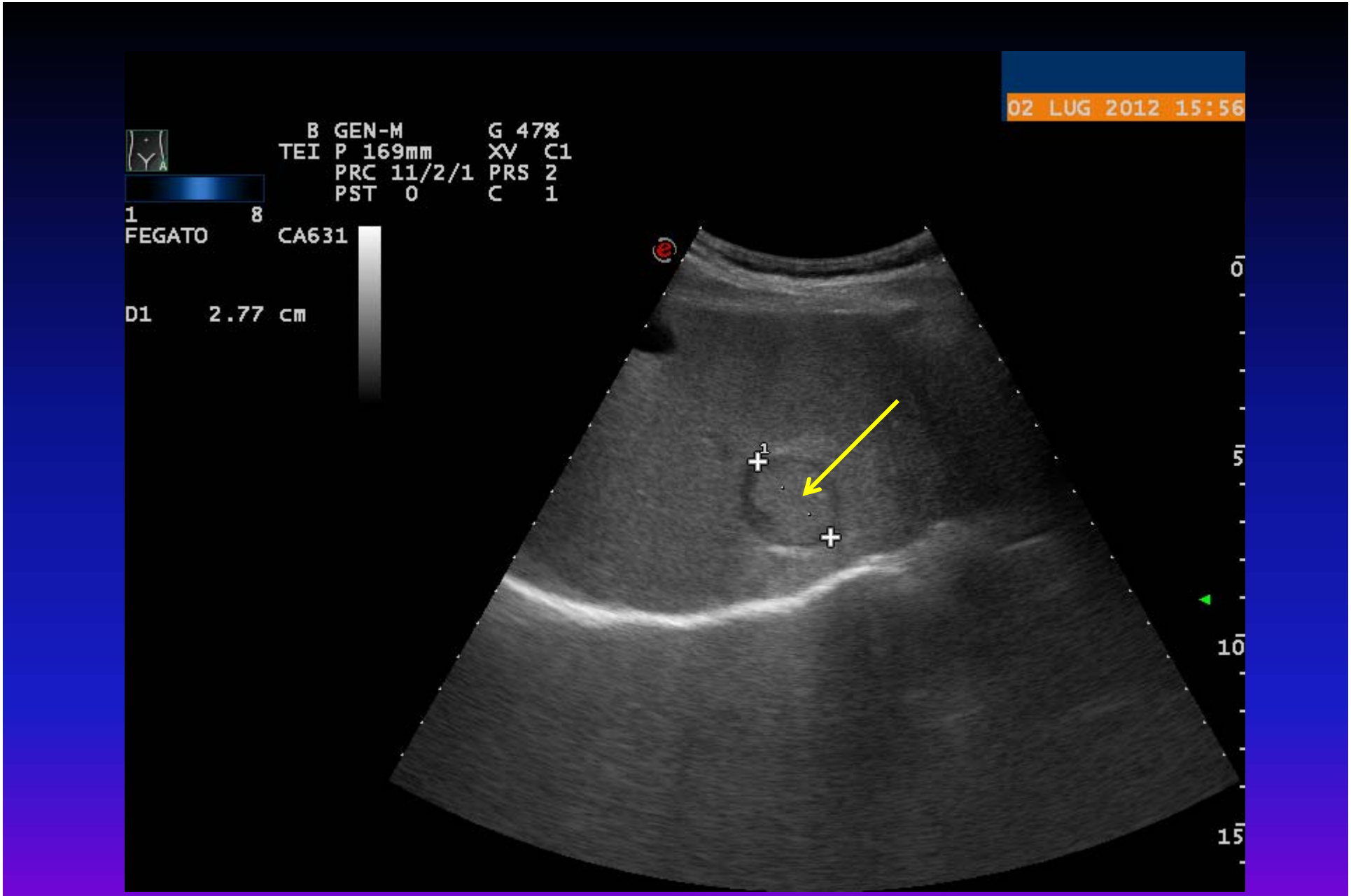


Barcelona Clinic Liver Cancer Staging System (BCLC-SS)

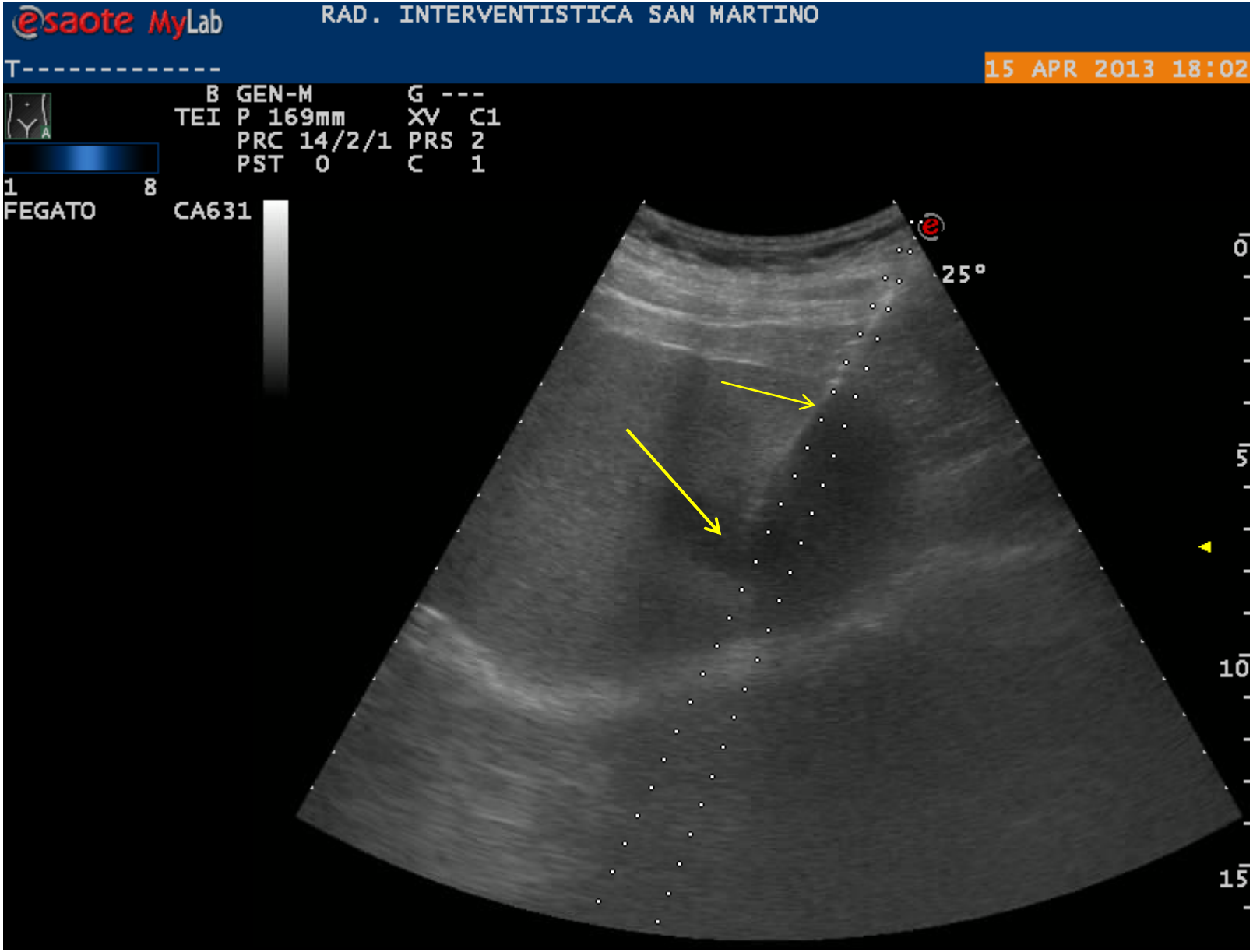
Llovet et al, Semin Liver Dis 1999; Bruix and Llovet, Lancet 2009



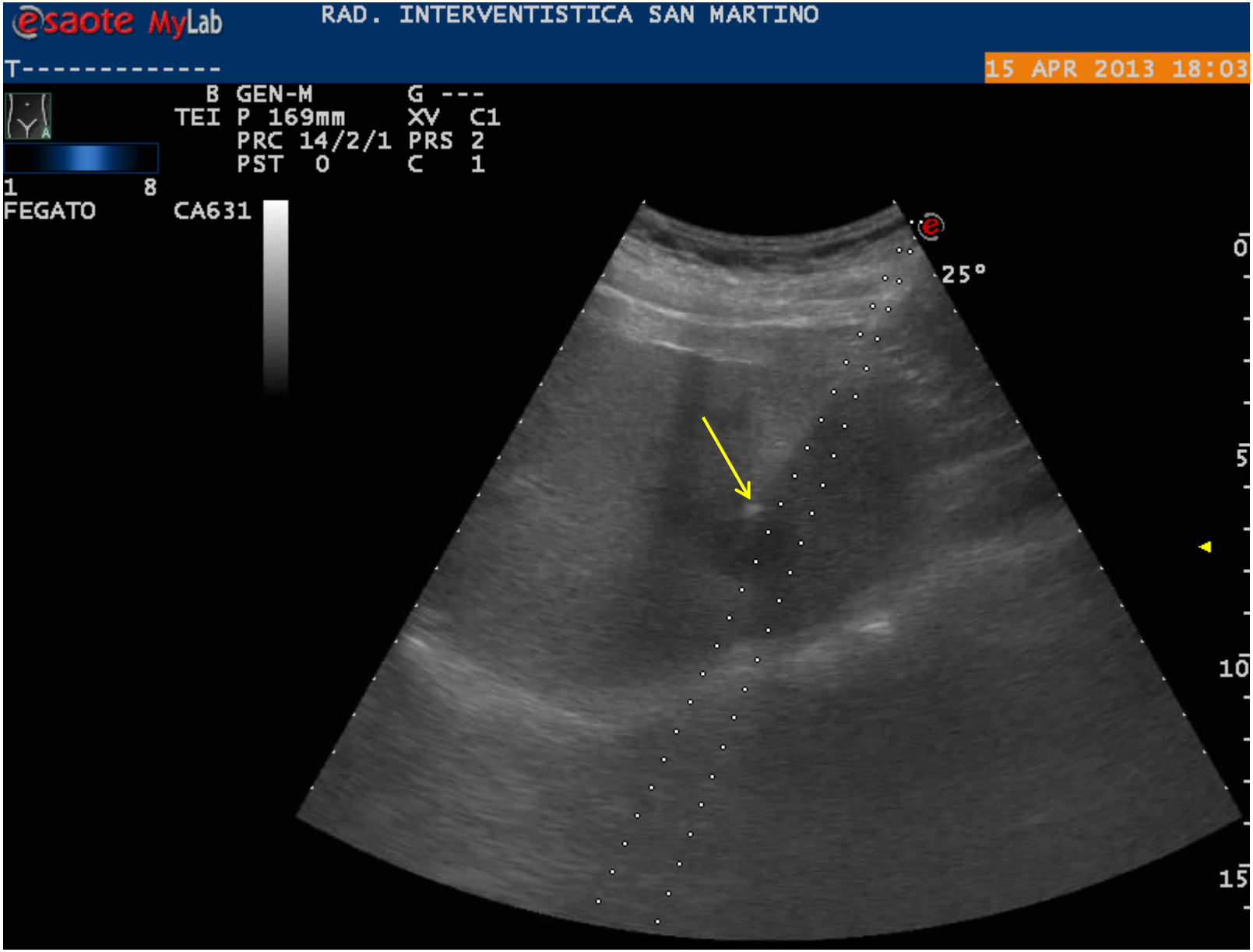
Paolo Borro – Centro Alcologico Regionale Ligure, IRCCS San Martino-IST, Genova



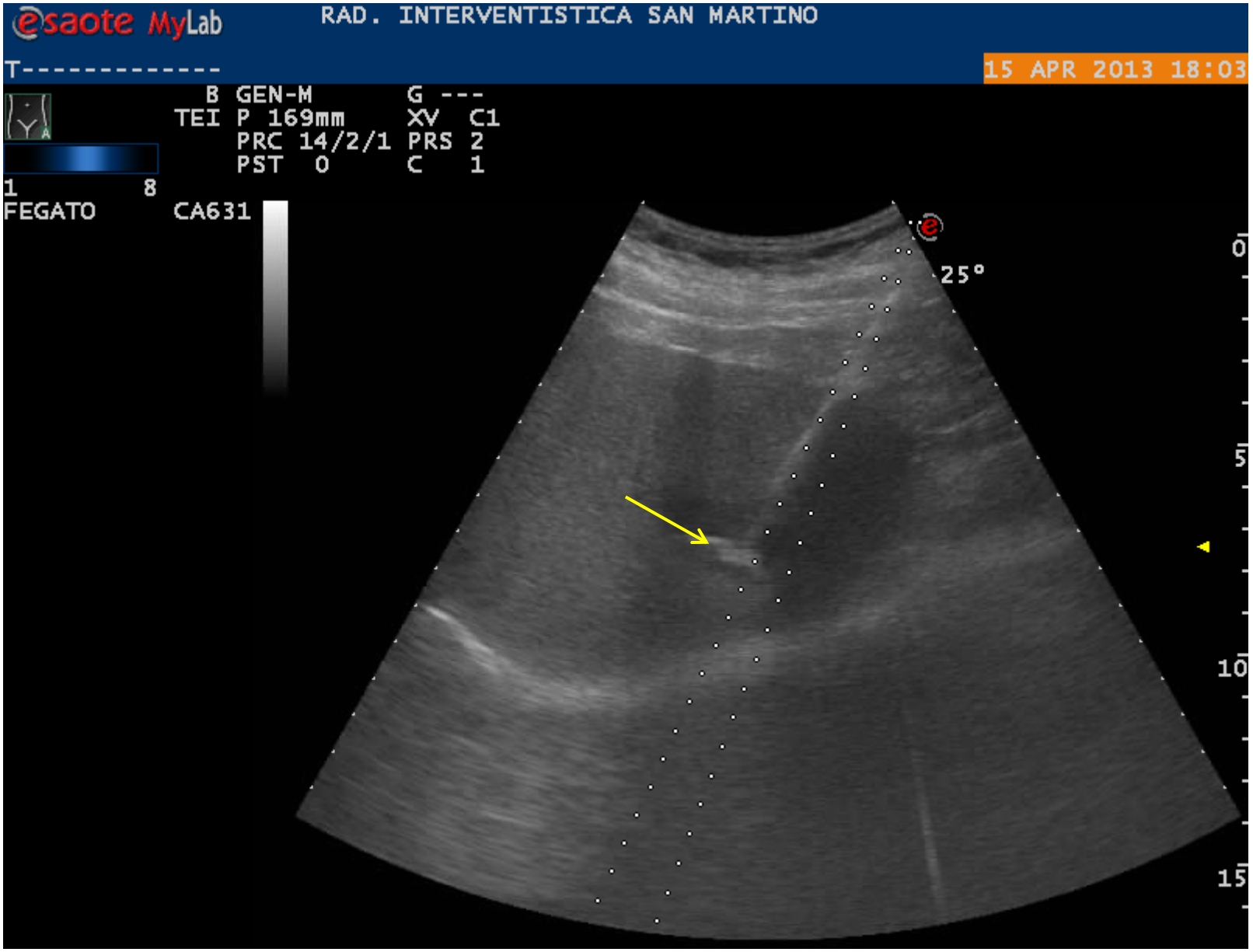
Paolo Borro – Centro Alcologico Regionale Ligure, IRCCS Ospedale San Martino-IST, Genova



Paolo Borro – Centro Alcologico Regionale Ligure, IRCCS San Martino-IST, Genova

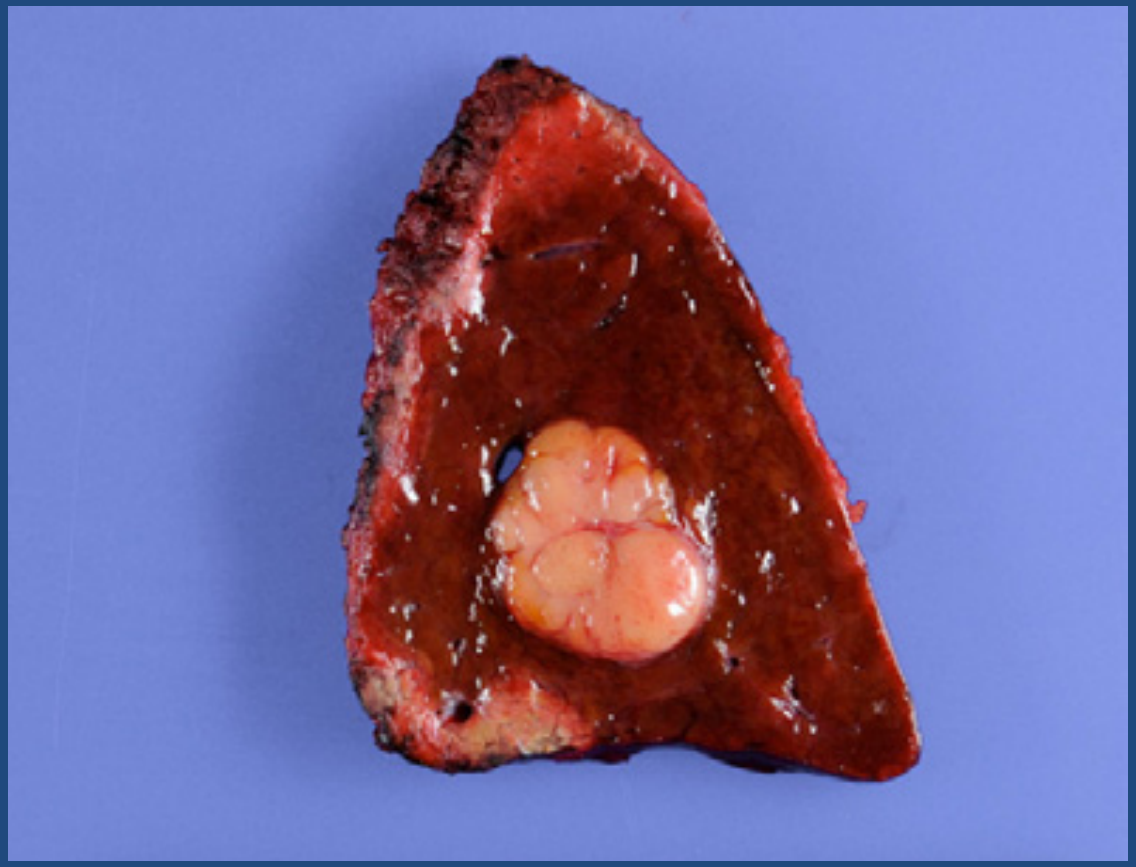


Paolo Borro – Centro Alcologico Regionale Ligure, IRCCS San Martino-IST, Genova



Paolo Borro – Centro Alcologico Regionale Ligure, IRCCS San Martino-IST, Genova

Hepatocellular Carcinoma (HCC)



Small HCC of 2 cm in size of an alcoholic patient (BCLC 0 stage) treated by surgical resection of S VI. Pathology examination: microscopic vascular invasion (High risk of recurrence → Indication of liver transplantation (*« ab initio»* indication)

An International Consensus for Medical Leadership on Alcohol

. . . . . Medical professionalism includes the responsability to speak out, to lead, and to voice advocacy. It is every clinician's responsability to address alcohol harm, both on a daily basis with individual patients and in the wider context of health harms and inequalities at the population level.

The voice of doctors is valued and trusted within societies, and therefore we call on all doctors to show effective leadership by holding ministries of health accountable for their lack of action in the face of such robust evidence.

We ask governments to act urgently and to champion evidence-based initiatives for the implementation of effective alcohol strategies at all levels to improve the health of populations worldwide.

Coltard C et al, Lancet 2011; vol 378: 1215

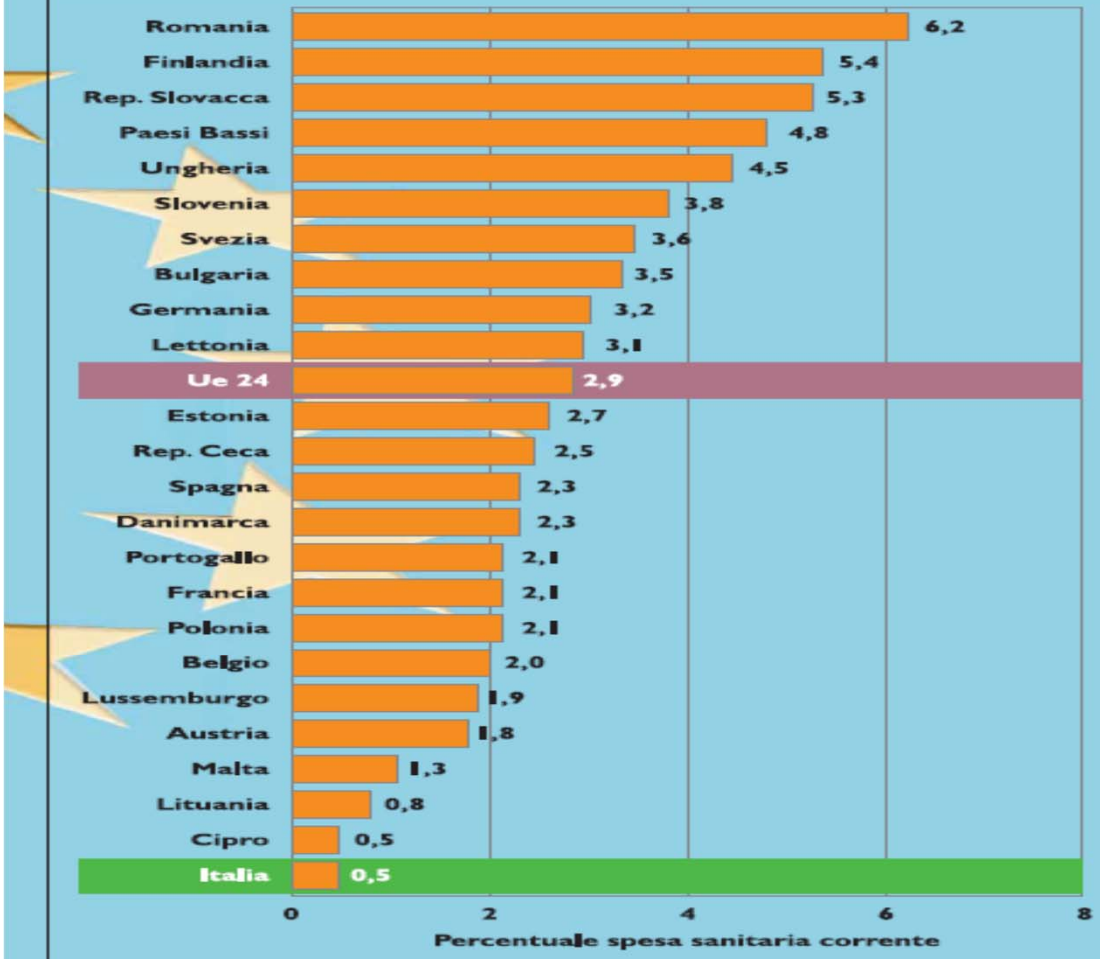
ALCOHOL CONSUMPTION AND CANCER

"THE ANALYSIS WAS UNABLE TO IDENTIFY A THRESHOLD LEVEL OF ALCOHOL CONSUMPTION BELOW WHICH NO INCREASE RISK FOR CANCER IS EVIDENT "

Bagnardi et al, Alcohol Research and Health 2001

Institute National du cancer, Paris 2007
World Cancer Research Fund, American Institute for Cancer Research, 2010
Union for the International Cancer Control, 2010
Association of European Cancer Leagues, 2011
Cancer Council Australia, 2011
Public Health, 2011
OMS (IARC), 2012

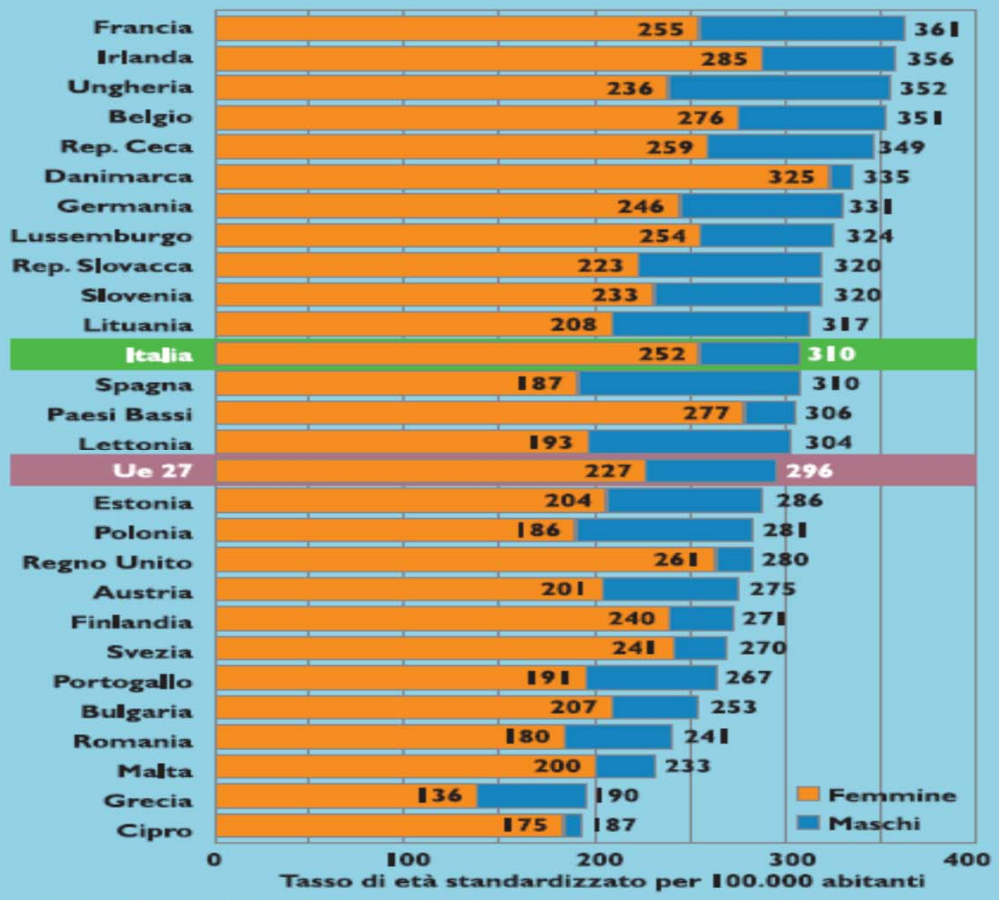
La spesa sanitaria destinata alla prevenzione (% sul totale)



Fonte: Ocse; Eurostat; Oms

La figura mostra la quota della spesa sanitaria assegnata alla prevenzione.
In media, gli Stati membri dell'Ue hanno stanziato meno del 3% della loro spesa per la salute alle attività di prevenzione come ad esempio i programmi di vaccinazione e le campagne su abuso di alcool e fumo.
L'Italia con lo 0,5% della spesa sanitaria totale destinata a politiche per la salute collettiva e a campagne di prevenzione, si trova all'ultimo posto tra i partner comunitari. Precedono l'Italia, nella parte bassa della classifica, Malta, Lituania e Cipro.
Chi investe di più in prevenzione e campagne per la promozione di stili di vita corretti sono invece Romania (6,2%), Finlandia (5,4%), Repubblica slovacca (5,3%), Paesi Bassi (4,8%).

Tasso di incidenza dei tumori (2008)



Fonte: Ferlay e altri (2010)

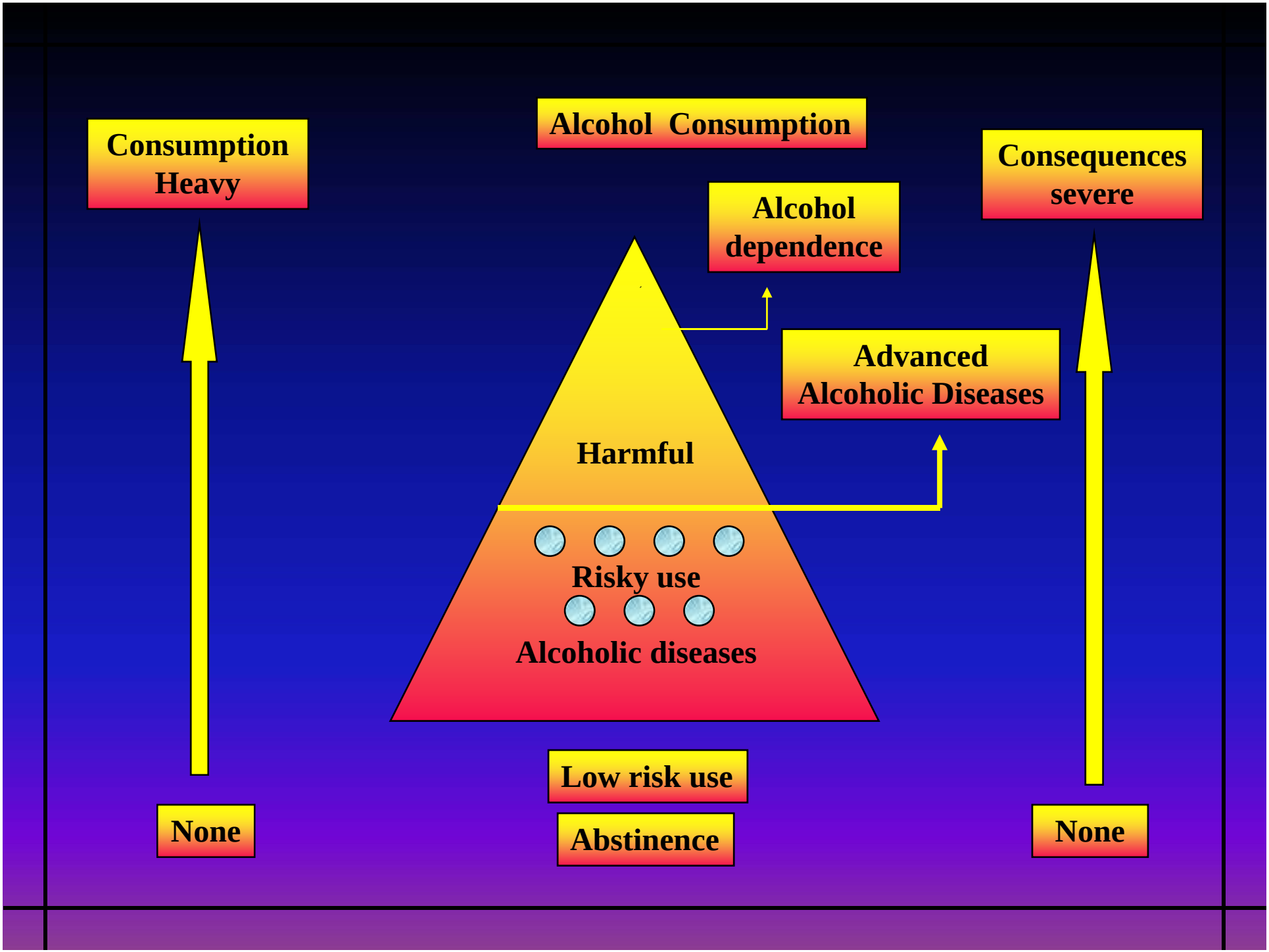
Nel 2008 in Europa 296 persone su 100mila hanno ricevuto una diagnosi di tumore.
La soglia più bassa di incidenza delle malattie tumorali si registra a Cipro (187, Grecia (190), Malta (233) e Romania (241); quella più alta in Francia (361), Irlanda (356), Ungheria (352) e Belgio (349).
L'Italia supera di qualche unità la media europea con 310 ammalati su 100mila abitanti, lo stesso tasso registrato in Spagna.

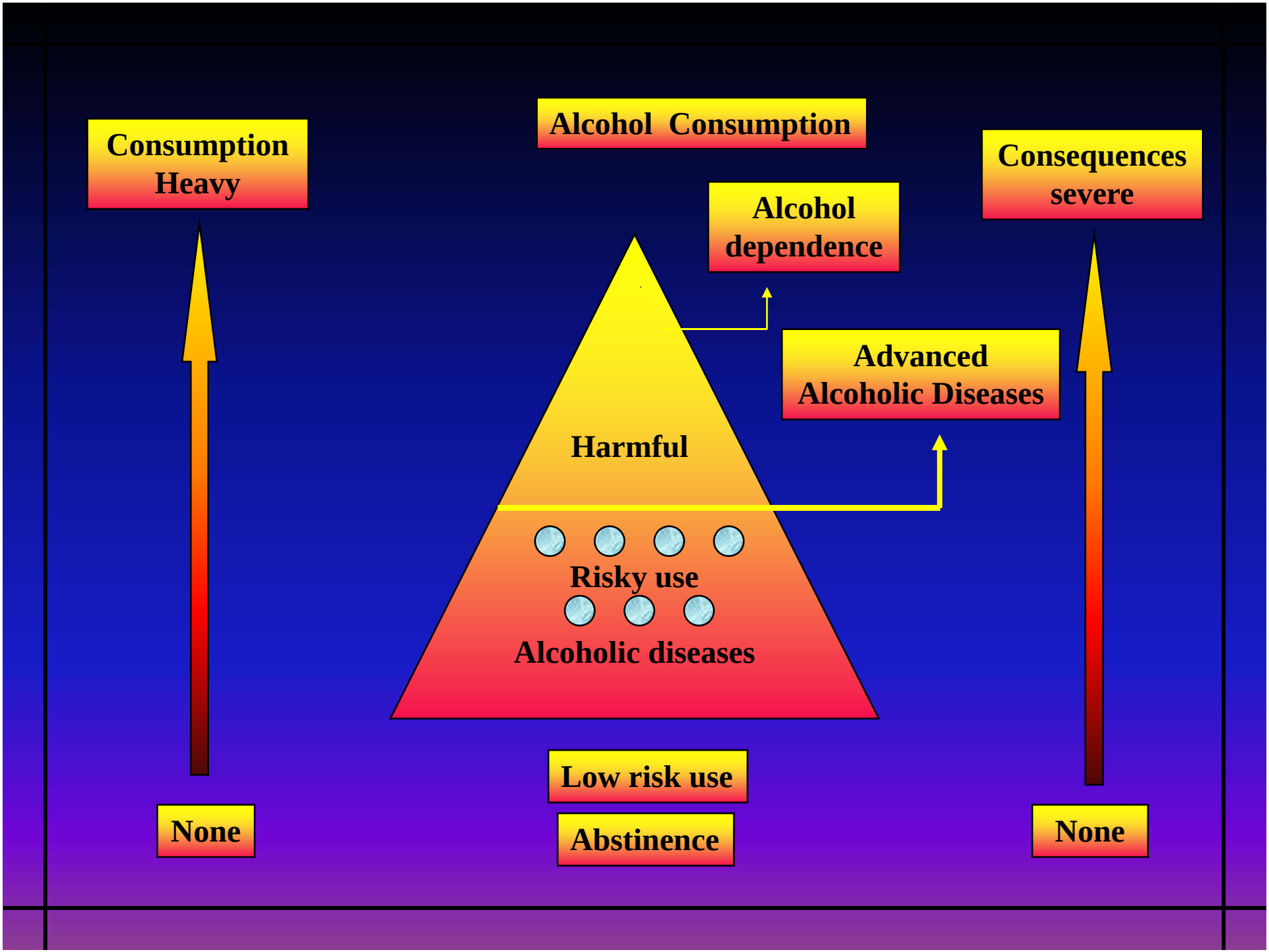
SOGGETTI CON CONSUMO RISCHIOSO/DANNOSO E ALCOLDIPENDENTI

PRIMA VALUTAZIONE – PREVENZIONE SECONDARIA

Migliorare anamnesi alcologica/ Esame Obiettivo

Testa-Collo	Visita Neurologica/ETG Collo
Cavita' Orale, Faringe, Laringe	ORL (Laringoscopia)
Esofago-Stomaco	Infezione da Hp/ Endoscopia con biopsie
Colon-Retto	Sangue occulto feci/colonscopia (clisma TAC colon/ colonscopia virtuale)
Fegato e regione bilio-pancreatica	Valutazione HBV/ HCB/ HIV - ETG ogni 6 mesi
Polmone	Rx Torace
Prostata	PSA tot. e libero con rapporto (tot/libero) al di sotto dei 70 anni
Mammella	ETG se sotto i 40 anni Mammografia e/o ETG se oltre i 40 anni


Alcohol Consumption
Consumption Heavy
Consequences severe
Alcohol dependence
Advanced Alcoholic Diseases
Harmful
Risky use
Alcoholic diseases
Low risk use
Abstinence
None
None


Consumption
Heavy
Alcohol Consumption
Consequences
severe
Alcohol
dependence
Advanced
Alcoholic Diseases
Harmful
Risky use
Alcoholic diseases
Low risk use
Abstinence
None
None


Grazie