

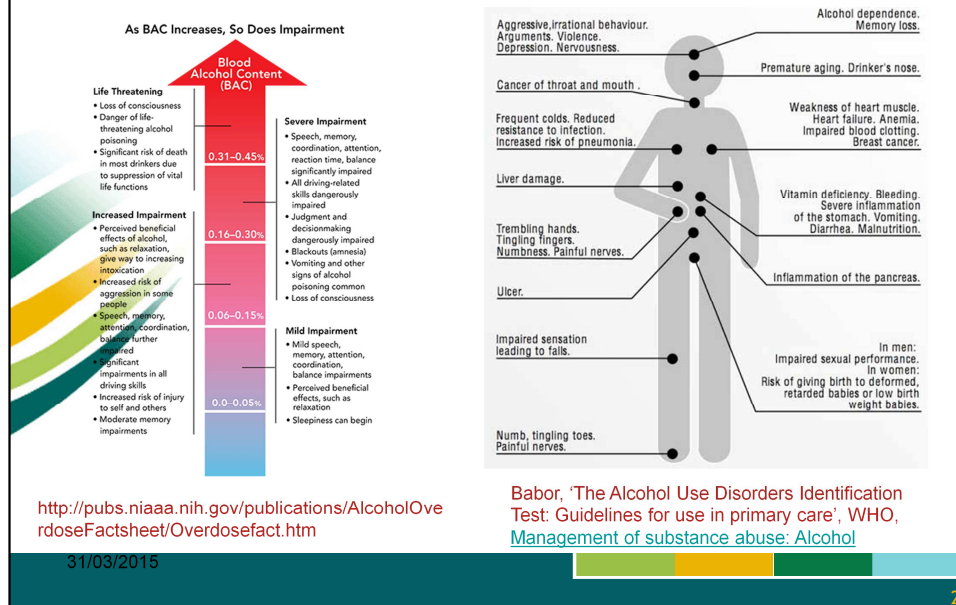


Per molti ma non per tutti: le differenze di età e
di genere sull'assorbimento e sul metabolismo dell'alcol

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SISA
29 Gennaio 2015

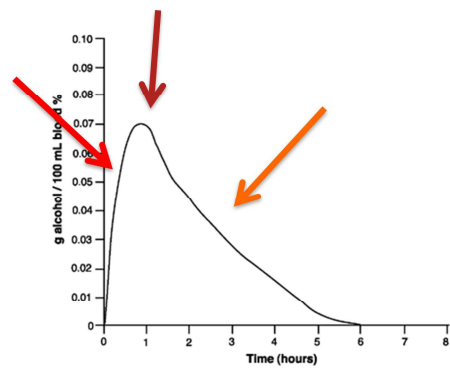
Effetti dell'alcol sull'organismo



Alcolemia

(Blood Alcohol Concentration: BAC)

- Assorbimento
- Metabolismo
- Distribuzione
- Eliminazione

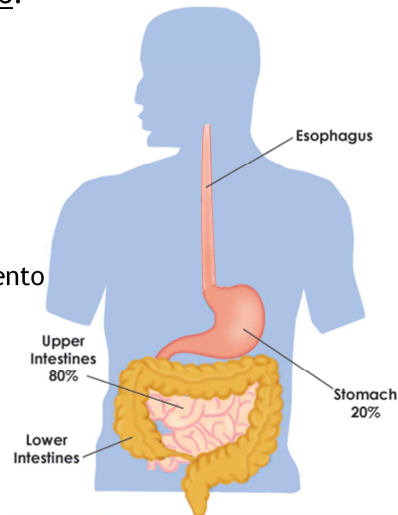


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Assorbimento

Fattori che influenzano l'assorbimento:

- Concentrazione dell'etanolo
 - quantità consumata
 - grado alcolico della bevanda
- Tipo di bevanda
- Proprietà irritanti dell'etanolo
- Velocità di ingestione
- Presenza di cibo
- Flusso sanguigno al sito di assorbimento



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Distribuzione

Fattori che influenzano la distribuzione:

- Acqua corporea
- Fattori che governano la circolazione
 - Vasocostrizione
 - Ormoni
 - Attività muscolare
 - Temperatura

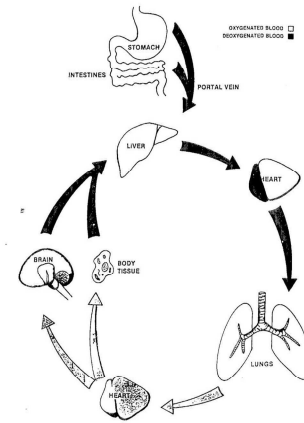
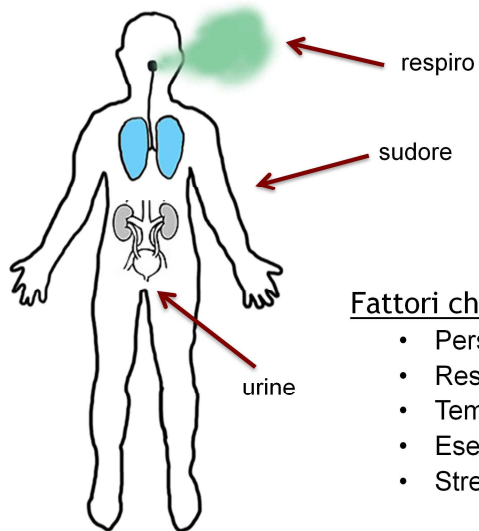


FIGURE 2: A Representation of the Alkaloid Distribution Pathways



Eliminazione



Fattori che influenzano l'eliminazione:

- Perspirazione
- Respirazione (frequenza)
- Temperatura e Umidità (ambiente e corpo)
- Esercizio fisico
- Stress

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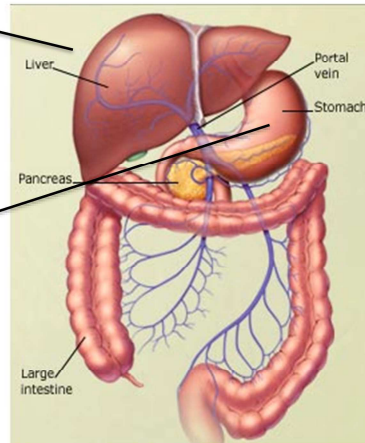
Metabolismo

Fattori che influenzano il metabolismo:

- Abitudine al consumo
- Genetica
- Sesso
- Uso di farmaci

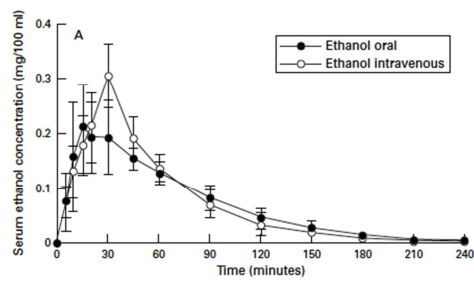
85%

15%



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First Pass Metabolism



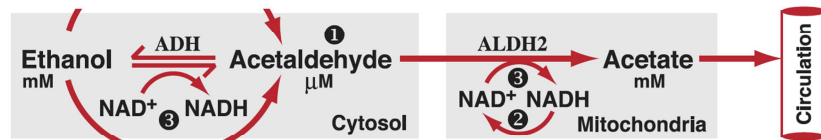
Oneta, 1998

Fattori che influenzano il FPM:

- sesso
- età
- genetica
- farmaci
- quantità/concentrazione ingerita
- tempo di svuotamento gastrico
- morfologia dello stomaco
- presenza di *Helicobacter pylori*

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Metabolismo ossidativo

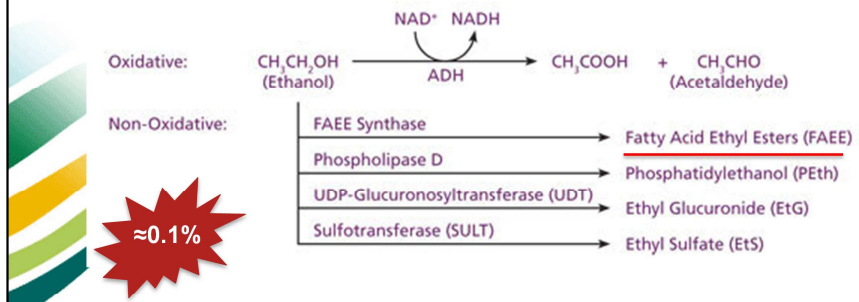


K_m ADH classe I <1mM

K_m ALDH 1-200μM

K_m CYP2E1 10mM

Metabolismo non ossidativo



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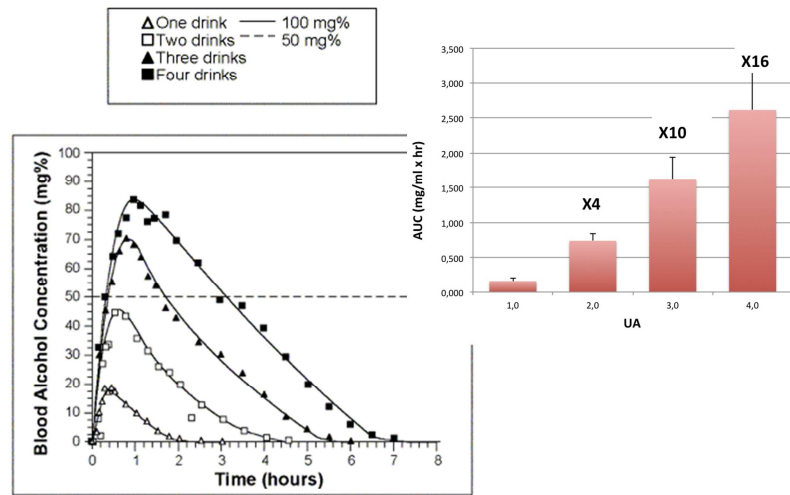
10

Fattori che influenzano l'alcolemia

- Caratteristiche della modalità di consumo
 - Quantità
 - Tipo di bevanda alcolica
 - Modalità di consumo (velocità/frequenza/binge)
 - Presenza di cibo
- Caratteristiche individuali
 - Sesso
 - Età
 - Peso
 - Abitudine al consumo
 - Polimorfismi enzimi del metabolismo
 - Patologie o carenze nutrizionali
 - Consumo farmaci

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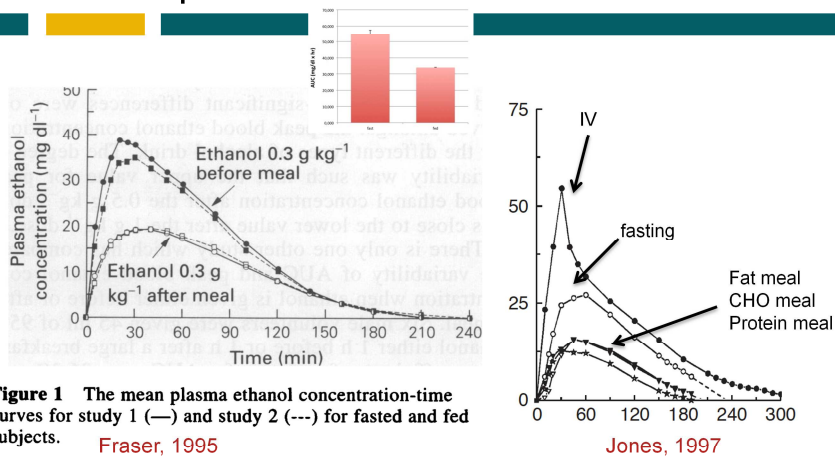
Quantità



Wilkinson, 1977

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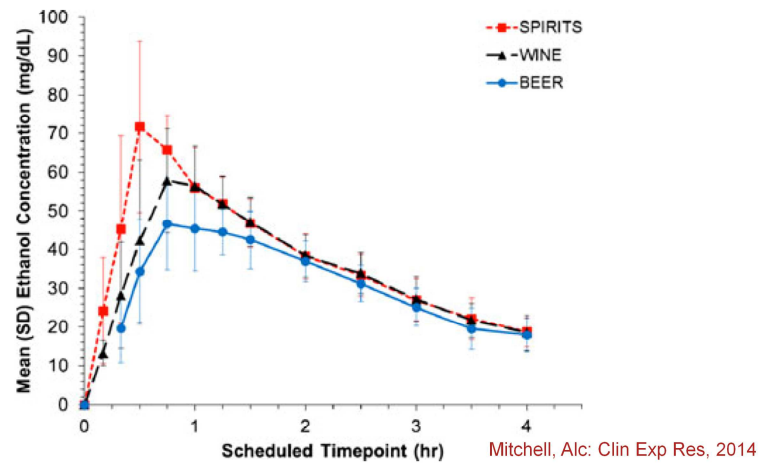
Presenza di un pasto



- rallenta l'assorbimento
- aumenta la velocità di eliminazione

Tipo di bevanda/concentrazione EtOH

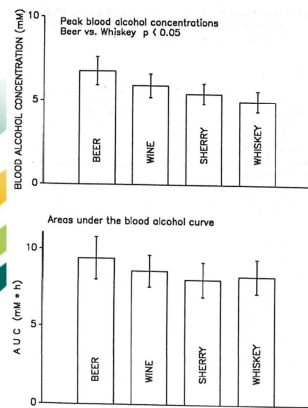
a digiuno



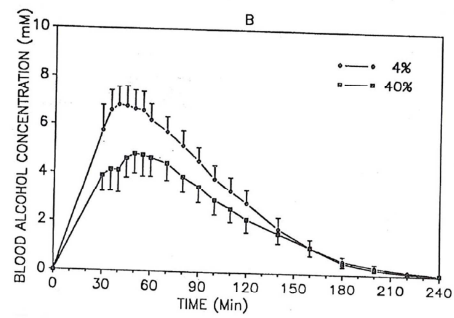
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Tipo di bevanda/concentrazione EtOH

Post-prandiale



Roine, Alc: Clin Exp Res, 1993



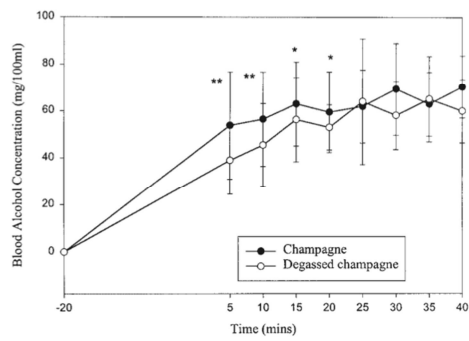
Roine, Alc: Clin Exp Res, 1991

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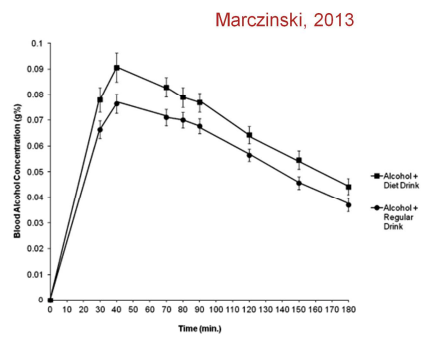
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	Tempo svuotamento gastrico	Ref
Volume	↑	Hunt, 1985
Contenuto calorico Zuccheri	↑	Velchik, 1989; Lin, 1989
Temperatura/Freddo	↑	Sun, 1988
Presenza CO ₂	↓	Roberts, 2007
Pasto	↑	Sedman, 1976; Fraser, 1995
Densità energetica Grassi	↑	Hunt, 1975; Hunt, 1985
Consistenza/Solido Viscosità	↑	Horowitz, 1989; Zhu. 2013
pH/Acido	↑	Lin, 1990
Fumo	↑	Johnson. 1991
Attività fisica PP	↓	Franke, 2008
Antiacidi	↓	Gupta, 1995; Arora, 2000
Aspirina	↑	Kechagias, 1997
Antibiotici	↓	Kondo, 1998

Giusto qualche esempio:



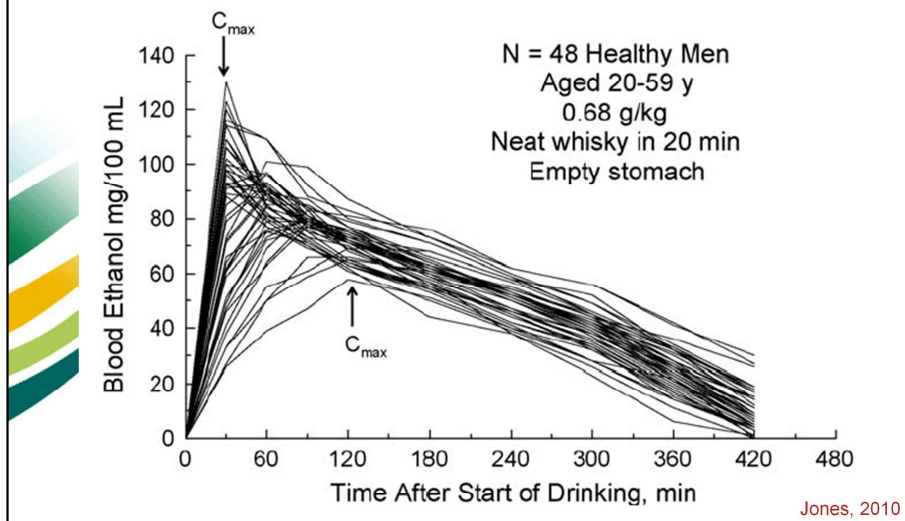
Ridout, 2003



Marczinski, 2013

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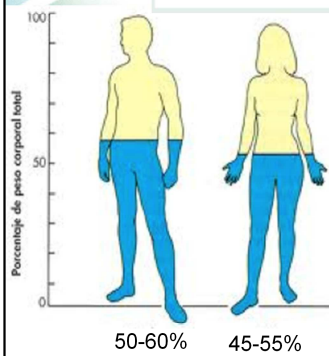
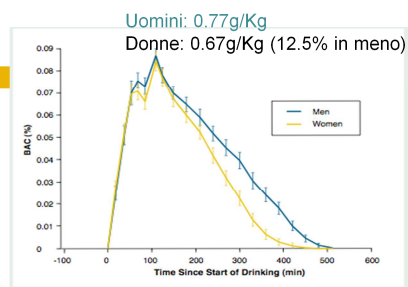
Variabilità inter-individuale



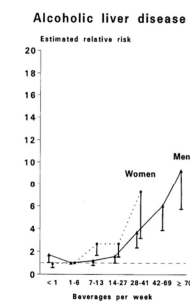
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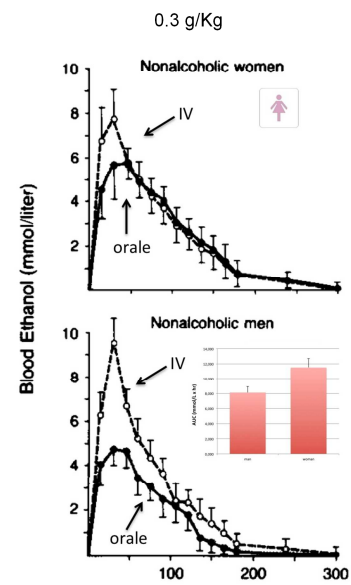
Sesso



Taylor, 1996



Becker, 1996



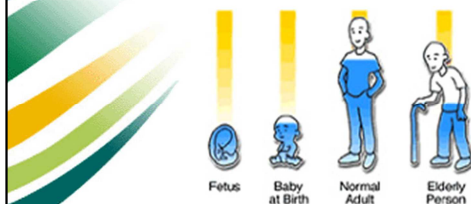
Frezza, NEJM, 1990

Età

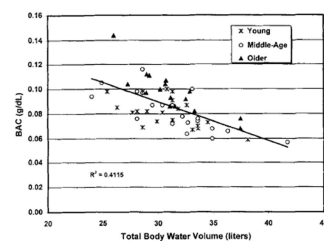
Age group	Age	Height (cm)	Weight (kg)	% H ₂ O	% Fat	TBW (liters)	LBM (kg)	IMP. IND.	Obs. BAC
Young									
Mean	21.75	163.6	60.9	51.3	29.90	30.80	42.09	41.3	.0811
(\pm SD)	(1.1)	(7.41)	(10.8)	(4.6)	(6.5)	(3.02)	(4.24)	(4.8)	(.012)
Middle-Age									
Mean	42.30	163.3	67.9	47.3	35.50	31.52	43.00	41.6	.0818
(\pm SD)	(3.4)	(6.66)	(14.0)	(4.9)	(6.8)	(4.04)	(5.46)	(6.6)	(.016)
Older									
Mean	68.94	162.6	70.7	45.0	37.51	31.20	43.34	42.8	.0975
(\pm SD)	(7.9)	(3.96)	(13.8)	(4.9)	(6.7)	(3.12)	(4.33)	(6.3)	(.018)



Davies, 1999



< acqua corporea
< attività dell'ADH gastrica



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Gravidanza e allattamento

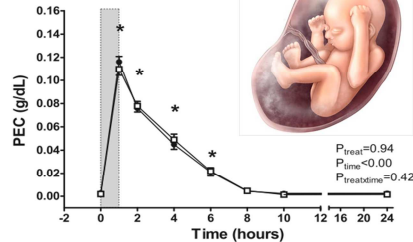
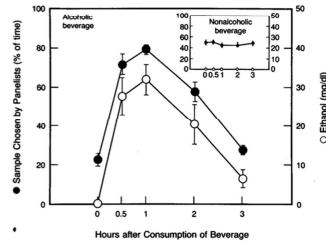


Fig. 1. Maternal (●, $n = 8$) and fetal (□, $n = 7$) plasma EtOH concentrations (PEC) measured following a 1-h maternal ethanol (EtOH) infusion (0.75 g EtOH/kg maternal body wt; shading). For each animal, PEC was measured on days 131–133 of gestation, and the values were averaged. Data are presented as means \pm SE. * $P < 0.05$, compared with time = 0 h for both maternal and fetal data.

Kenna, 2011

metabolismo materno è la via principale di eliminazione
feto solo 3-4%

< attività metabolica
< funzione renale



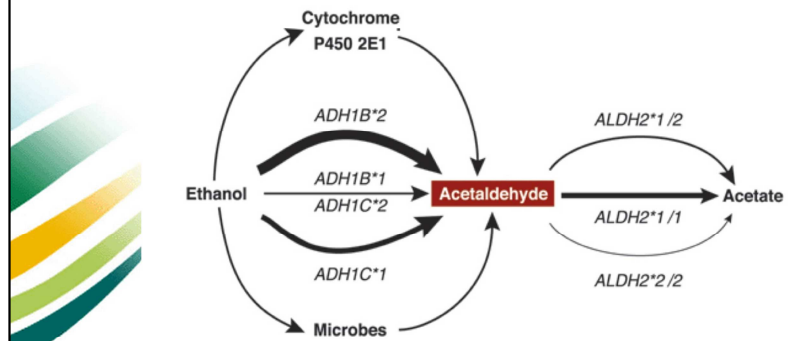
Mennella, 1991

Ethanol and acetaldehyde content of the milk and peripheral blood of lactating women at various intervals after peroral administration of 0.6 g of ethanol per kg maternal body weight

Sample		30 minutes	60 minutes	90 minutes	120 minutes
Milk	Ethanol (μmoles/ml. milk)	15.8 \pm 5.4	16.9 \pm 2.5	14.1 \pm 2.5	11.3 \pm 2.6
Milk	Acetaldehyde (nmoles/ml. milk)	0	0	0	0
Blood	Ethanol (μmoles/ml. blood)	19.1 \pm 6.5	18.2 \pm 2.5	15.0 \pm 2.1	12.4 \pm 2.4
Blood	Acetaldehyde (nmoles/ml. blood)	44.4 \pm 21.1	31.5 \pm 13.7	26.7 \pm 10.5	19.3 \pm 7.5

Kesaniemi, 1974

Genetica-Polimorfismi



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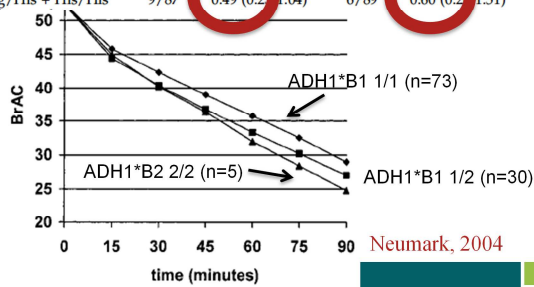
Polimorfismi ADH

Frequency of ADH Alleles in Racial Population Bosron, 1993; Crabb, 1995

	ADH1B*1	ADH1B*2 ↑	ADH1B*3	ADH1C*1	ADH1C*2
White-American	>95%	< 5%	< 5%	50%	50%
White-European	85%	15%	< 5%	60%	40%
Japanese	15%	85%	< 5%	95%	5%
Black-American	85%	< 5%	15%	85%	15%

	Oral		Pharynx		Larynx		Esophagus	
	Cases/controls	OR (95% CI)	Cases/controls	OR (95% CI)	Cases/controls	OR (95% CI)	Cases/controls	OR (95% CI)
ADH1B R48H								
Arg/Arg (slow)	144/635	1.00	100/650	1.00	288/650	1.00	163/792	1.00
Arg/His + His/His	9/87	0.49 (0.21-1.04)	6/89	0.60 (0.21-1.51)	26/89	0.57 (0.31-0.96)	4/95	0.19 (0.01-0.53)

Hashibe, 2006



Neumark, 2004

Polimorfismi ALDH

Polymorphism of ALDH2

Subunit	Gene	Codon 487
Active	ALDH2*1	GAA(Glu)
Inactive	ALDH2*2	AAA(Lys)

Tanaka, 1996

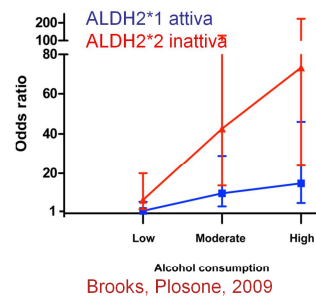


Wall, 1997

TABLE 3. Incidence of ALDH2 Genotypes

	No.	ALDH2*1/*1	ALDH2*1/*2	ALDH2*2/*2
Control	66	26 (39.4%)	35 (53.0%)	5 (7.6%)
Alcohol dependents	90	86 (95.6%)*	4 (4.4%)‡	0 (0%)
Alcoholic liver disease	31	25 (80.6%)†	6 (19.4%)§	0 (0%)

Rischio tumore esofago



Brooks, Plosone, 2009

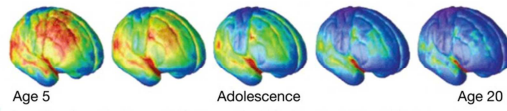
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Conclusioni

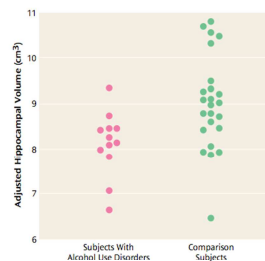
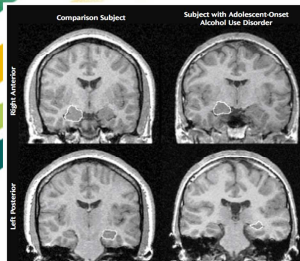
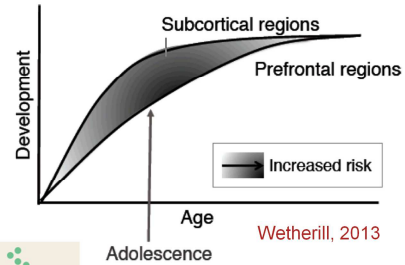


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Conclusioni: e i giovani?



Source: "Dynamic mapping of human cortical development during childhood through early adulthood," Nitin Gogtay et al., Proceedings of the National Academy of Sciences, May 25, 2004; California Institute of Technology.



De Bellis. 2000



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Grazie!

A tutti voi per l'attenzione

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