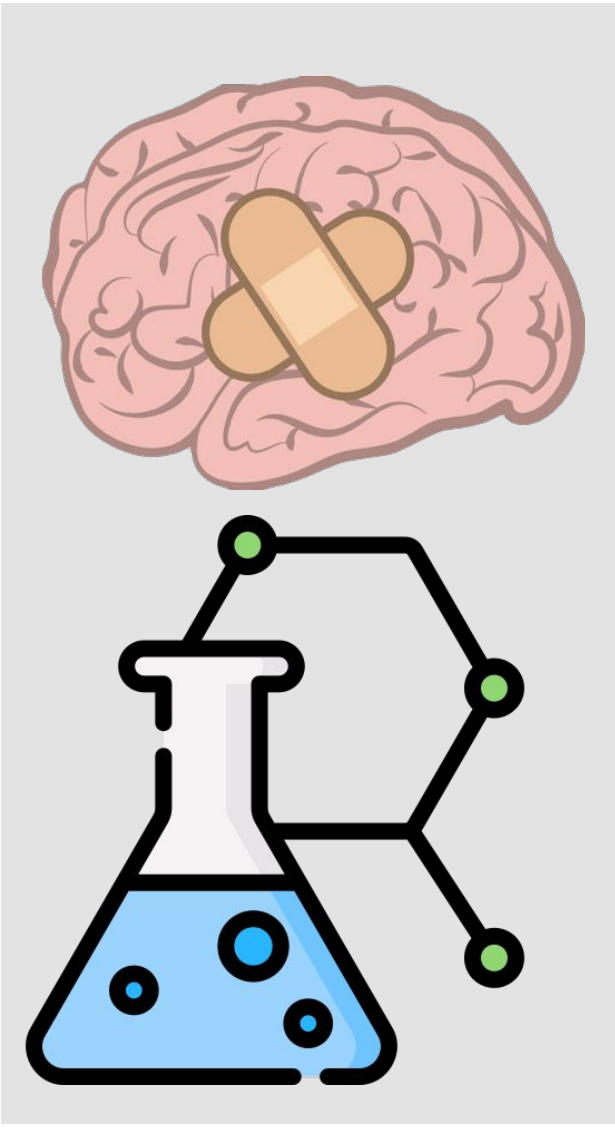
L’impatto dei biomarcatori nella gestione del paziente traumatico

Mirco Ravazzini

AOU Modena – Trauma Center di Baggiovara (MO)



Il caso…

curiosità, novità e aggiornamenti in medicina d'urgenza empills

Trauma cranico lieve: che fare…

di **Davide Tizzani** 30 Maggio 2024

355 0

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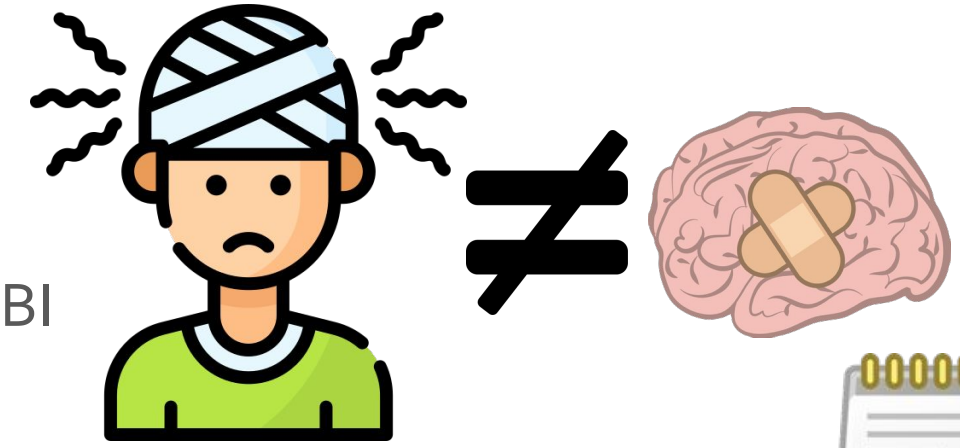
DEFINIZIONI (1)

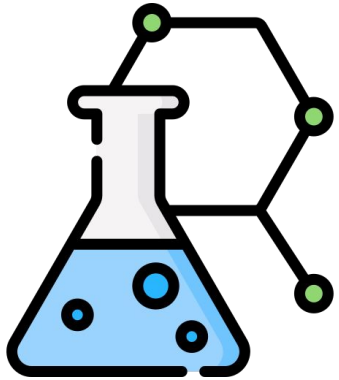
- Trauma cranico ≠ TBI



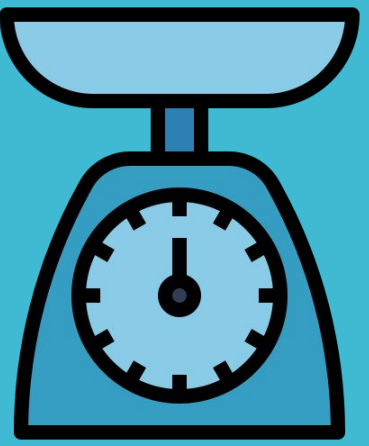
- La definizione "sintomatologica" (1993–> 2023)

- La presenza di fattori **confondenti**

- L'integrazione con i dati neuroradiologici… e I biomarkers



BURDEN



- 28 - 69 M / anno

- Di cui 80-90% **lieve** (sicuramente sottostimato…)
- Fascia d'età **trimodale**

DEFINIZIONI (2)

- ACRM – WHO – DoD – DVA ecc.
- Lavoro di armonizzazione da parte della ACRM (2019->2023)
- mTBI

1993

Definition of mild traumatic brain injury

Developed by the Mild Traumatic Brain Injury Committee of the Head Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine

DEFINIZIONI (3)

2023

MECCANISMO DI DANNO CAUSATO DA UNA FORZA ESTERNA

(con presentazione a 30' con GCS 13-15)

AND

Almeno 1 **segno:**
- PdC
- Amnesia
- Alterazione mentale
- Segni neurologici acuti
- Crisi epilettica

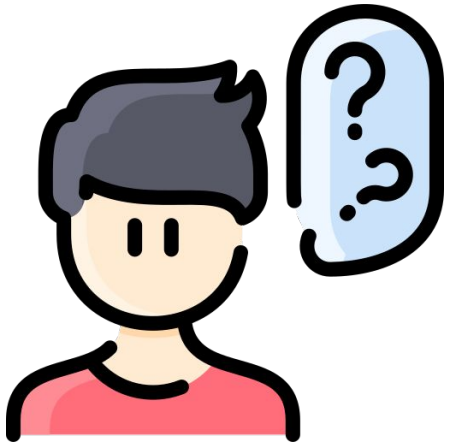
OR

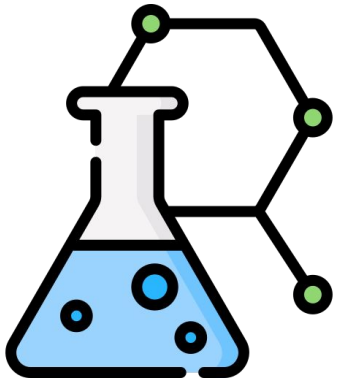
Almeno 2 **sintomi:**
- Comportamentali
- Emozionali
- Psicologici

e alterazione dei biomarkers

OR

Alterazioni post-Traumatiche a TAC o RM





DEFINIZIONI (4)

- E… la concussione?

- Il "sospetto" e il ruolo dei fattori confondenti…

Classificazioni CLINICHE

- GCS . . . (e il numero 13?)

- FOUR score

Validity of the FOUR Score Coma Scale in the Medical Intensive Care Unit

VIVEK N. IYER, MD; JAYAWANT N. MANDREKAR, PHD; RICHARD D. DANIELSON, RN; ALEXANDER Y. ZUBKOV, MD, PHD; JENNIFER L. ELMER, RN; AND EELCO F. M. WIJDICKS, MD, PHD

Classificazioni RADIOLOGICHE

- Marshall
- Rotterdam

NEUROIMAGING

VS

TAC sì o no? Clinical Decision Rules

CCHR

GCS <15 a 2 h dal trauma
- Frattura aperta/depressa del cranio
- Frattura della base cranica
- Perdite di liquido cefalo-rachidiano)
- 2 o più episodi di vomito
- Età >65 anni

Amnesia retrograda oltre 30 min prima del trauma
- Dinamica traumatica maggiore (pedone investito da veicolo a motore – eiezione da veicolo a motore – caduta da >3 m o >5 gradini)

NOC

Cefalea diffusa
- 2 o più episodi di vomito
- Età >60 anni
- Evidenza di intossicazione da alcol o droghe
- Amnesia anterograda persistente
- Convulsioni
- Segni evidenti di trauma al di sopra delle clavicole

NEXUS - II

- Evidenza di frattura cranica
- Deficit neurologici
- GCS uguale o minore di 14
- Coagulopatia
- Vomito persistente

TAC sì o no? Clinical Decision Rules

- Canadian (CCHR)

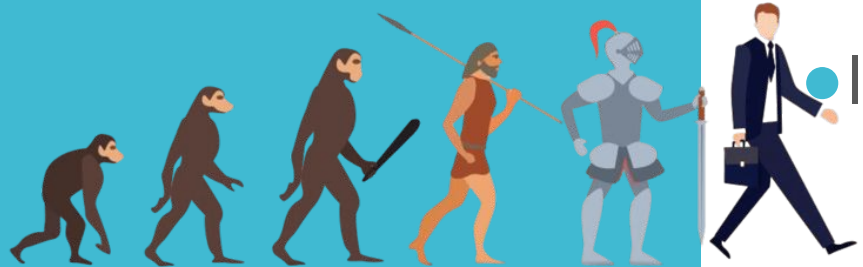
- NEXUS – II

- New Orleans (NOC)

TAC sì o no? Clinical Decision Rules

2007 (ASSR –SINCH)

Negli ultimi 20 anni. . .

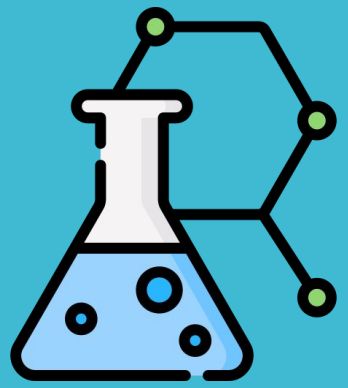


- I limiti di età sono ancora validi?
- E i farmaci?
- Il fattore tempo?

E allora...

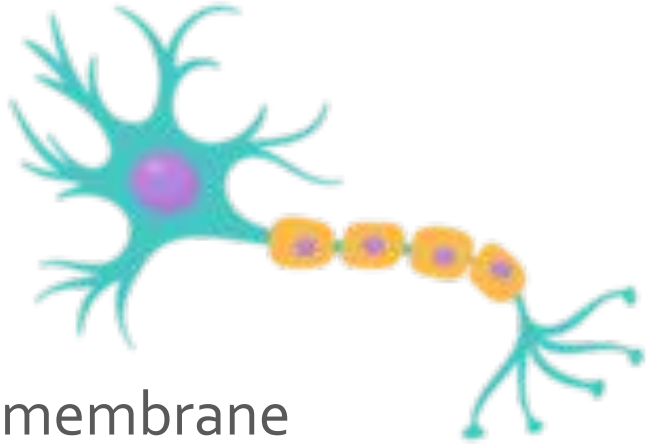
FISIOPATOLOGIA

Ritorno alla FISIOPATOLOGIA



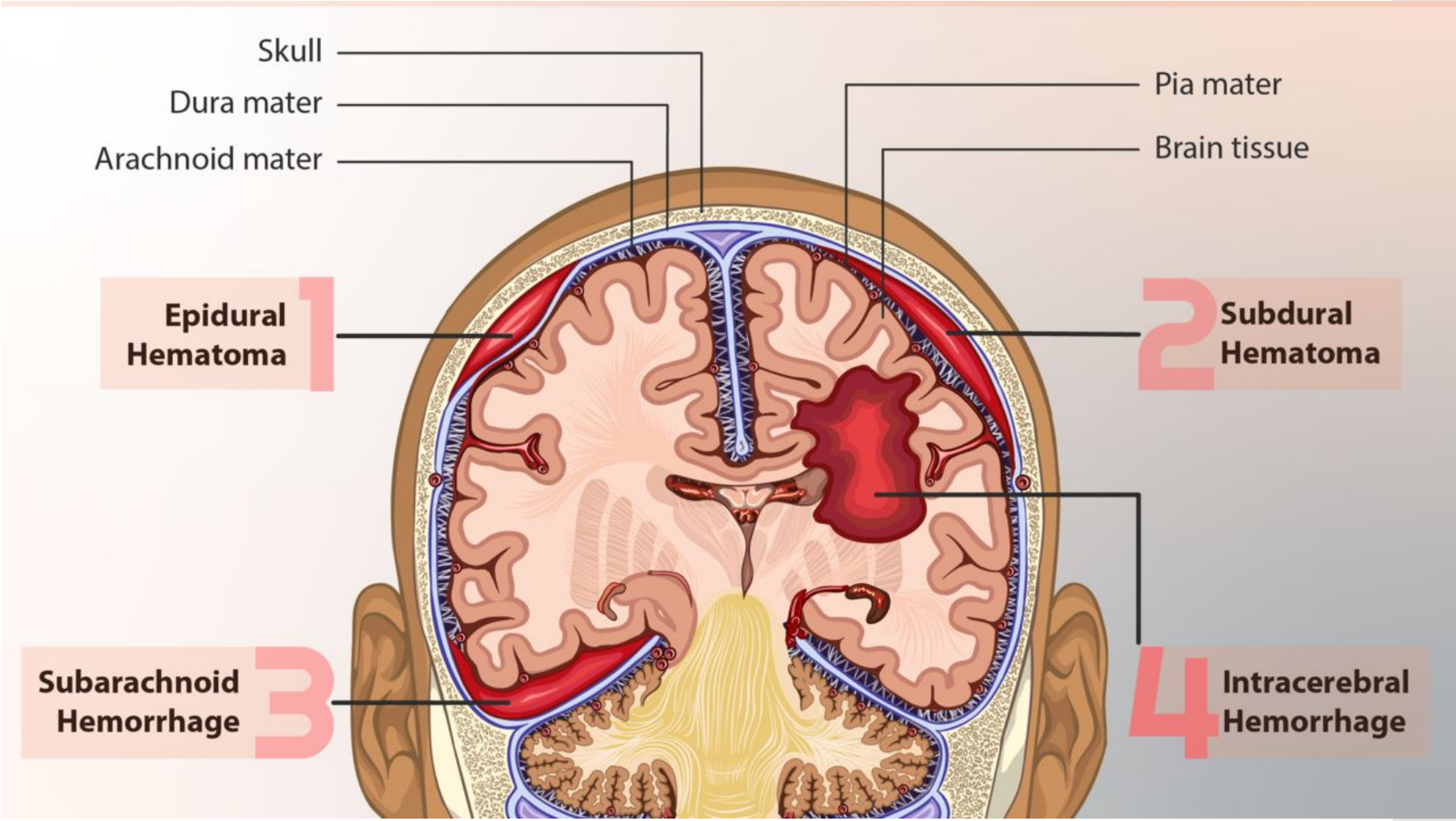
- Cercare il **danno neuronale** e non la **lesione TAC**
- Migliorare l'accuratezza della **stratificazione del rischio**
- Implementare l'iter diagnostico in DEA
- Fornire informazioni **prognostiche**

Danno SECONDARIO…

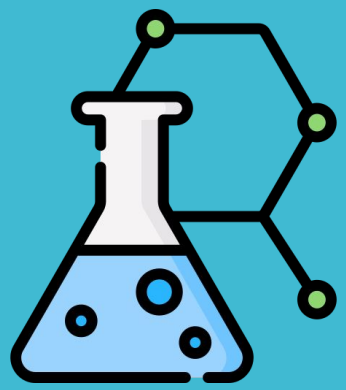


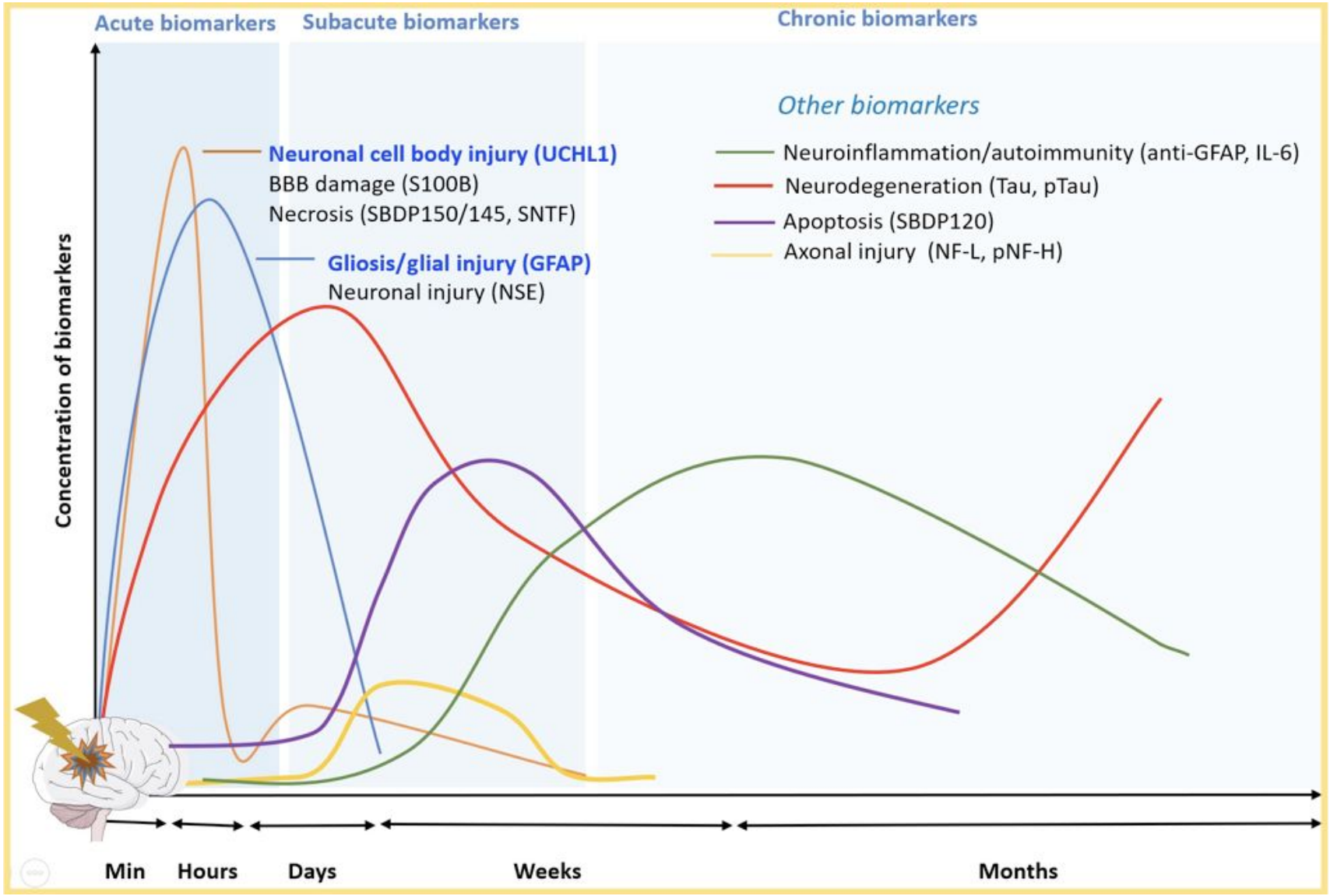
- Interruzione dei microtubuli
- Alterazioni elettrochimiche delle membrane
- Accumulo di neurofilamenti del citoscheletro assonale
- Accumulo di Beta-amiloide / aggregazione Tau
- Rilascio di neurotrasmettitori, radicali liberi, citochine

…e danno PRIMARIO!



BIOMARCATORI (1)





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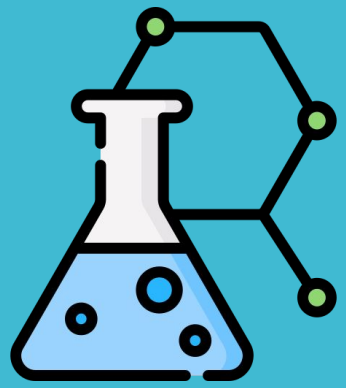
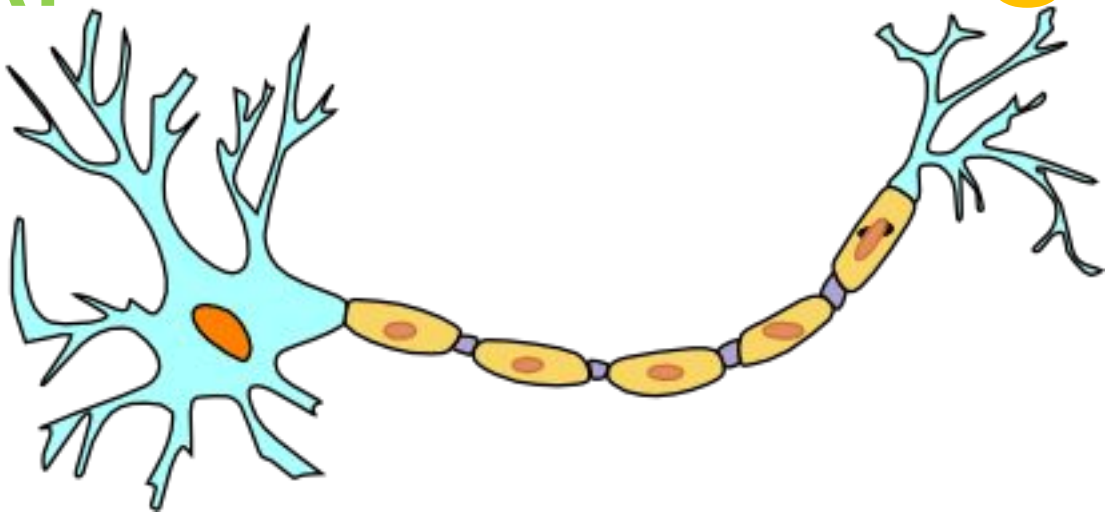


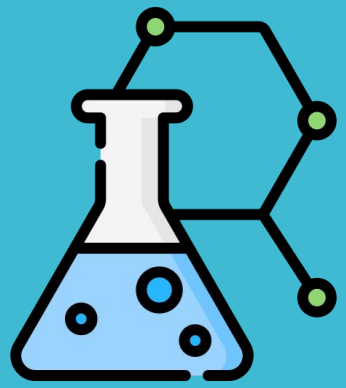
GFAP

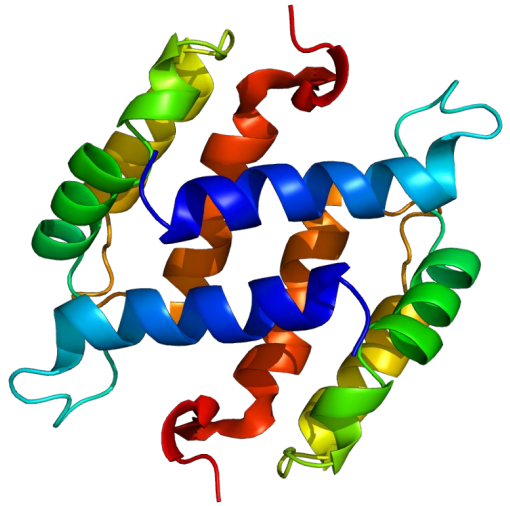
UCH-L1



S100B

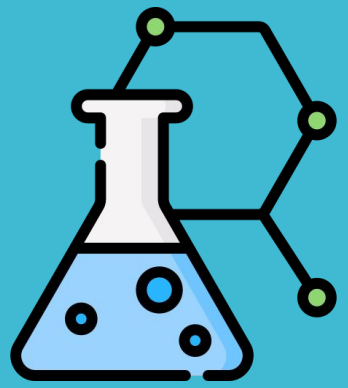
BIOMARCATORI (S100b)

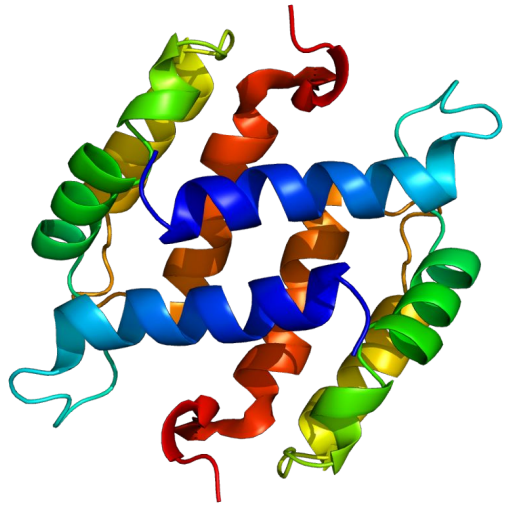




- Astrociti
- Adipociti, **melanociti,** condrociti
- ***Primo studio multicentrico*** *Bierthaler et al. (2001)*
- Linee guida scandinave (cut off 0.10mcg/L)
- **Recente metanalisi** (2021)

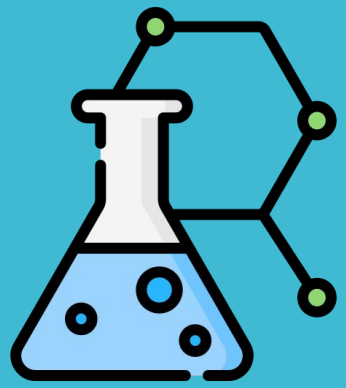
BIOMARCATORI (S100b)





- **ACEP 2008**: livello di evidenza II
- **Metanalisi 2021**: potenziale ruolo come strumento di screening per S100B
- **FDA:** non ancora approvato

BIOMARCATOR I (S100b)



All adult patients with minimal, mild and moderate head injury (GCS 9-15) within 24 hours of injury

See help sheet for explanations and more details

Moderate

GCS 9-13

No

Mild
high-risk

GCS 14-15 *and*

- Posttraumatic seizures
- Focal neurological deficits
- Clinical signs of depressed or basal skull fracture
- Shunt-treated hydrocephalus
- Therapeutic anticoagulation or coagulation disorders

No

Mild
medium-risk

GCS 14-15 *and*

- BOTH age ≥65 years *AND* anti-platelet medication

N

Mild
low-risk

GCS 14

or

GCS 15 *and*

- Suspected/confirmed loss of consciousness
- Repeated vomiting (≥2 episodes)

No

Minimal

GCS 15

Yes

CT

CT normal or abnormal

Yes

CT

- Consider admission for observation ≥12 hours after injury as an alternative option

CT abnormal

CT normal

Yes

S100B

- If <6 hrs after injury, sample serum for S100B analysis
- If ≥6 hrs, extracranial injury or if S100B is unavailable, do CT

< 0.10 µg/L

≥ 0.10 µg/L

CT

- Consider admission for observation ≥12 hours after injury as an alternative option

CT abnormal

CT normal

Yes

CT normal

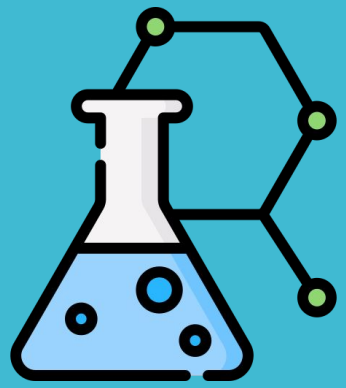
Admission for observation ≥24 hours

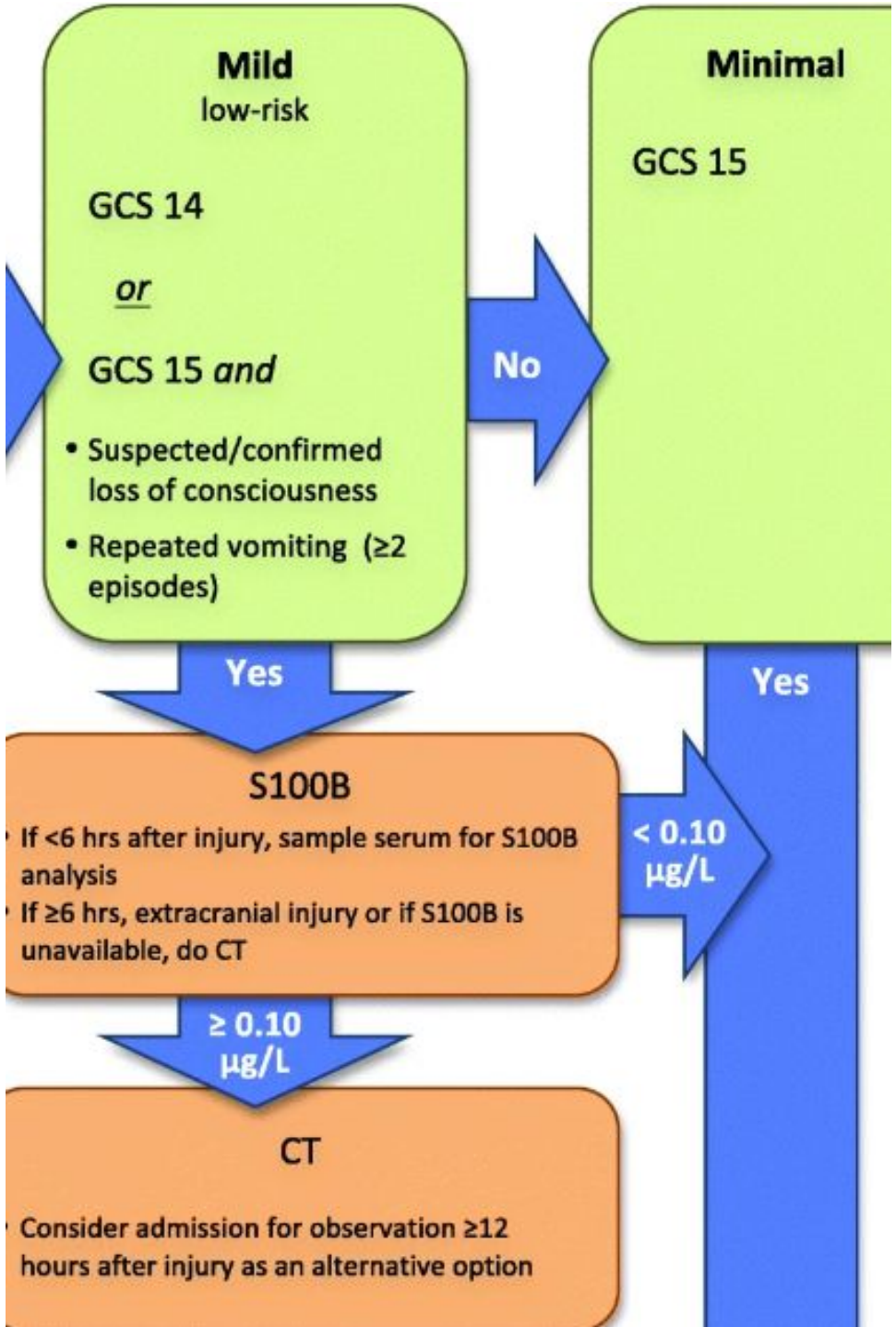
- Consider consultation with neurosurgeon
- Repeat CT if neurological and/or GCS (≥2 points) deterioration

Discharge with oral and written instructions

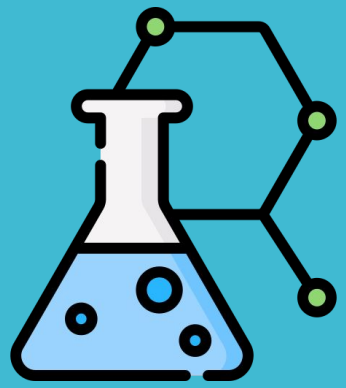
- Some patients may need admission for reasons other than their head injury

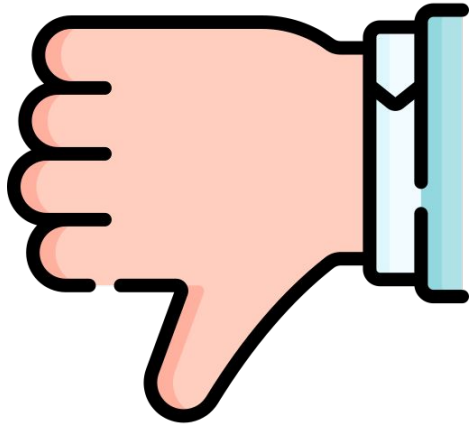
BIOMARCATORI (S100b)





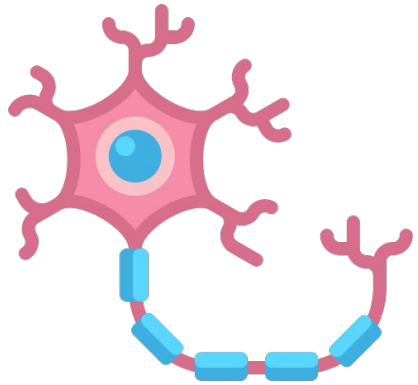
BIOMARCATORI (S100b)





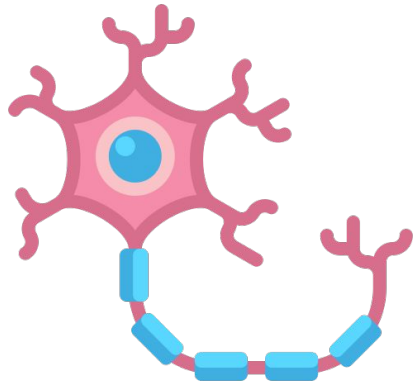
- Permangono comunque **falsi negativi** di potenziale interesse NCH
- **Politraumi** sono fattori confondenti

BIOMARCATORI (UCH-L1)



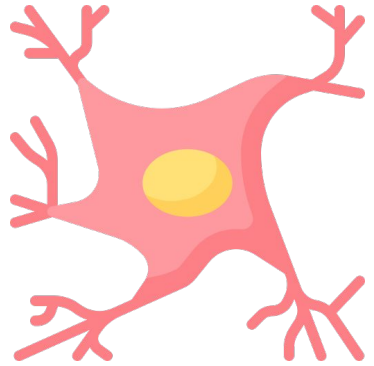
- Scanveger neuronale
- La più **"veloce"** tra i biomarkers di TBI
- Maggiore correlazione con il danno nel DAI e nel sTBI
- Rischia di arrivare **tardi**…

BIOMARCATORI (UCH-L1)



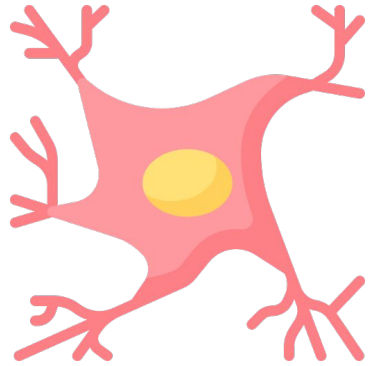
- **Papa et al.** (2012) buona accuratezza se entro le 4h (Sens 100% spec 21% VPN 100%)
- **Altri studi successivi** mostrano scarsa accuratezza rispetto a GFAP, soprattutto se fatta entro 24h o anche più tardivamente

BIOMARCATORI (GFAP)



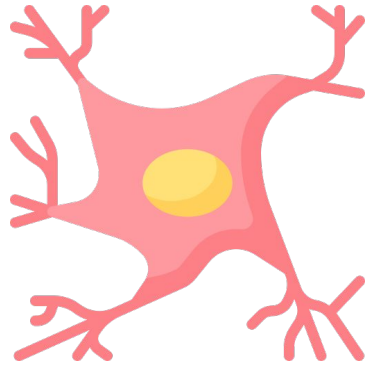
- **Astrociti**
- Osteociti, cellule di Leydig, condrociti
- **Studi diversi,** cut-off diversi
- Vs S100B: paz con lesioni extra-craniche
- Danno acuto **e** subacuto. . .

BIOMARCATORI (GFAP)



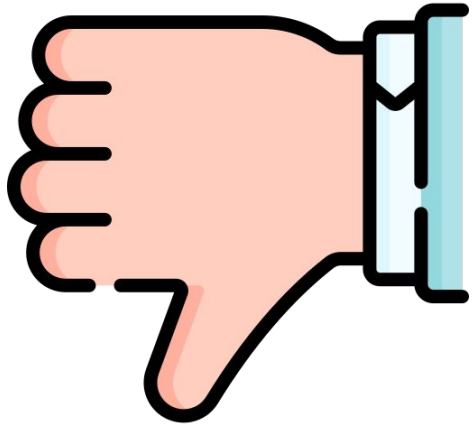
- **Metanalisi** 2023 (Archives of Academic Em Med): Sens 83% Spec 39%
- **Papa et al.** 2012: Sens 97% Spec 18% VPN 94%
- **Center TBI core study** (2020): GFAP **supera** i criteri clinici nel predire presenza e severità di lesioni TAC

BIOMARCATORI (GFAP)



- **GFAP** > di S100B (Papa et al. 2014, Czeiter et al. 2020)
- **Lesioni extracraniche**

BIOMARCATORI (GFAP)



- Disponibilità sul mercato
- **Cut-off** non ancora definiti?
- Rimane vasta variabilità interpretativa degli studi

Nuove applicazioni cliniche (1)

Bazarian et al. 2018

VPN 99.6%

Nuove applicazioni cliniche (2)

Bazarian et al. 2021

VPN 99.3%

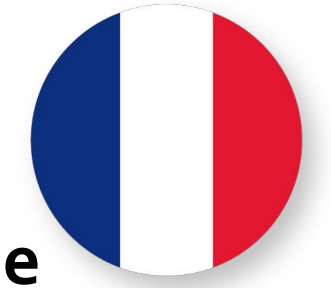
Nuove applicazioni cliniche (3)

FDA 2024

GFAP

UCH-L1

Nuove applicazioni cliniche (4)



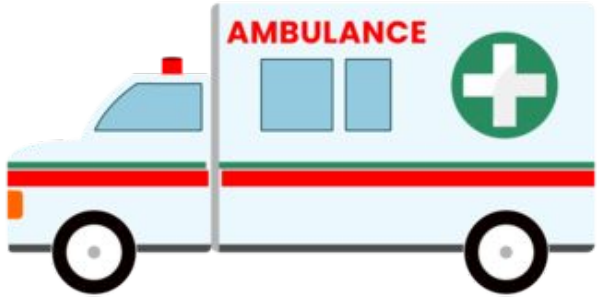
Oris et Al. (Aprile 2024): **comparazione** di Lab vs POCT

Walid et al. (Feb 2024): **validazione** del test rapido come strumento di triage

E… in Italia?

TRAUMA CENTER di Baggiovara (MO)

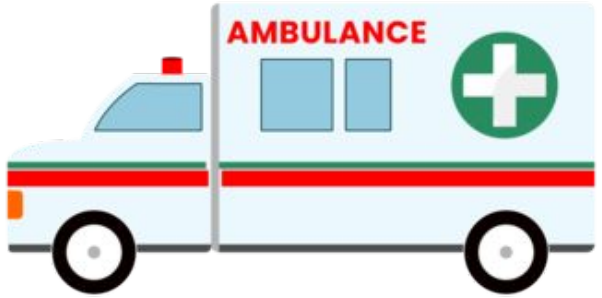
CONCLUSIONI (1)



- Il trauma cranico e la sua conseguenza neuropsicologica **TBI** sono per la maggior parte del loro percorso **a carico del DEA**

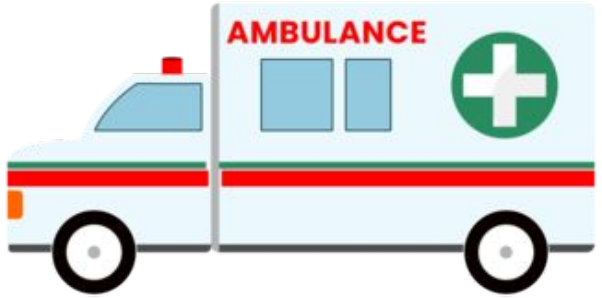
- E' necessario un continuo processo di **revisione e miglioramento di linee guida e protocolli interni** di gestione che siano condivisi e facilmente applicabili, dato che gli ormai vecchi score stanno mostrando i loro limiti

CONCLUSIONI (2)



- L'uso di **biomarkers ematici** per identificare la presenza di lesioni intracraniche può alleggerire il carico assistenziale del paziente in PS e favorire il processo decisionale in sicurezza
- **GFAP** da sola performa già bene per l'utilizzo che se ne farebbe in DEA
- La limitata disponibilità di strumentazione al momento non permette di studiarne l'impatto clinico su larga scala e su una popolazione diversa da quella degli studi (USA vs EU)

CONCLUSIONI (3)



- Si può cominciare a considerare il mTBI come un **continuum di gravità** di quadri con/senza lesioni TAC evidenti ma con dei valori decrescenti di biomarkers?

- Quale ruolo devono avere I nostri DEA non solo nell'identificare l'acuto, ma anche I follow-up? E quali markers possiamo usare in questi casi?

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