EUROPEAN UNION
European Structural and Investment Funds
Operational Programme Research,
Development and Education

MINISTRY OF EDUCATION, YOUTH AND SPORTS

MUNI


# HUMANS AND STRESS:

## Environment and disease

This work was supported from Operational Programme Research, Development and Education - Project „Postdoc2MUNI“ (No. CZ.02.2.69/0.0/0.0/18_053/0016952).

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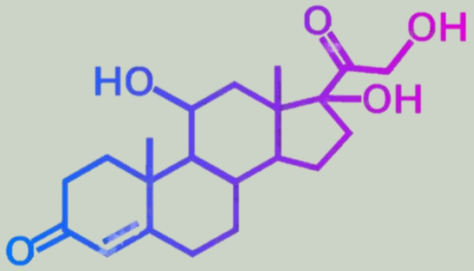
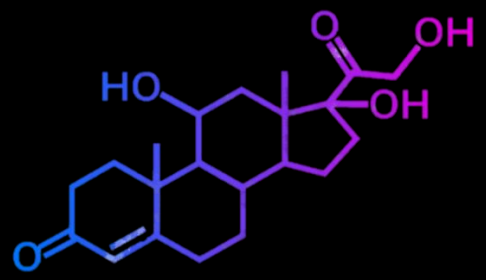



# Aims and Objectives

- **What is stress?**
- **Why is stress important to study?**

  What does stress experience tell us about individuals, populations and cultures?
- **What are stress-related diseases and how do they differ or relate to other types of disease?**
- **How is stress ‘viewed’ in the body? In the skeleton?**

  How is stress measured?
- **My current research! – Want to help or participate?**




# ‘I’m just so stressed out!’ Stresovanými!

- Stressors can be:
  - Physical- illness or injury
  - Psychological- a big exam or interview
  - Social- loneliness, subordination
  - Environmental- inadequate housing, noise pollution
- Why is ‘stress’ important?
  - Stress is linked to chronic diseases in modern populations
    - Cardiovascular disease
    - Metabolic syndrome and Diabetes (type 2)
    - Immunosuppression (HIV progression to AIDS impacted by stress)
  - Stress experience tells us something about the lives people lead (past and contemporary populations)
    - Many stressors? Few stressors?
    - How do populations cope?

# What is ‘Stress’?

Biological or physiological stress is an interaction

‘Stress’ is the result of stimuli (stressors) moving the body out of homeostasis, eliciting a physical reaction (stress response)

# Stressor = stimulus

What are they?

- ***Physiological/physical*** *- physical trauma, illness, resource scarcity, extreme temperature*
- ***Psychological****- a big exam or interview, public speaking (lucky me!)*
- ***Social****- loneliness, subordination*
- ***Environmental****- inadequate housing, noise pollution*
- ***'Real'*** *- harmful event occurring*
- ***Perceived*** *– harmful event anticipated (thinking about mortality)*

Many other ways to classify stressors!

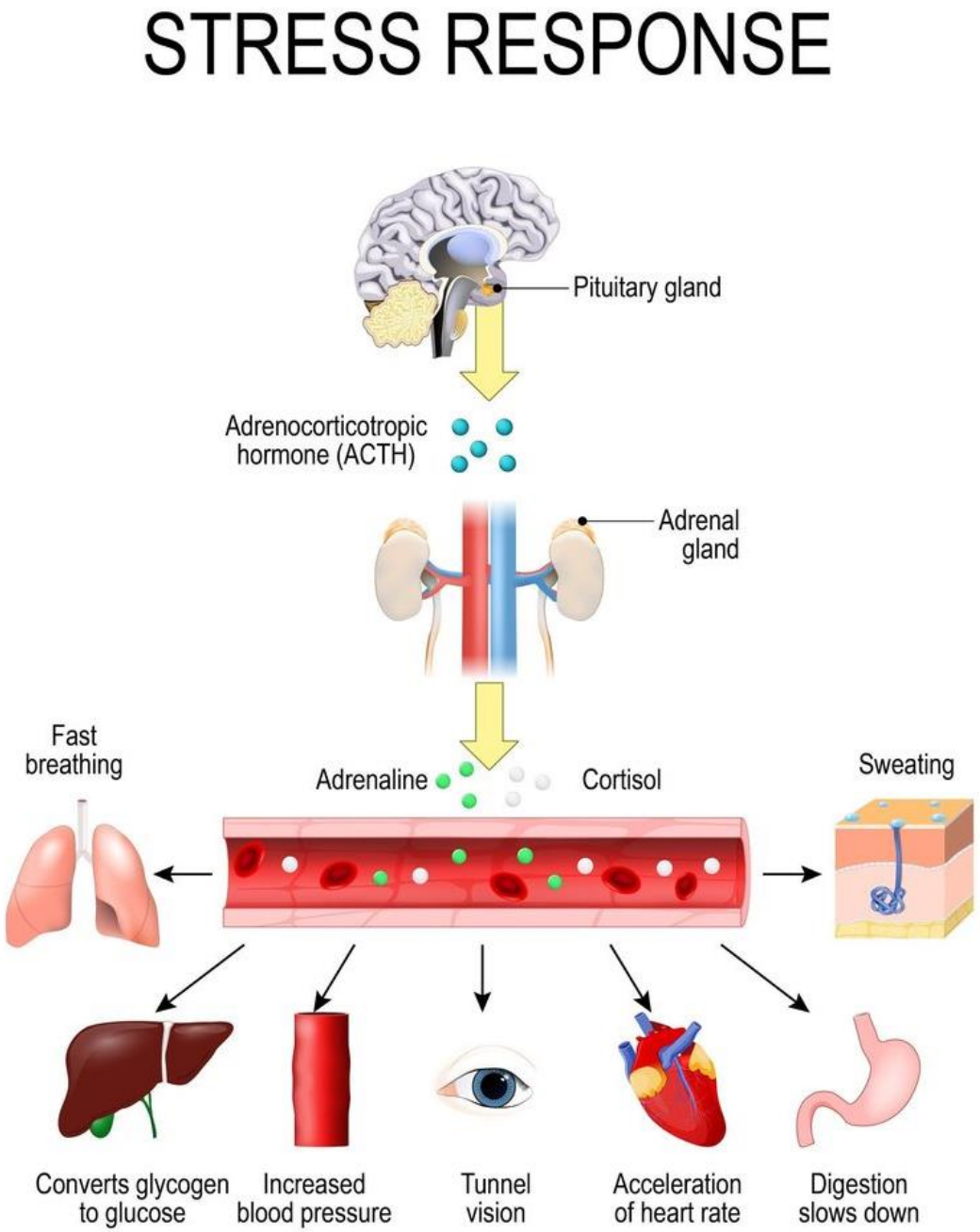

# Stress Response =

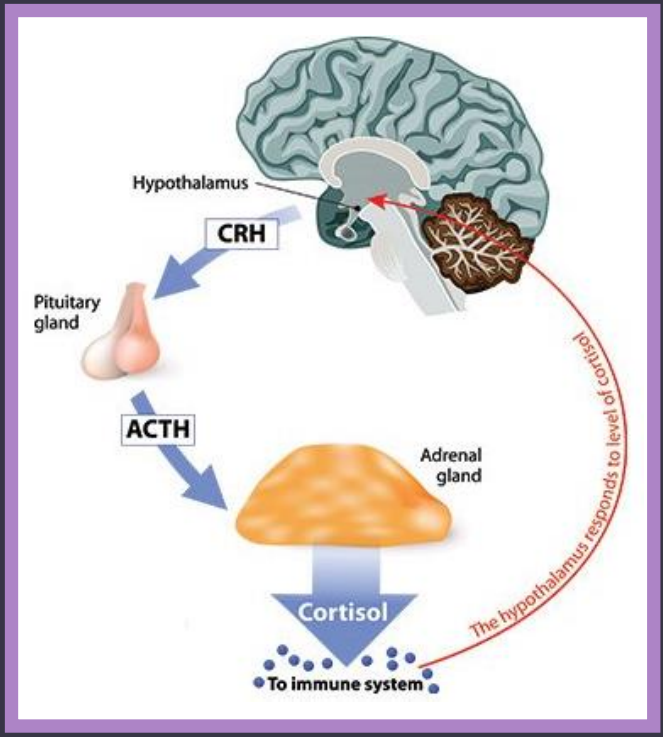
## the actions the body takes to respond to a stressor

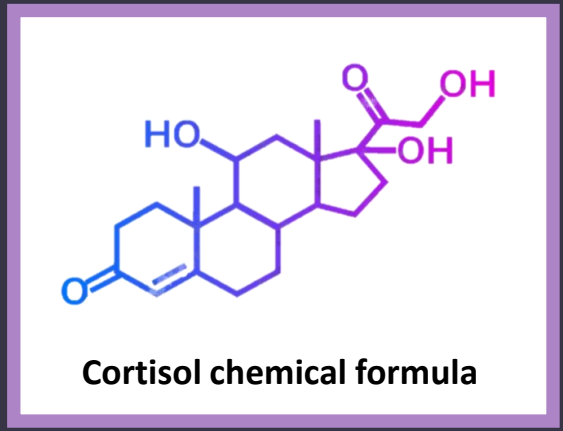
Heart rate increases, tissues transformed into energy, digestion slowed, growth delayed, reproductive activities suppressed

- *Autonomic Nervous system- Epinephrine/Nor-Epinephrine (Adrenaline)*
- ***Hypothalamic Pituitary Adrenal (HPA) Axis- Cortisol***

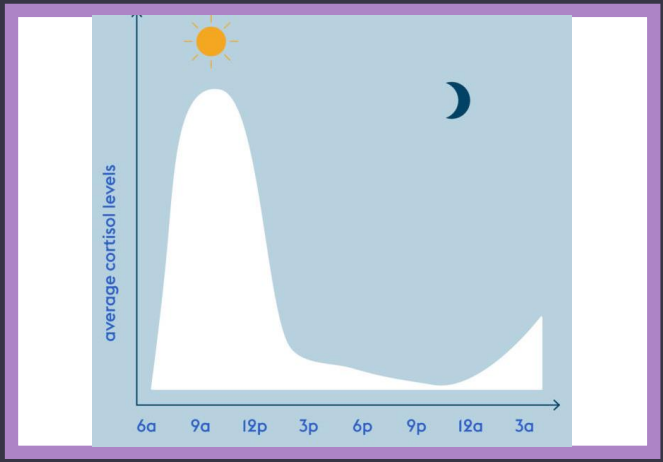
Non-specific – no matter the stressor, the pathway is the same

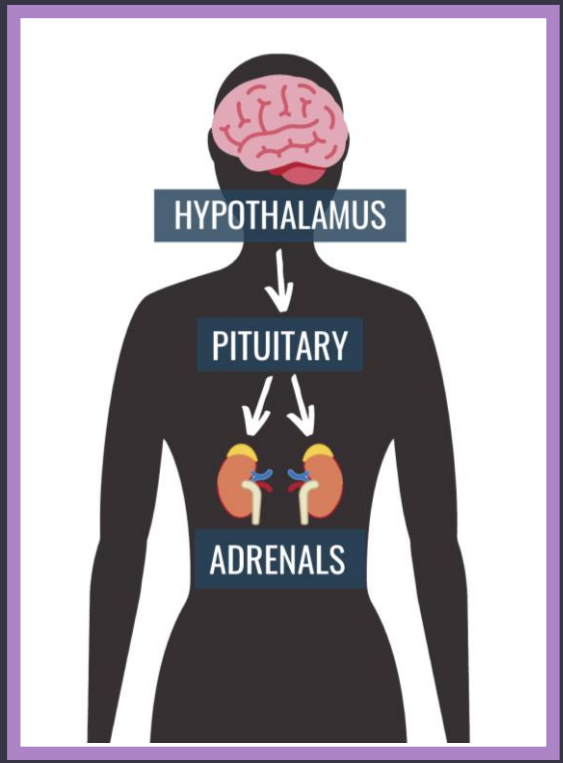




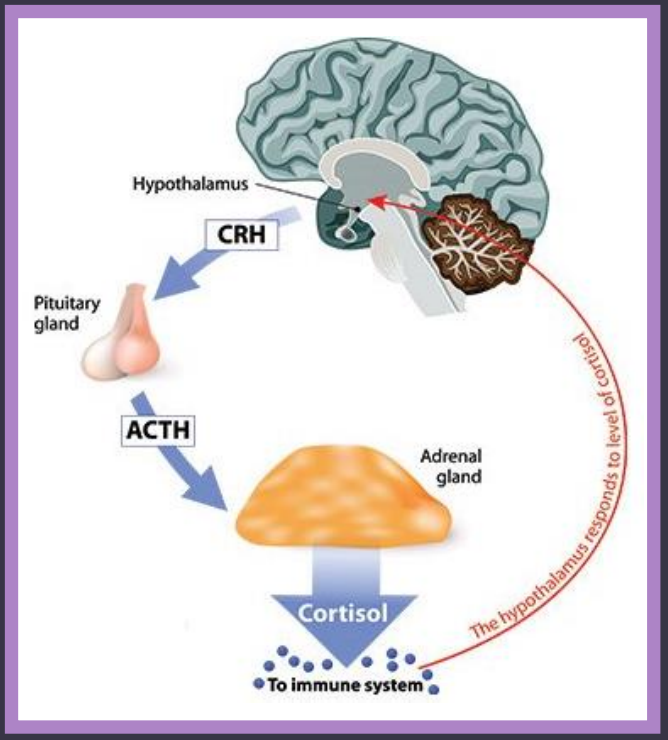

**Cortisol chemical formula**

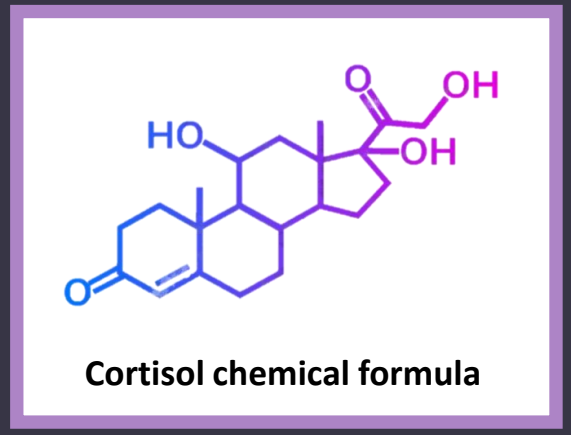



# Hypothalamic-Pituitary-Adrenal Axis (HPA)

- Cortisol is secreted from the adrenal glands and travels through the bloodstream
- Cortisol affects the transcription of genes within the cell nucleus to produce changes
- HPA Axis produces cortisol
  - in the presence of a stressor
  - Daily, following a circadian rhythm (high in the morning, low during sleep)
- Circadian rhythm of the HPA axis changes over the life course and is different between males and females
  - Cortisol production changes during adrenarche, puberty, pregnancy and menopause

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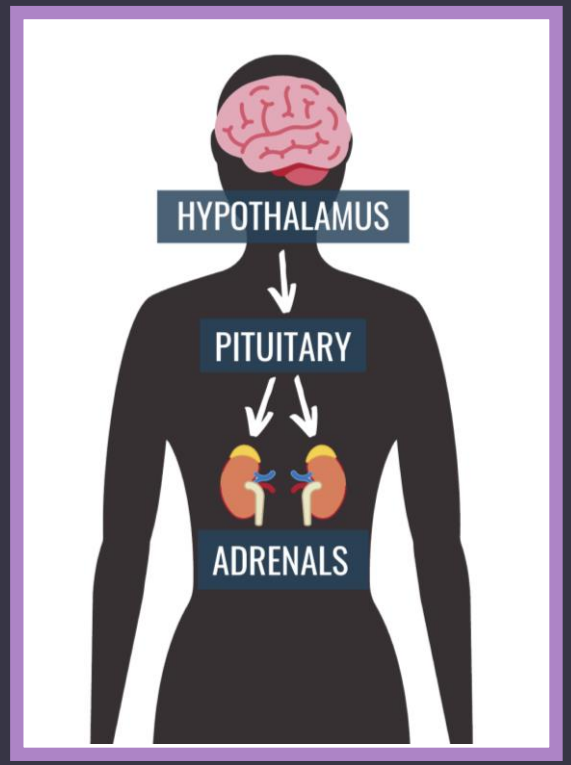
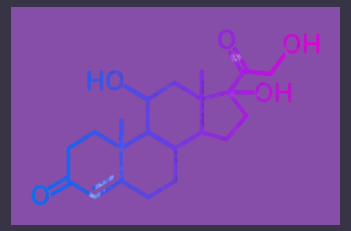



# HPA Axis Dysregulation

- HPA Axis Dysregulation- repeated or prolonged exposure to stressors
  - Less efficient stress response
    - Organism becomes more vulnerable to the stressor
  - Exposure to high levels of cortisol and the effects of the stress response
    - included an increased heart rate
    - overproduction of energy
    - suppression of growth, fertility and the immune system

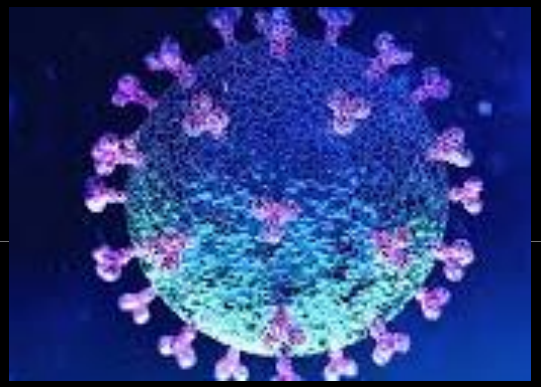

# Cortisol

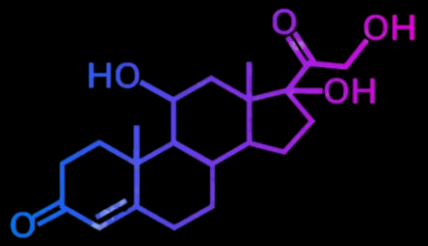
What is cortisol?

- Hormone = chemical messenger
- Glucocorticoid hormone, the ‘stress hormone’

What does cortisol do?

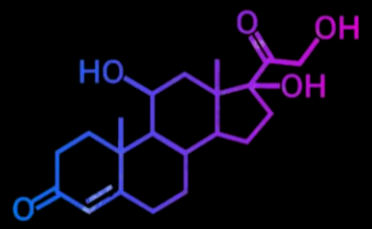
- Maintains homeostasis (balance in the body) in ‘stressed’ and ‘un-stressed’ states
- Regulatory functions in cardiovascular, metabolic, and immunological systems
  - suppresses overactive immune or inflammatory responses
  - maintains blood glucose levels
  - modulates cardiac output
- Communicates the presence of a stressor to organs and tissues, and initiates stress response activities



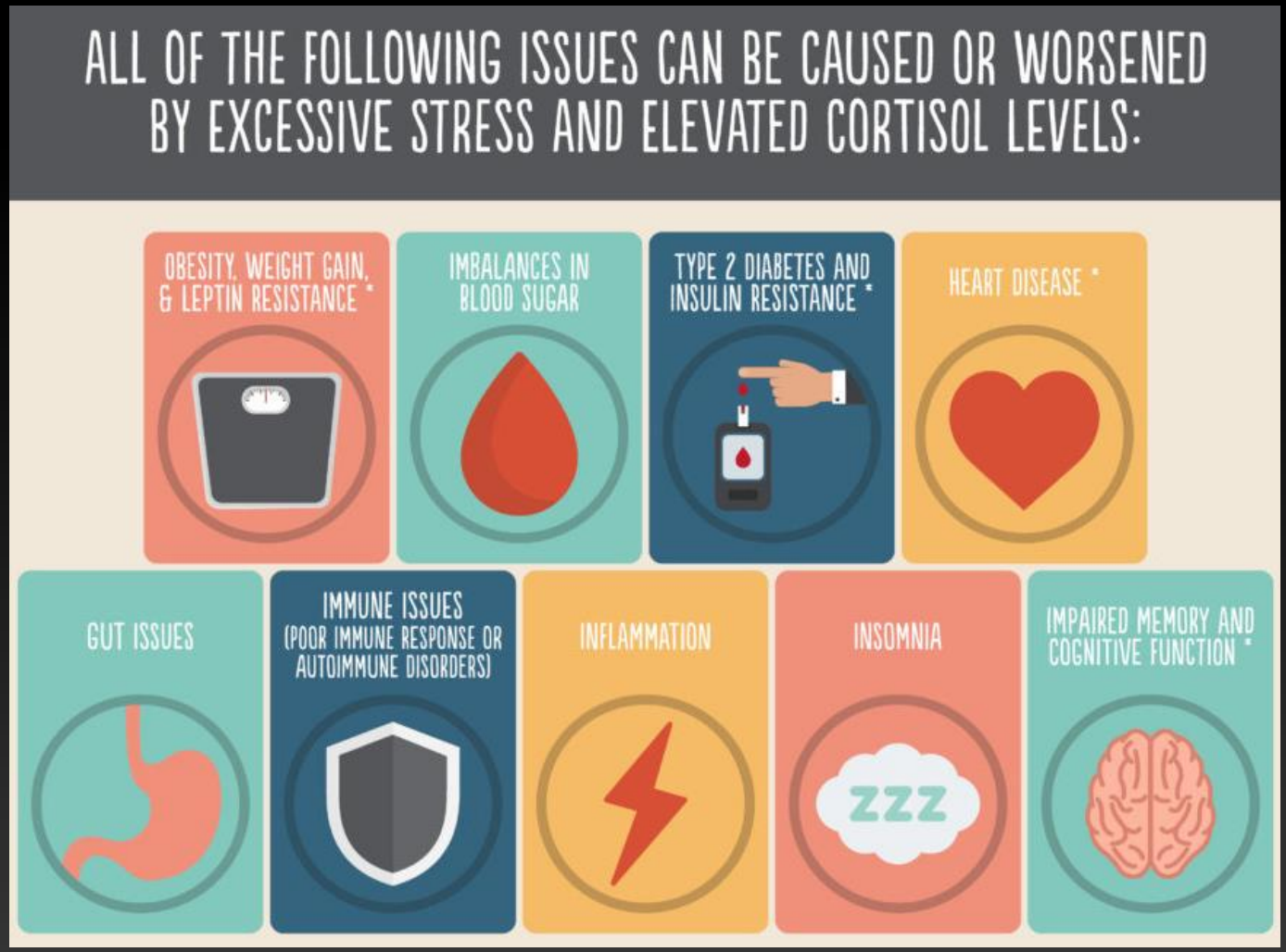

# The good...

- Cortisol is a corticosteroid hormone
- Extensively studied in a range of animals and contexts
  - controlled studies
- Used to treat inflammatory diseases
  - asthma, rheumatoid arthritis, lupus
- Facilitates organ transplants
- Important in treatment of respiratory distress and failure resulting from COVID 19



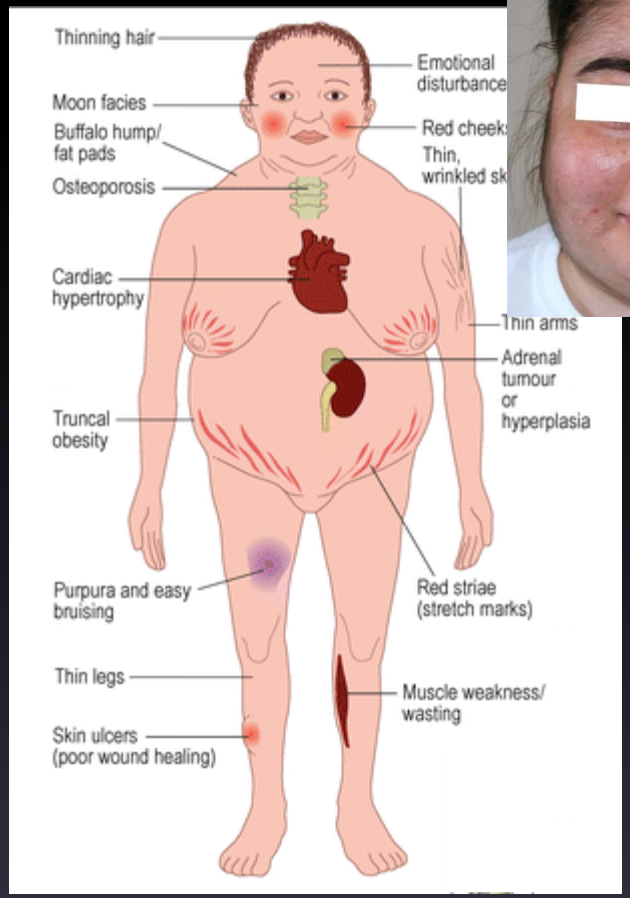

# The bad…

| Tissue | Ultimate effects |
|---|---|
| Brain | Depression<br>Altered cognition<br>Dementia<br>Psychosis/Neurosis |
| Cardiovascular | Cardiovascular Disease |
| Metabolic<br>Endocrine<br>Musculo-skeletal<br>Gastro-intestinal | Decreased Growth<br>Suppression of appetite and digestion<br>Delays puberty<br>Suppression of reproduction<br>Osteoporosis<br>Muscle atrophy<br>Peptic ulcers |
| Anti-Inflammatory<br>Hematologic<br>Immunological | Hyperglycemia<br>Suppressed inflammatory reaction<br>Slowed Wound Healing<br>Immunosuppression<br>Increased risk of infection |



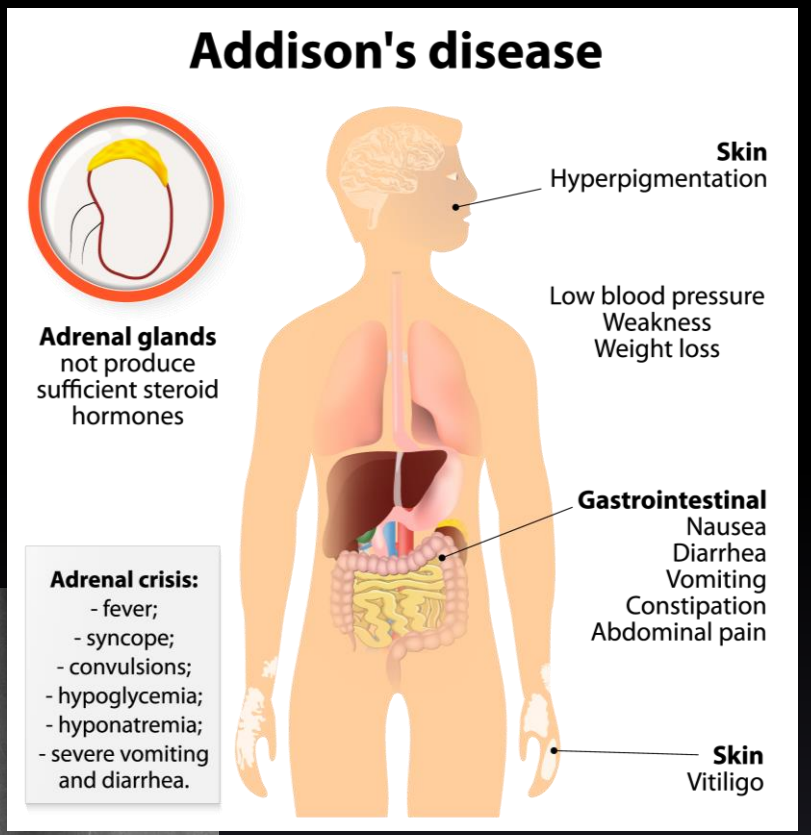
# Cushing’s Syndrome

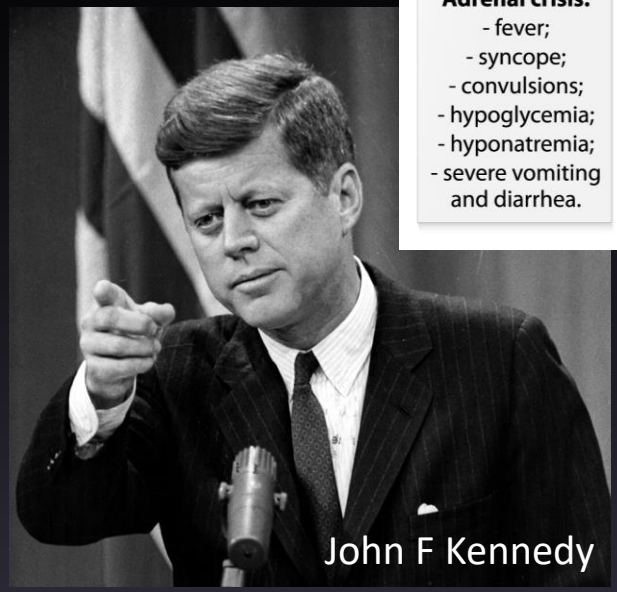
Too much cortisol





King Henry VIII of England
(very speculative case)



John F Kennedy

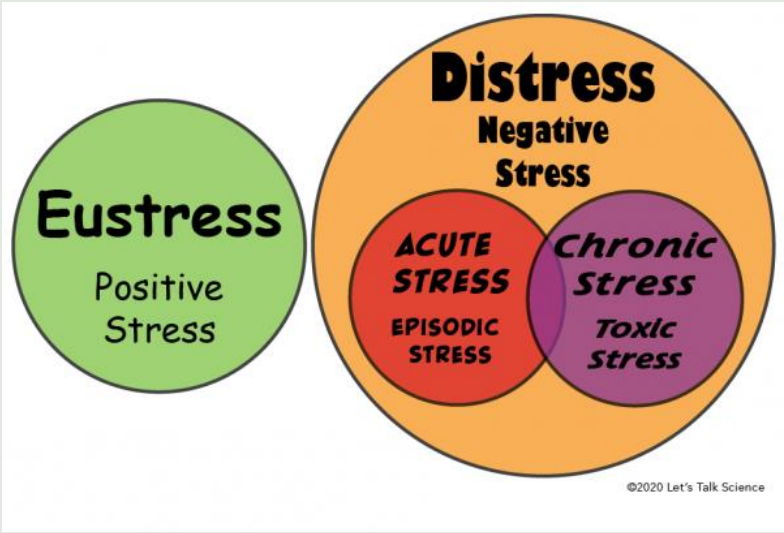
# Addison’s Disease

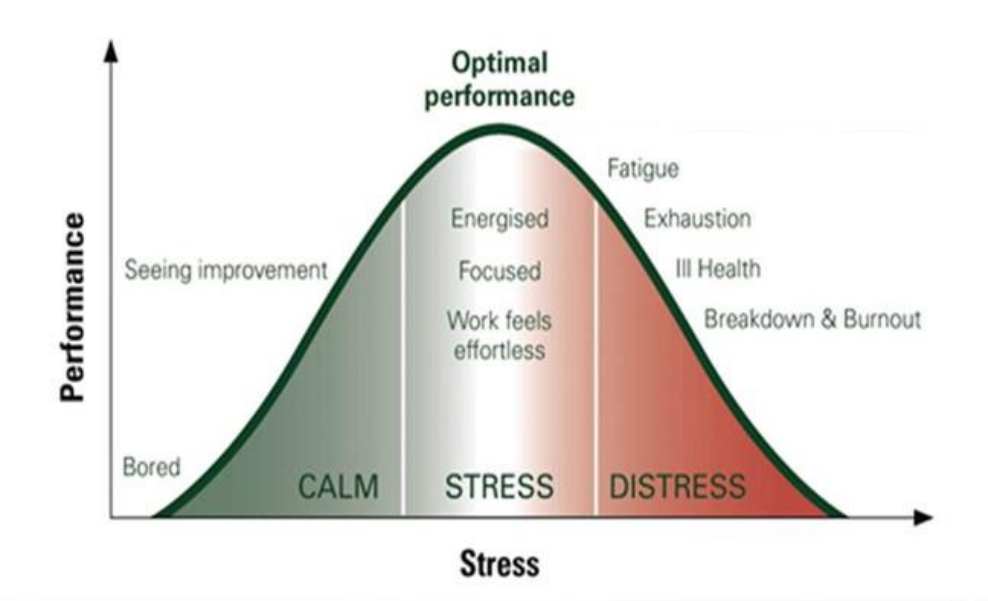
Too little cortisol

# Not all stress is bad!

Some stress is positive!

- we need a functioning stress response to handle stressors
- Eustress- positive challenges
- Distress- too many challenges, they are too severe or last too long

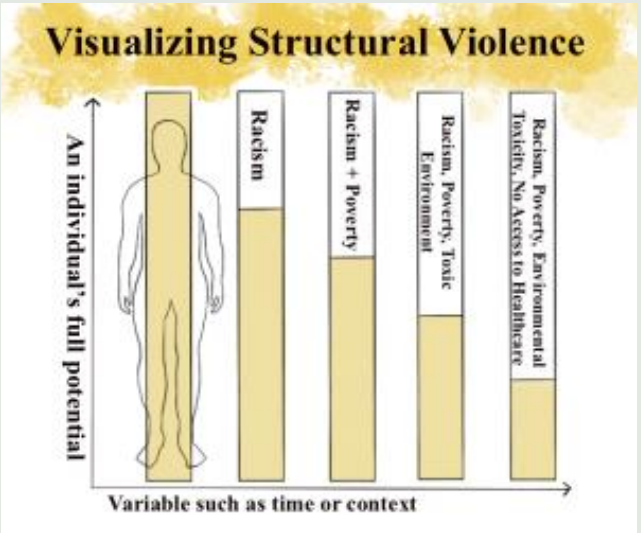


# Social, Cultural and Political Stressors

**Structural Violence**- ‘harm done to individuals or groups through the normalization of social inequalities in political-economic organization

(Farmer et al., 2006; Nystrom, 2014)




# Social, Cultural and Political Stressors

**Arabic mothers in the USA after 9/11 tragedy were more likely to have low birth weight babies (Lauderdale, 2006)**

- **Result of social stigma and harassment during pregnancy**

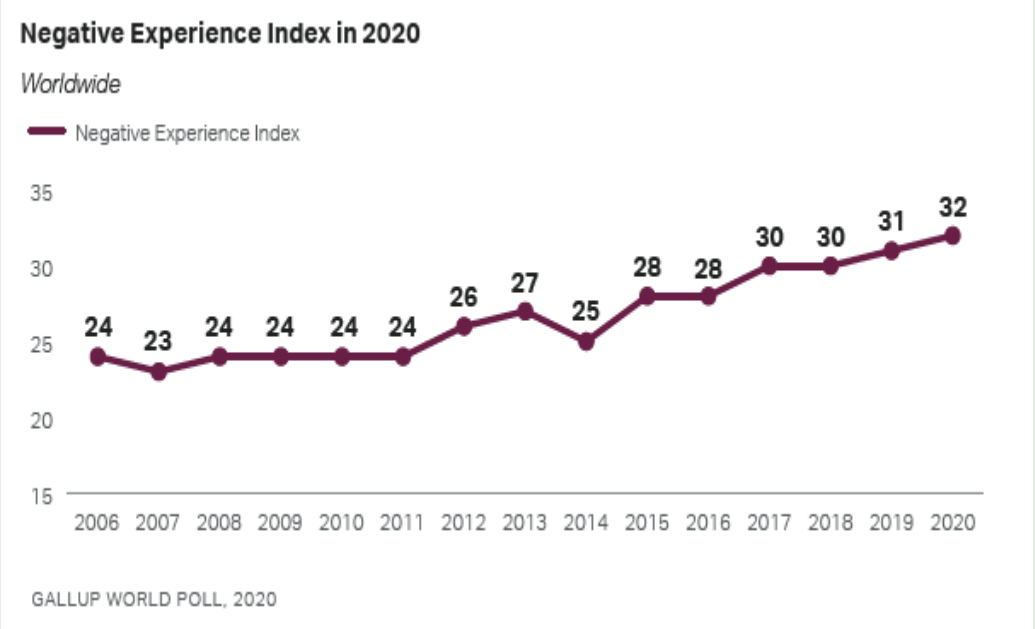
**Low Birth Weight Baby= < 2500 grams**

- **Increased mortality**
- **Increased susceptibility to infection**
- **Problems with cognitive development**

# Recent Stress Experience- ‘The Worst and Most Stressful Year’

“More people reported feeling stressed, sad, angry and worried in 2020 than at any point in Gallup’s global tracking” – Gallup Poll, 2021

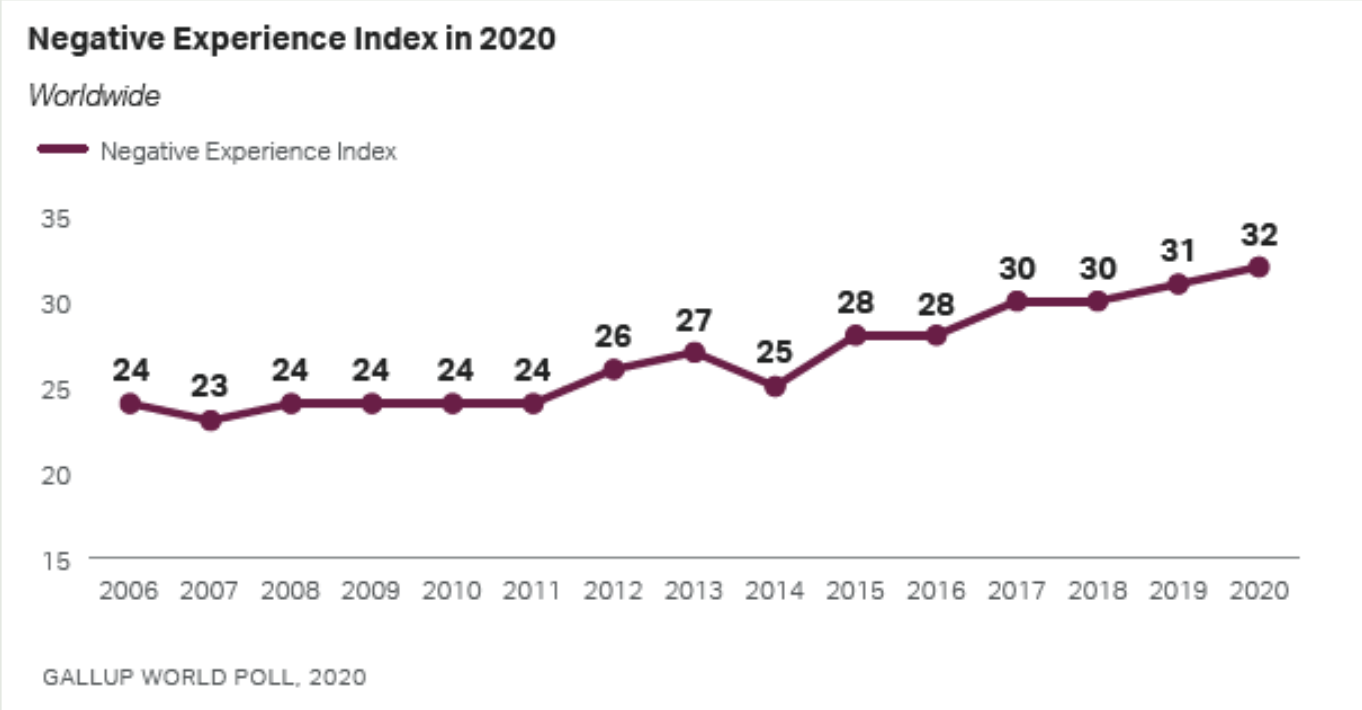
based on nearly 160,000 interviews with adults in 116 countries and areas in 2020 and early 2021

# Is it all COVID-19?

other things may be contributing to the trend in global rise in negative emotions:

- Political and economic turmoil (in some areas- Lebanon, Greece)
- increasing global hunger
- a lack of freedom
- rising corruption
- income inequality



# Stress and Infection

**Stress and infection have an important relationship**

- **cortisol suppresses the immune system- person more susceptible to infection**
- increased risk for infection arises in just days
- molecular immune changes identified within as little as five minutes of stressor onset
- dose-responsive, increasing with greater glucocorticoid concentration
- cortisol can modulate illness duration and severity

# Stress and Infection: COVID 19


Maternal viral infections during pregnancy have been associated with developmental delays in the fetus

Shuffrey et al., 2022 tested this relationship with COVID-19

They found that **stress experience** during the pandemic, rather than actually having the disease/infection, **negatively affected neurodevelopment**

# Stress, infection and the marginalized

"Bioarchaeology and other social sciences have repeatedly demonstrated that these kinds of crises play out along the preexisting fault lines of each society," says Gwen Robbins Schug,

Those ‘who faced discrimination in ways that damaged their health or limited their access to medical care even in prepandemic times. In turn, the pandemics themselves affected societal inequality, by either undermining or reinforcing existing power structures.’

From Black Death to fatal flu, past pandemics show why people on the margins suffer most

By Lizzie Wade | May. 14, 2020 , 8:00 AM


In this 1625 illustration, Londoners fleeing the plague are barred by country dwellers.NEW YORK PUBLIC LIBRARY/SCIENCE SOURCE

Pandemics' historical role in creating inequality

Liliana M. Dávalos[1,*], Rita M. Austin[2,3,4], Mairin A. Balisi[5,6], Rene L. Begay[7], Courtney A. Hofm…
+ See all authors and affiliations

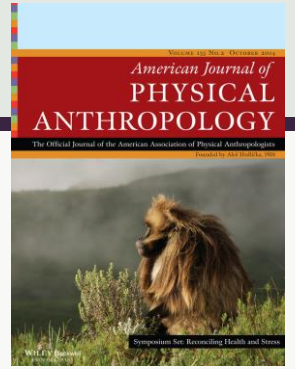
# QUICK BREAK!

See you in 5 minutes!

# Stress in Bioarchaeology

Stress, 2010 by Cuban sculptor #YoanCapote created from 17 tons of concrete supported by the bronze teeth






# What is health?

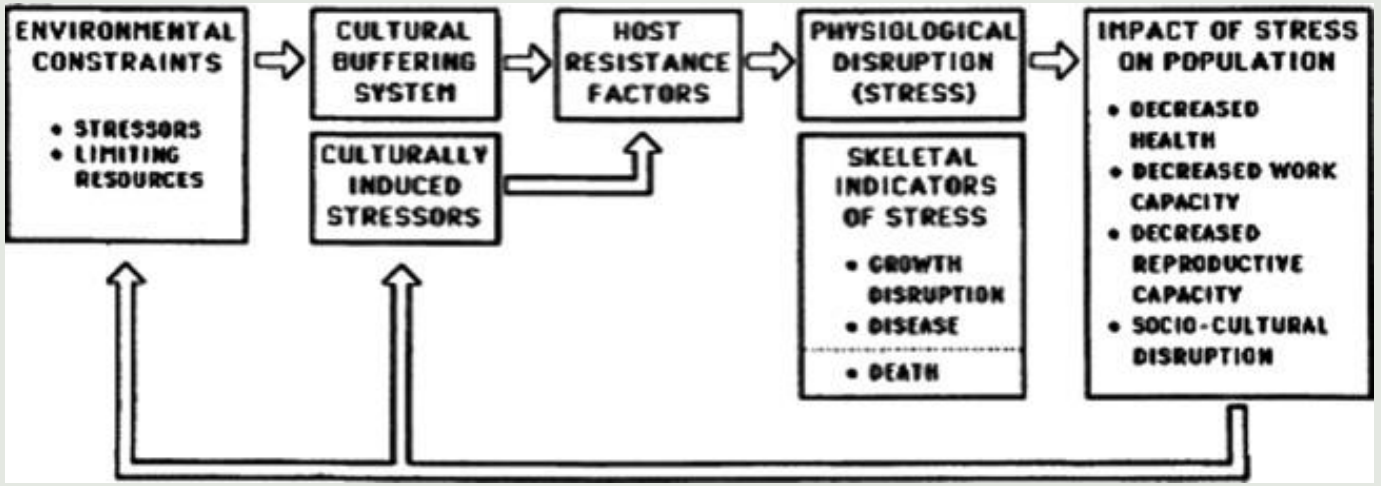
**Health is a state of complete physical, mental, and social well-being and not merely the absence of disease, or infirmity (WHO)**

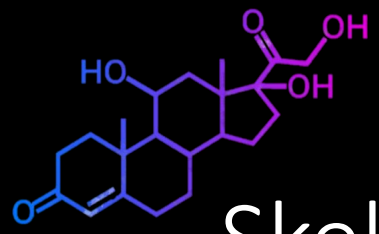
**Although we may never be able to agree on what represents "healthy," we may be able to agree that physiological changes in the body as a result of stress are "unhealthy" (Reitsema and McIlvaine, 2014)**

**Stress can be a useful proxy for health in past populations**

# Non-specific stress indicators

A general model for the study of stress in skeletal populations (Goodman and Armelagos, 1989; revised from Goodman et al., 1984).





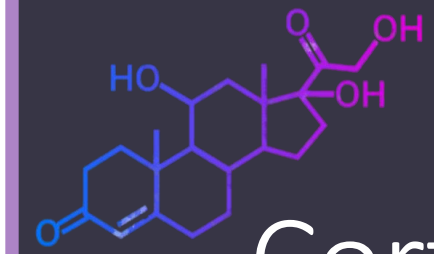

# Skeletal Stress Markers

- Bioarchaeological methods
  - Growth disruption, dental enamel hypoplasia, cribra orbitalia, periosteal reaction, mortality
  - Osteological Paradox
    - Individual needs to survive long enough to produce skeletal changes
    - How do we interpret the presence/absence of a lesion
  - Indirect and non-specific measures of stress
  - Unknown ‘threshold of stress’ needs to be met for development of the lesions
  - Many markers don’t often connect with modern studies

Cribra Orbitalia

Periosteal Reaction

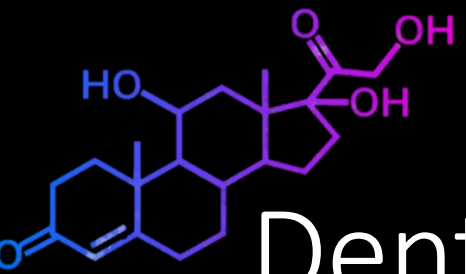
Dental Enamel Hypoplasia


# Cortisol Testing

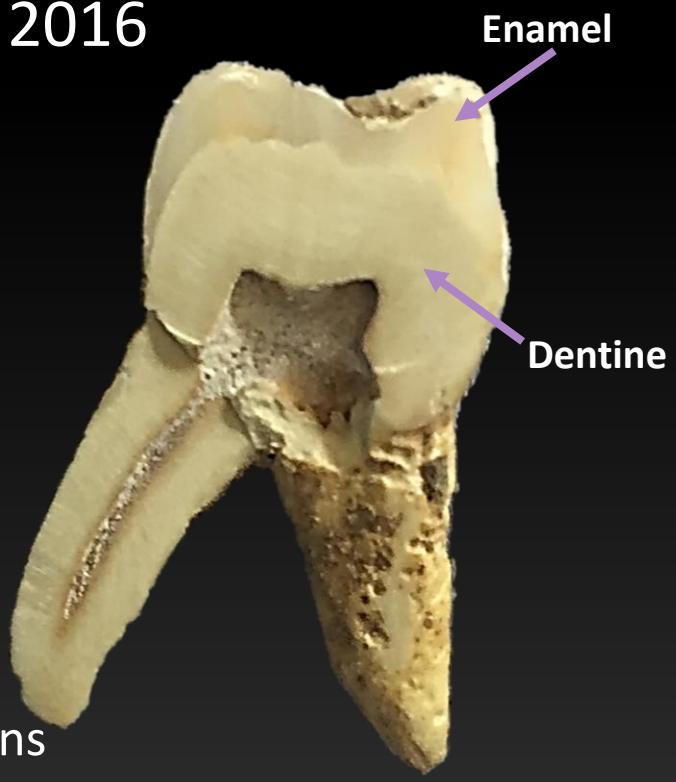
- Direct indicator of stress, used in modern studies
  - Blood
  - Urine
  - Saliva

  } Acute Stress and daily HPA rhythm
  Approx. 1-24 hours
  - Hair- chronic stress, weeks to months
- Cortisol found in archaeological hair
  - cortisol preservation over hundreds of years
    (Webb et al., 2015a, 2015b, 2010)
- BUT…
  - cortisol may be removed from hair when washed
  - very few archaeological individuals have hair




# Dental Cortisol

Cortisol detected in modern tooth dentine -Nejad et al., 2016

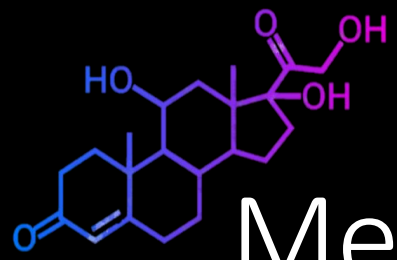



## Cortisol in archaeological teeth? – Let's find out!

- 69 teeth from 65 individuals (1st to the 7th century France)
- 29 teeth sampled twice to test dentine and enamel (96 samples)

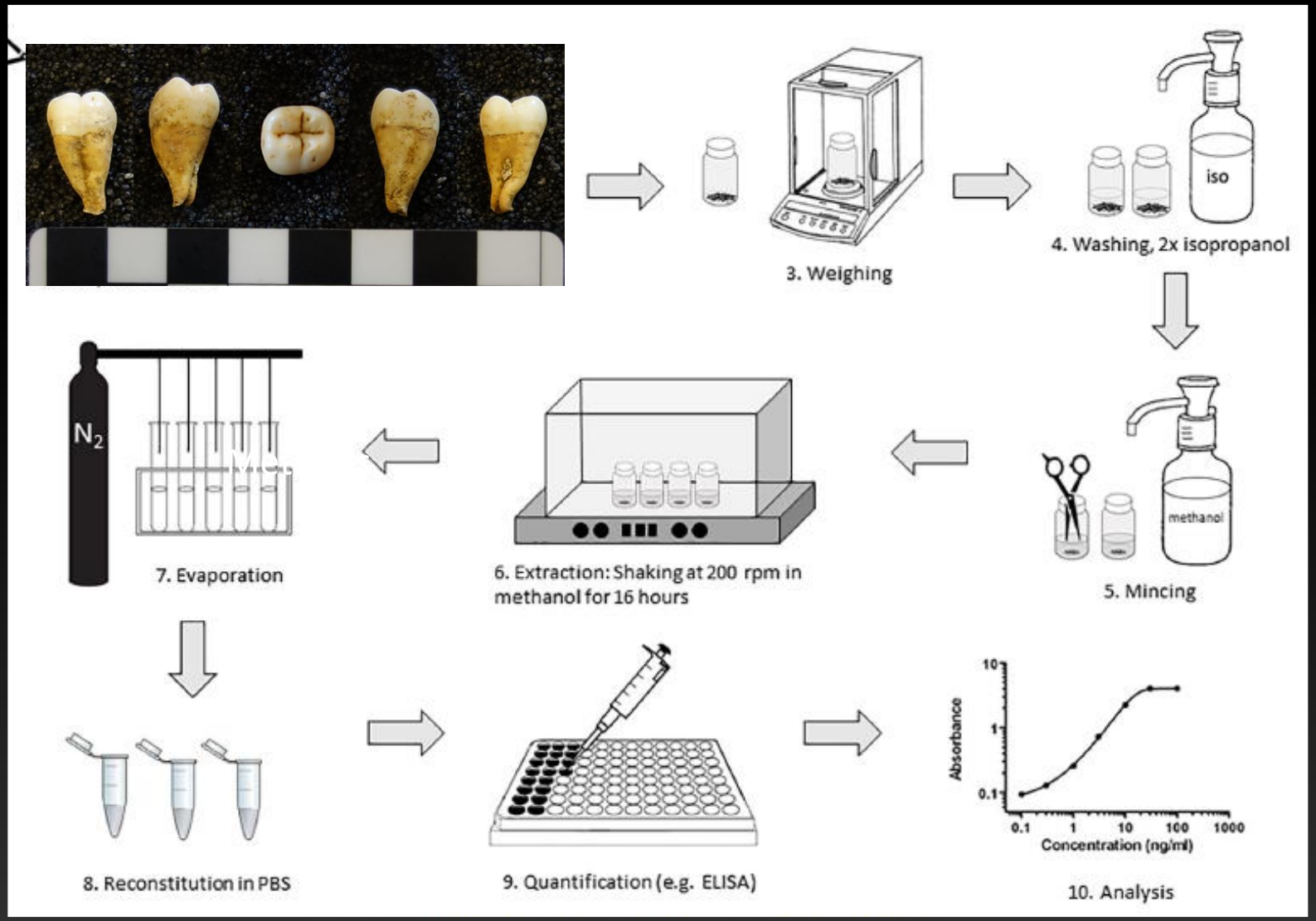
## Objectives:

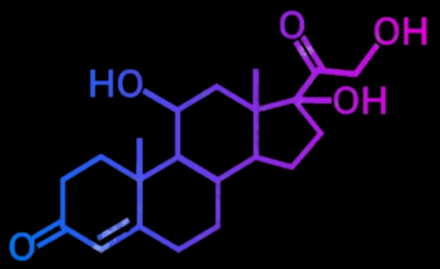
1. Can cortisol concentrations can be obtained from archaeological dentine or enamel
2. To investigate possible correlations between cortisol concentrations in dentine and enamel
3. To assess cortisol concentration variation between males and females




# Method

- Photograph
- Wash
- Grind
- Weigh
- Extract cortisol
- Evaporate solvent
- Reconstitute samples
- Detect and quantify cortisol through ELISA
  - Enzyme Linked Immunosorbent Assay

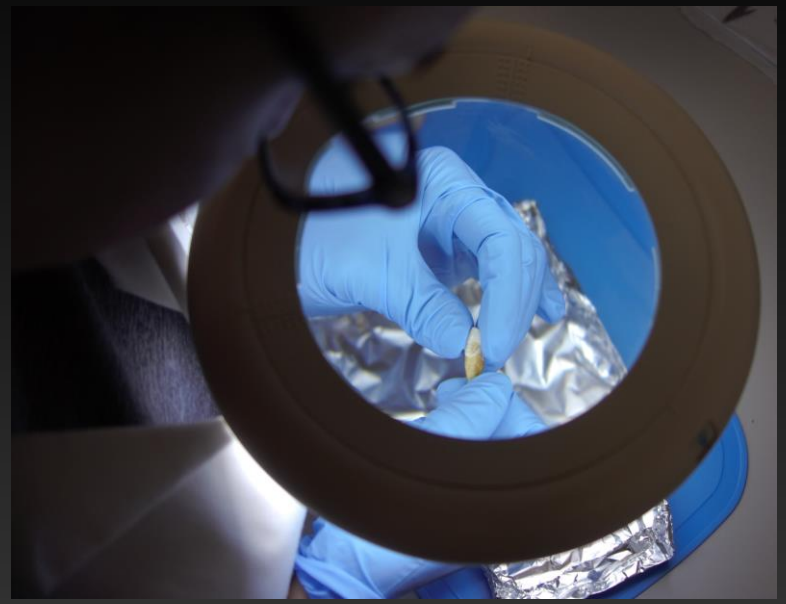


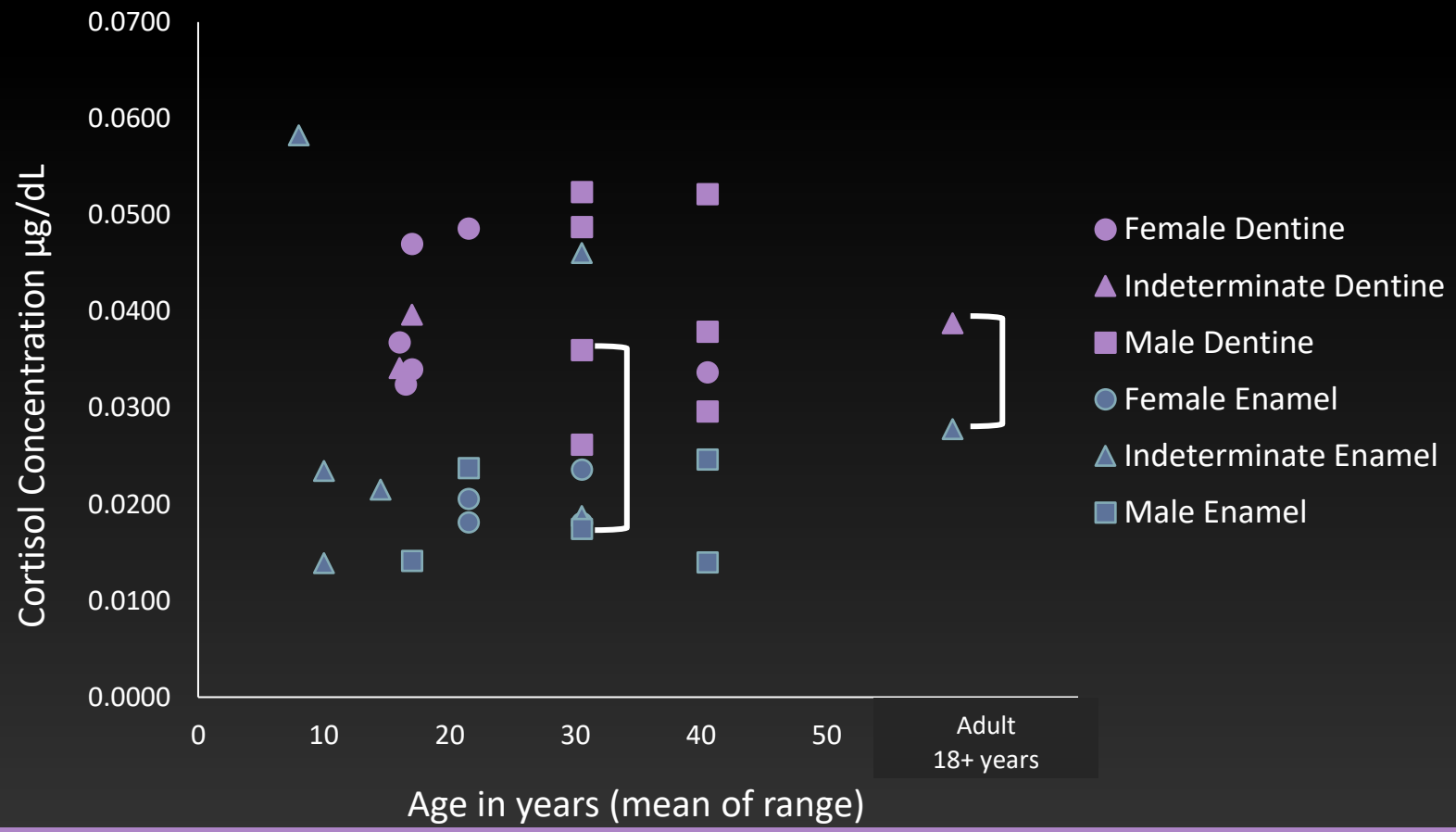


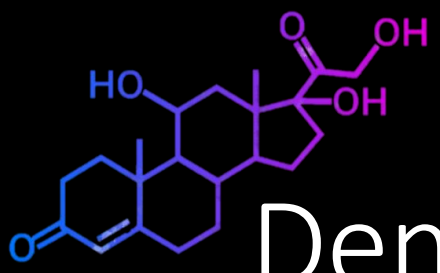

# Results- It's there!

Cortisol detected!

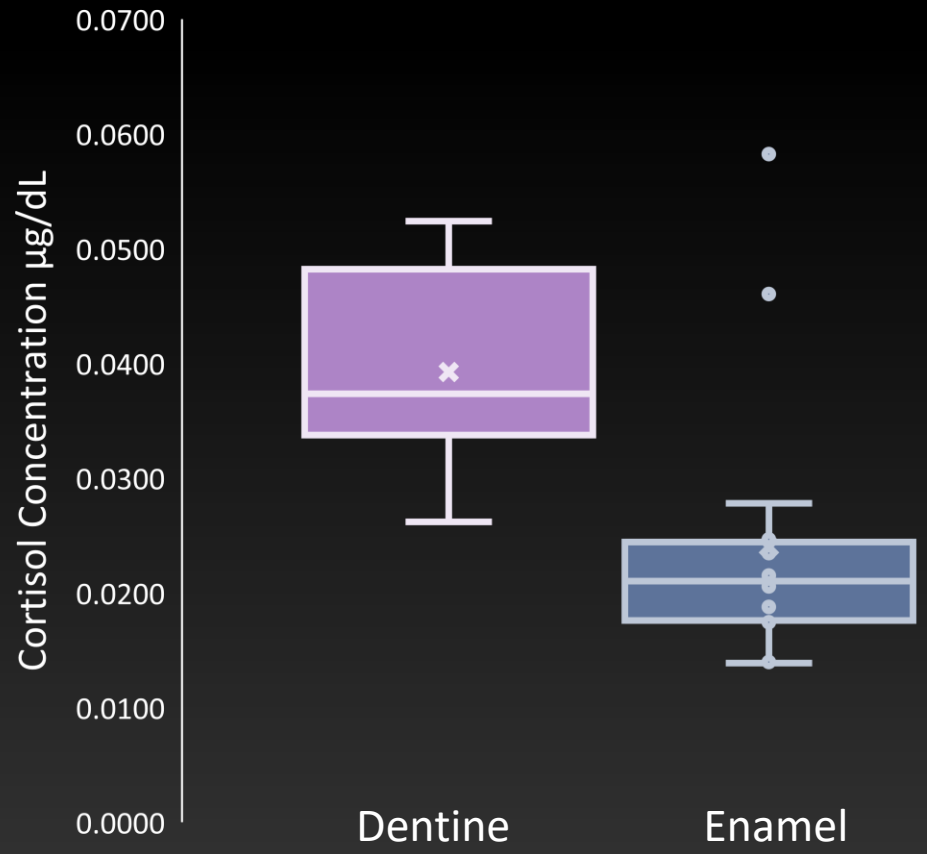
- 16 dentine samples
- 16 enamel samples



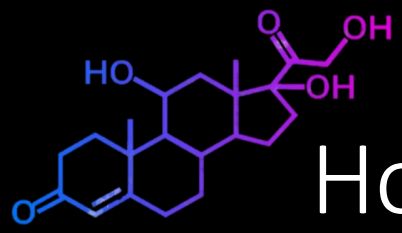





# Dentin and Enamel- Why are they different?




- Dentine values higher than enamel
  - Within and between teeth
  - In two teeth that generated dentine and enamel samples, dentine cortisol values were higher
  - Studies of other biochemicals show similar results
- Dentine may accept cortisol more easily into its structure
  - Enamel is more highly mineralised than dentine
    - Enamel- 96% inorganic materials
    - Dentine- 70% inorganic materials



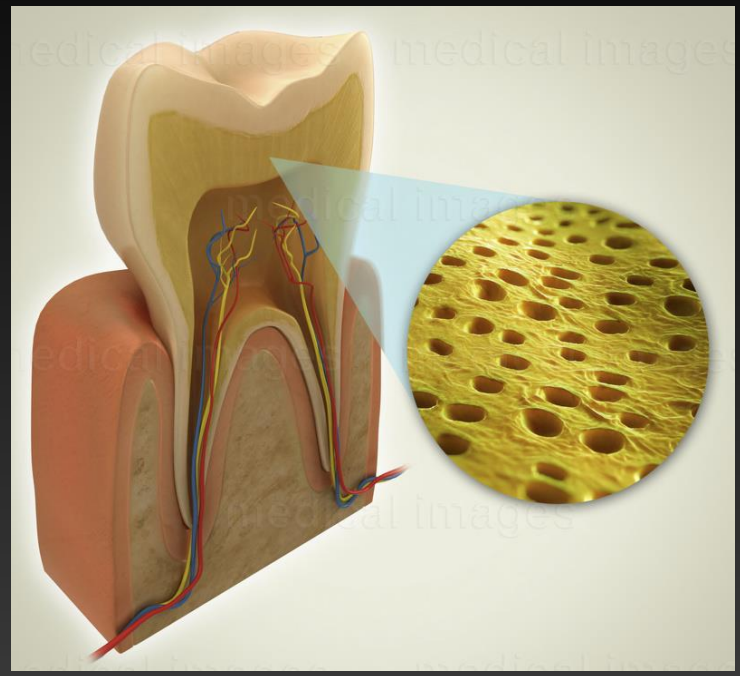

# How does cortisol get into tooth structures?

We don't know exactly …

- Enamel and dentine (also hair) may incorporate cortisol during development of the tissue
  - If correct, cortisol concentrations in teeth reflect cortisol from childhood

BUT…

- Dentinal tubules- connect dentine with the blood supply
  - could transmit chemicals or substances in pulp/blood to dentine throughout life
- Dentine cortisol levels are higher because …
  - Dentine collects cortisol during development and throughout life through dentinal tubules AND/OR
  - Dentine collects cortisol 'better' than enamel (less mineralised)

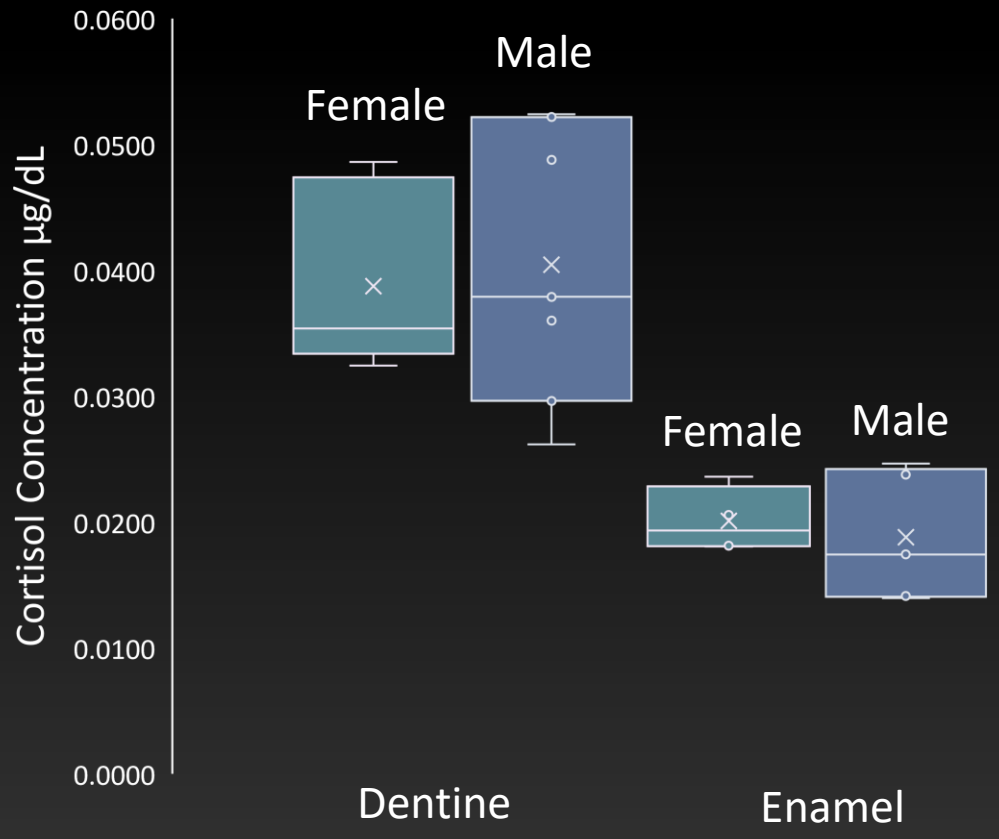


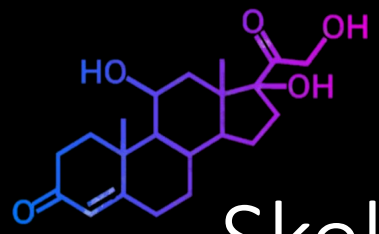
# Sex-based Differences?

No differences in dentine or enamel cortisol concentrations between males and females

Why?

- Small sample size?
- Overall low values?
- Results might reflect cortisol from before puberty
  - Sex-based differences in cortisol are thought to develop at puberty
  - Could explain these results in both this analysis and in modern dentine






# Skeletal Stress Markers

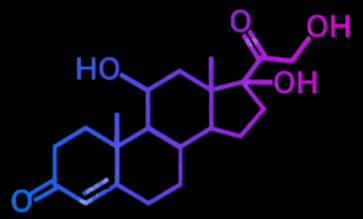
- Bioarchaeological methods
  - Growth disruption, dental enamel hypoplasia, cribra orbitalia, periosteal reaction, mortality
  - Indirect and non-specific measures of stress

Correlations with other skeletal stress indicators? Some preliminary data…

Cribra Orbitalia

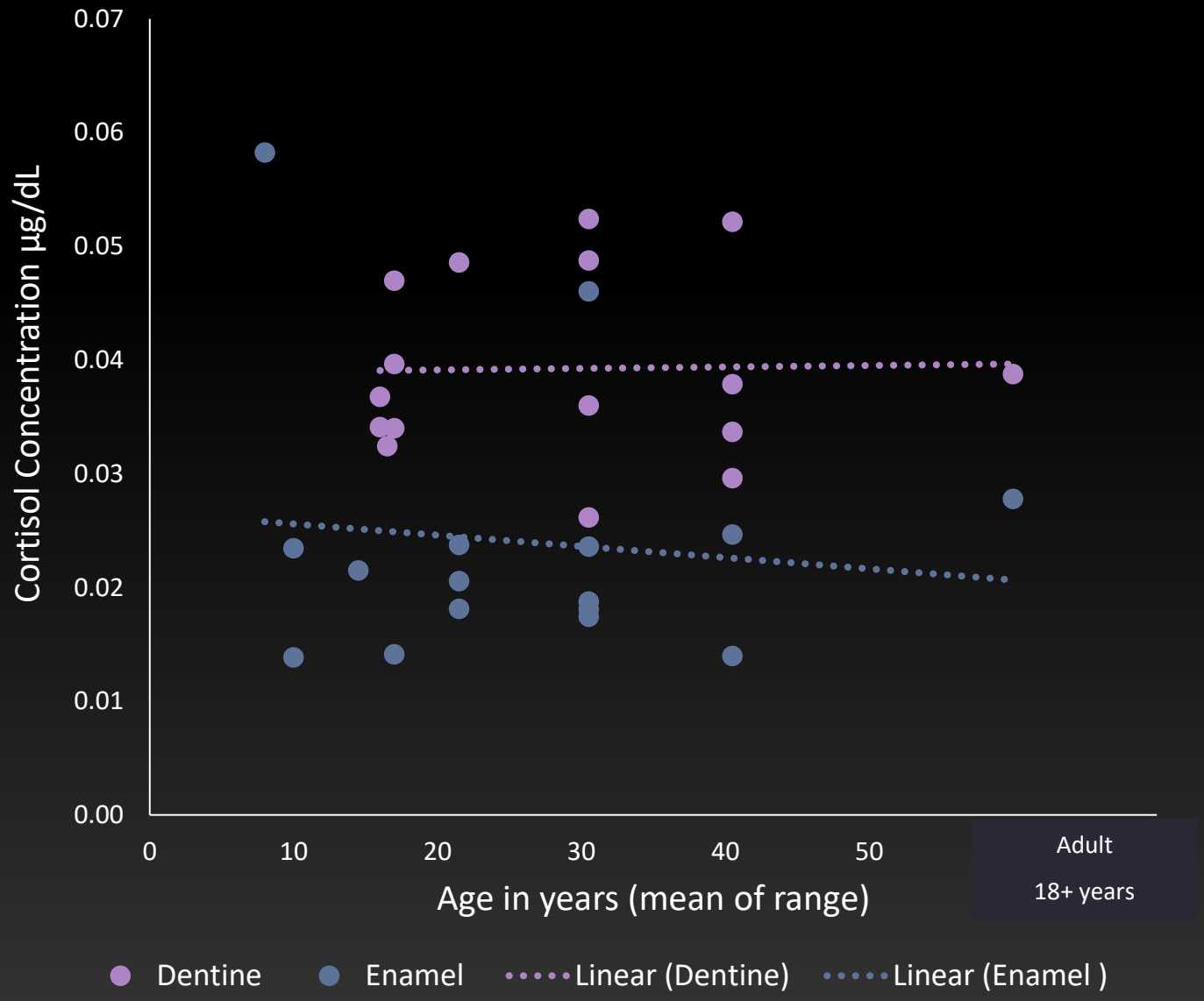
Periosteal Reaction

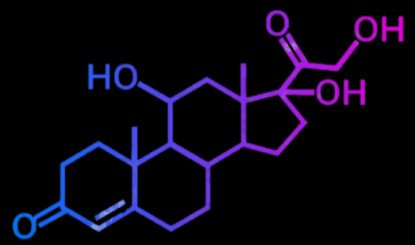
Dental Enamel Hypoplasia




# Mortality

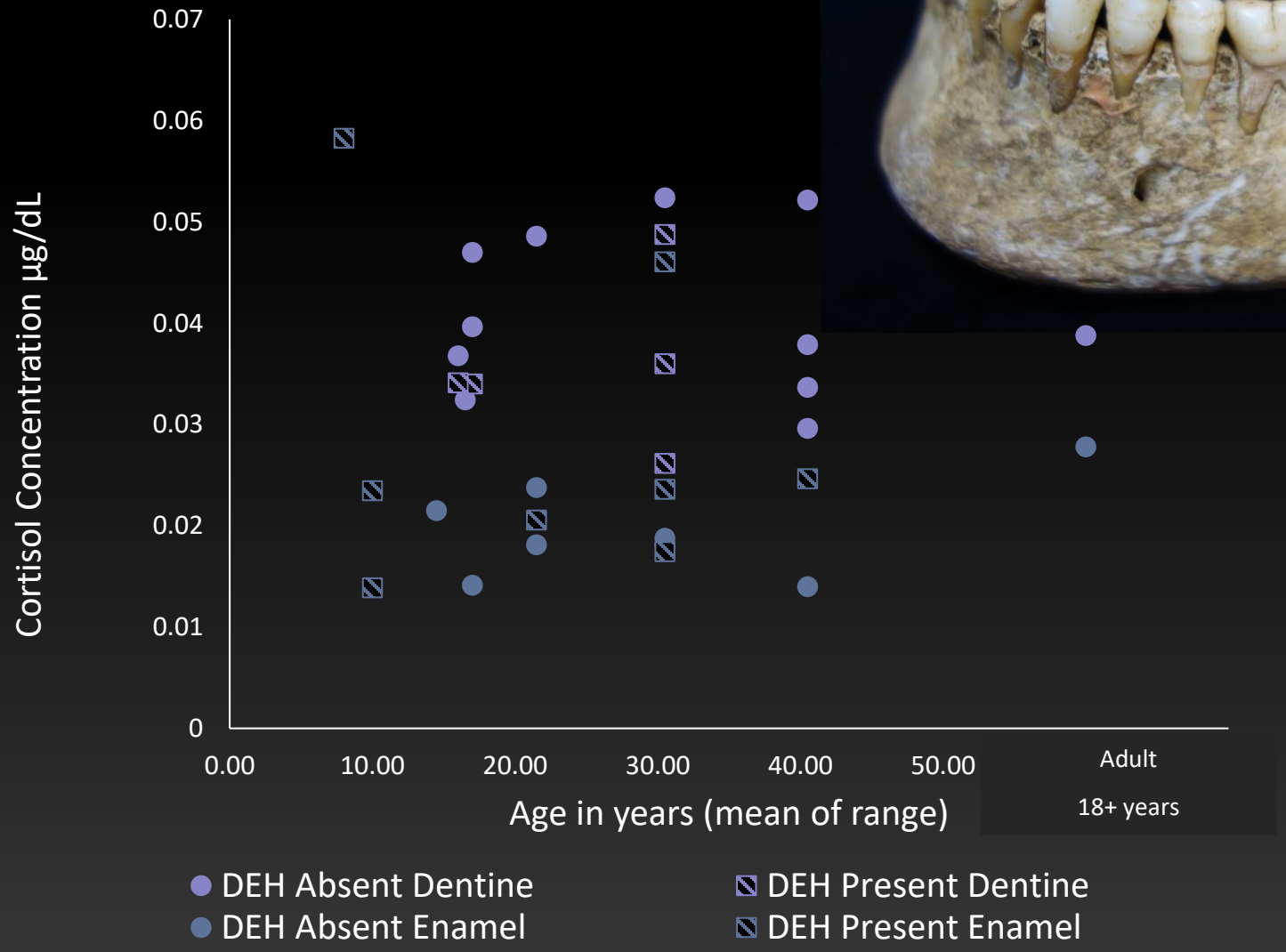
- Premature death= ultimate sign of inability to adapt
- Dysregulated cortisol is associated with premature death in modern populations
  - usually the result of cortisol's secondary effects – immunosuppression, etc
- Even small or short periods of stress affect the immune system
- Long term effects of cortisol dysregulation are of interest to palaeopathologists
  - High mortality from infectious diseases in the past
- No clear relationship between dental cortisol and age-at-death

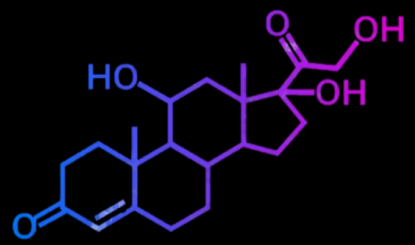





# Dental Ename Hypoplasia

- Defects in enamel
  - Form during development as a result of illness, nutritional deficiencies or deprivation
- No clear pattern
  - High and low cortisol present in teeth with and without DEH
- BUT… the two enamel samples with very high cortisol have DEH
  - a concurrence between biochemical and macroscopic indicators of stress in extreme cases?



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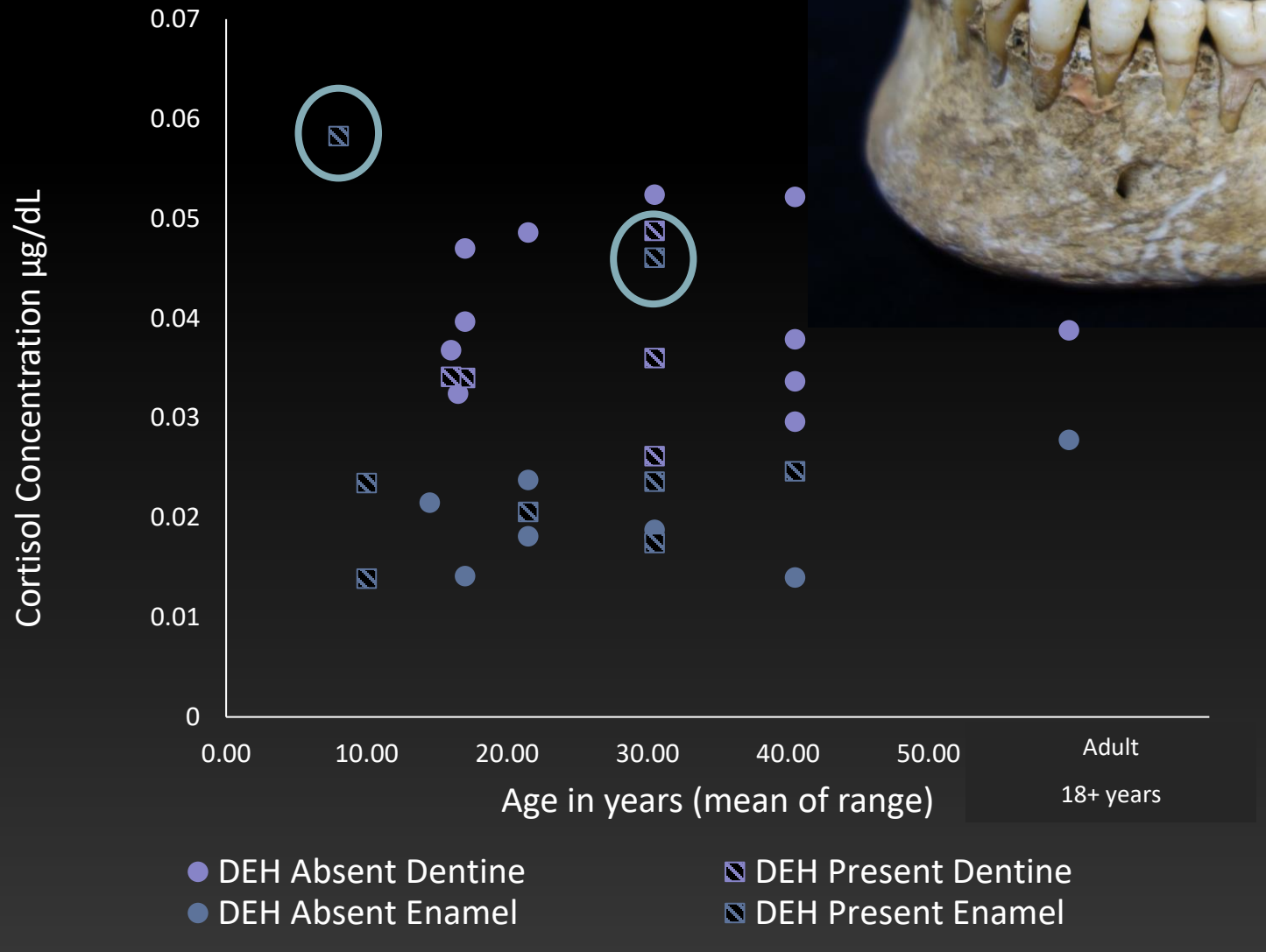
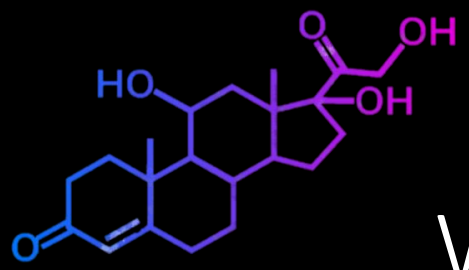
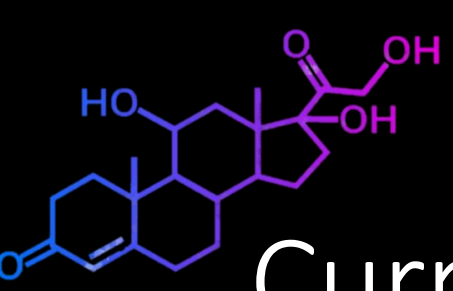





# What does it mean?

- Cortisol can be detected in archaeological tooth structures
  - Clarifies chronic stress experience in the past
  - Links palaeopathological data with modern data, research and interests
- Opportunities for future research:
  - Further testing of the cortisol method
  - Timing and duration of cortisol uptake
  - No consistent patterns between dental cortisol and skeletal stress markers




# Current Research

1) Build upon and refine dental cortisol method and analysis

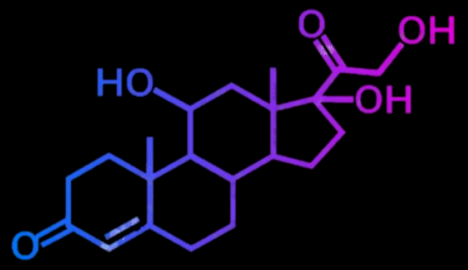
2) Examine dental cortisol concentrations in relation to:

- known occurrences of stress
- skeletal manifestations of stress

3) Encourage interdisciplinary collaborations surrounding stress and cortisol


# Refine & expand dental cortisol method

- Validate and refine method
  - testing for precision, robustness, trueness
- Generate more data
  - required to identify and interpret patterns in cortisol concentrations
  - Explore variation in uptake mechanisms between dentine and enamel
- Analyze cortisol in baby (deciduous/milk) teeth for the first time!
  - Likely reflects maternal health and stress

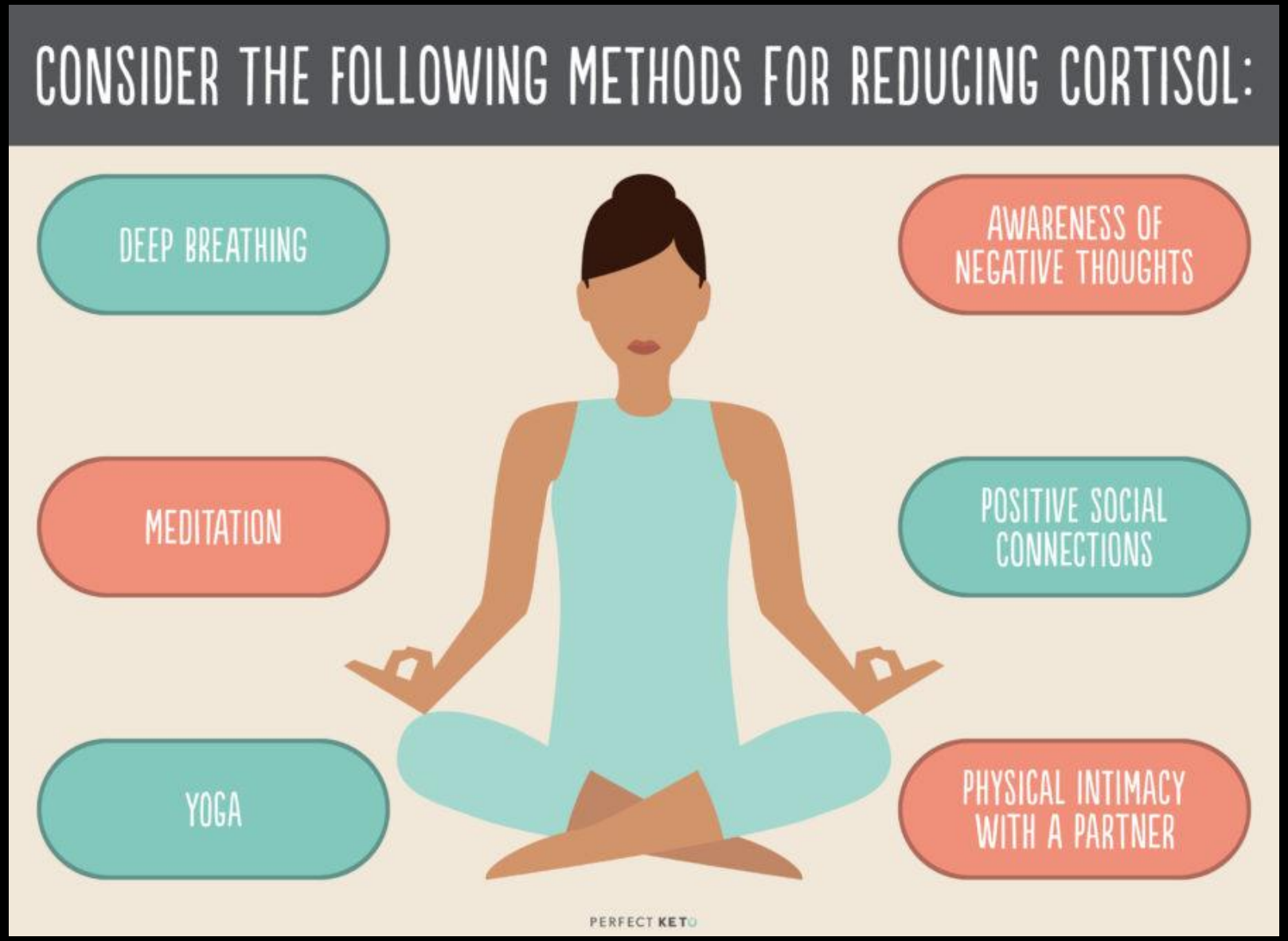


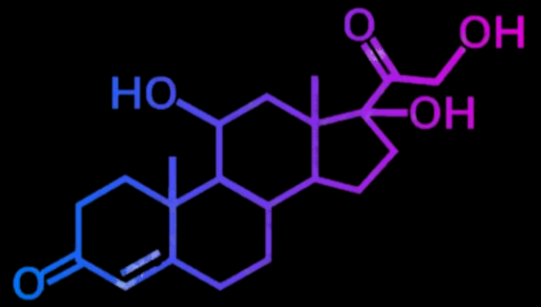

# What do dental cortisol concentrations mean?

Cortisol concentrations in relation to:

- Sex/Age
- Known stress events and health outcomes
- Physiological signs of stress- growth stunting/stature, dental defects, maturity or fertility

- European Longitudinal Study of Pregnancy and Childhood (ELSPAC) study
  - Known health and stress data
  - Teeth!
- Archaeological teeth




# HAVE SOME TEETH?

**Or interested in learning more?**

**Thank you!**
**quade@sci.muni.cz**

# Recommended Reading


2014. American Journal of Physical Anthropology. Volume 155, Issue 2 Special Issue: Symposium Set: Reconciling Health and Stress, Pages: 181-317- WHOLE ISSUE

Armelagos, G.J., Goodman, A.H., Harper, K.N. and Blakey, M.L., 2009. Enamel hypoplasia and early mortality: Bioarcheological support for the Barker hypothesis. Evolutionary Anthropology: Issues, News, and Reviews: Issues, News, and Reviews, 18(6), pp.261-271.

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Farmer, P., 2004. An anthropology of structural violence. Current anthropology, 45(3), pp.305-325. (This is a little dense!)

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Goodman, A.H., Armelagos, G.J. and Rose, J.C., 1980. Enamel hypoplasias as indicators of stress in three prehistoric populations from Illinois. *Human biology*, pp.515-528.

Quade, L., Chazot, P.L. and Gowland, R., 2021. Desperately seeking stress: A pilot study of cortisol in archaeological tooth structures. *American Journal of Physical Anthropology*, *174*(3), pp.532-541.

Shuffrey, L.C., Firestein, M.R., Kyle, M.H., Fields, A., Alcántara, C., Amso, D., Austin, J., Bain, J.M., Barbosa, J., Bence, M. and Bianco, C., 2022. Association of Birth During the COVID-19 Pandemic With Neurodevelopmental Status at 6 Months in Infants With and Without In Utero Exposure to Maternal SARS-CoV-2 Infection. JAMA pediatrics, pp.e215563-e215563.

Wade, L., 2020. From Black Death to fatal flu, past pandemics show why people on the margins suffer most. Science.