



CORTICO- STEROIDI E CUORE

Prof. Felice Strollo
IRCCS San Raffaele Pisana, Roma

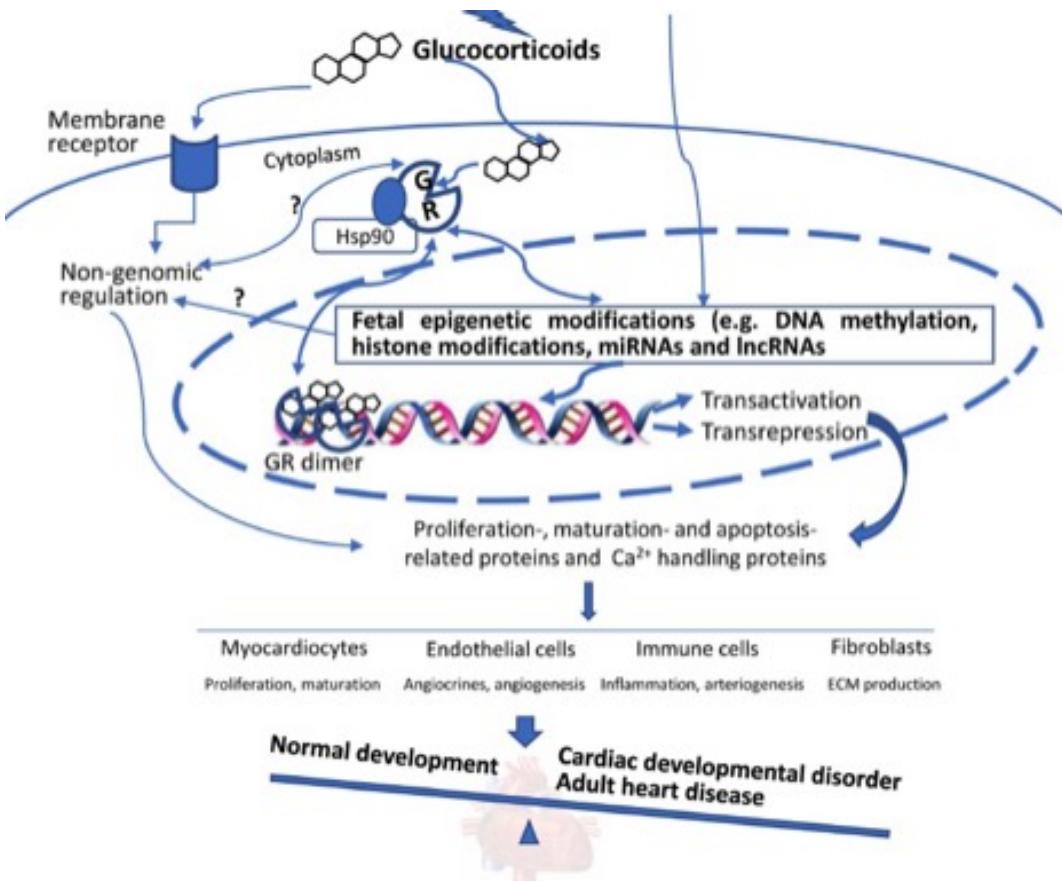
 **IRCCS San Raffaele**

Differenza fra cortisolo e corticosteroidi

| Molecola | Potenza glico-attiva | Potenza mineralo-attiva | Emivita(h) | Picco h) |
|---------------------------|----------------------|-------------------------|------------|--------------|
| Cortisolo / idrocortisone | 0,8/1 | 1 | da 8 a 12 | 1 |
| Deflazacort | 4 | 1 | < 12 | 1 |
| Prednisolone | 4 | 0,8 | da 12 a 36 | 1 |
| Prednisone | 4 | 0,8 | da 12 a 36 | 2 |
| Metilprednisolone | 5 | 0,5 | da 12 a 36 | da 1.1 a 2.2 |
| Triamcinolone | 5 | 0 | da 12 a 36 | da 1 a 2 |
| Betametasone | 25 | 0 | da 36 a 72 | 1 |
| Desametasone | 25 | 0 | da 36 a 72 | da 1 a 2 |

STRESS MATERNO & EPIGENETICA CARDIACA

GENOMIC AND NONGENOMIC EFFECTS OF GLUCOCORTICOIDS play a critical role in late gestational cardiac maturation



Song R et al. J Endocrinol. 2019 July 01; 242(1): T121-T133.

Glucocorticoids

- are required for the **DEVELOPMENT** of lung, brain, gastrointestinal, renal and **CARDIOVASCULAR SYSTEM**.
- in the maternal heart can induce
 - direct non-genomic effects (cellular signaling pathway activation)
 - genomic effects (altered gene expression through transactivation or transrepression)
- **IN THE FETAL HEART CAN INDUCE EPIGENETIC EFFECTS** (DNA methylation, histone acetylation, miRNAs and lncRNAs).

This **alters fine-tuning proliferation-, maturation- and apoptosis-related proteins and Ca^{2+} handling proteins**, resulting in modification of the activities and functions of **CARDIOMYOCYTES AND SUPPORTING CELLS**

The binding of **EXCESS** glucocorticoids to GR in **LATE GESTATION** contribute to the development and progression of **ADULTHOOD HEART DISEASE**.

Glucocorticoidi: effetti fisiologici e maladattativi

| Acute, Adaptive Physiological Roles | Chronic, Maladaptive Effects | Pathological Outcomes |
|---|---|-----------------------|
| Regulation of glucose homeostasis | Hyperglycaemia Insulin resistance | Diabetes mellitus |
| Maintenance of energy homeostasis | Visceral adiposity General weight gain | Obesity |
| Maintenance of vascular tone and blood pressure | Impaired vasodilation Increased contractility Plasma volume expansion | Hypertension |
| Regulation of lipid metabolism | Elevated cholesterol Elevated triglycerides | Dyslipidaemia |
| Heart development and function | Bradycardia Cardiac hypertrophy | Heart failure |
| Regulation of clotting factors and fibrinogen | Hypercoagulability | Thrombosis |

Effetti del M. di Addison sul cuore

Il **deficit di forza** muscolare coinvolge anche il miocardio ed è aggravato dall'**iperkaliemia**.

Trattamento

- Cortone 25 mg: 3/4 – 1+1/2 cp/die fraz.**
- Hydrocortisone 10 mg: 1+1/2 – 4 cp/die fraz**
- Plenadren 5 o 20 mg: 25 - 30 mg h.8**

ma mai esagerare, altrimenti

forte aumento della probabilità di cardiopatia ischemica,
soprattutto

- nelle donne ($F = 2xM$),
- in rapporto ad alte dosi sostitutive di corticosteroidi.

| IPERKALEMIA | | |
|--------------------------|---|---|
| Livello K+ sierico | Aspetto dell'ECG | Anomalia dell'ECG |
| lieve (5.5-6.5 mEq/L) |  | Onde T a picco Segmento PR prolungato |
| moderato (6.5-8.0 mEq/L) |  | Perdita dell'onda P Complesso del QRS prolungato Elevazione del tratto ST Battiti ectopici e alterazioni di ritmo |
| severo (>8.0 mEq/L) |  | Slargamento del complesso QRS Fibrillazione ventricolare, asistoliam, deviazione dell'asse BB, blocchi fascicolari |

Effetti di M.i di Cushing e Conn sul cuore

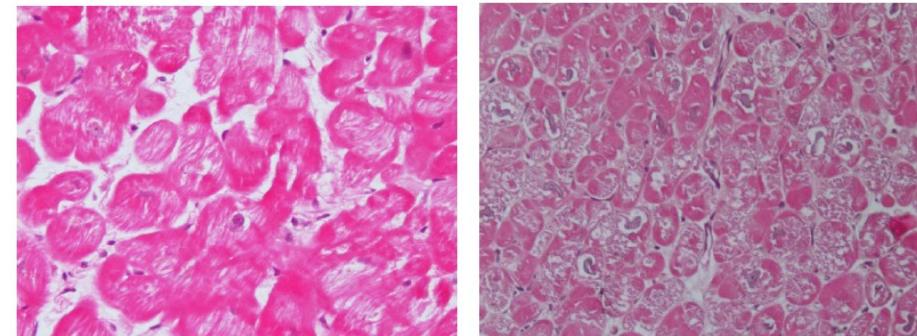
The excessive activation of MRs by cortisol / aldosterone has deleterious effects on the cardiovascular system through sympatho-excitation
elevated salt appetite } hypertension & K^+
renal retention of salt
heart fibrosis and remodelling à atrial and ventricular arrhythmias

Sztechman D et .al. DOI: 10.26402/jpp.2018.6.01heart

IPERKALEMIA

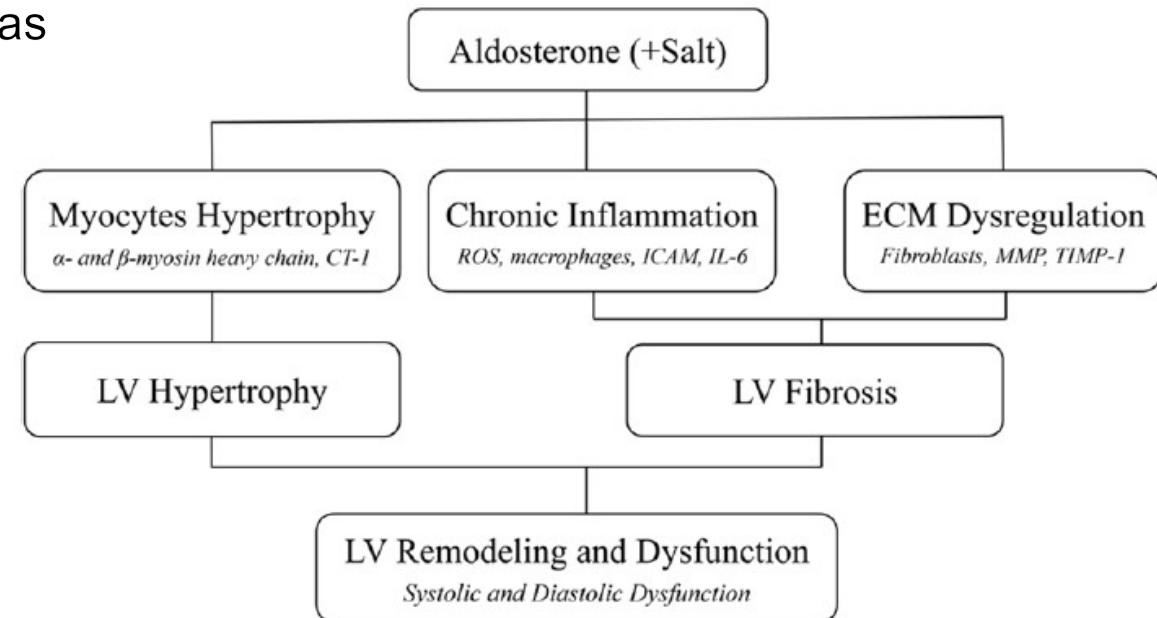
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reduction in contractile elements because of **gluconeogenesis** due to cortisol overproduction in Cushing's syndrome



enlarged and vaculated mycardiocytes due to **water accumulation** in aldosterone excess conditions

Tsai C-H et al. J Hum Hypertens (2021) 35:131–147



Petramala L et al Int. J. Mol. Sci. 2020, 21, 5047; doi:10.3390/ijms21145047

Sarcoidaìosi ed altre gravi malattie autoimmuni

Table 2. Summary of Arrhythmia-Associated Mortality In Individual Autoimmune Diseases

| Autoimmune disease | Arrhythmia-associated mortality (% total deaths) |
|------------------------------|---|
| Sarcoidosis | 24–65* |
| Systemic lupus erythematosus | 7.3*–21 |
| Scleroderma | 6.0–15 |
| Type 1 diabetes | 8.0–15 |
| Graves' disease | 8.0 |
| Rheumatoid arthritis | 0.8 |
| Ankylosing spondylitis | 0.5 |

Inflammatory processes and oxidative stress lead to cardiomyocyte necrosis in severe autoimmune disease, causing

- generalized inflammation → sympathetic overactivation and parasympathetic function decline
- myocardial inflammation } → ARRHYTHMIAS
- fibrosis

DIAGNOSI E TERAPIA della SARCOIDOSI CARDIACA

| Stage | Rest MPS (Viability) | FDG-PET (Inflammation) | LGE CMR (Fibrosis) |
|-----------------------------------|-------------------------|---------------------------|-----------------------|
| Normal | Normal | | Absent |
| Early | Normal | | Absent |
| Progressive | Mild defect | | Absent |
| Peak active | Moderate defect | | Abnormal |
| Progressive myocardial impairment | Severe defect | | Abnormal |
| Fibrosis/ Burnt out | Severe defect | Absent | Absent |

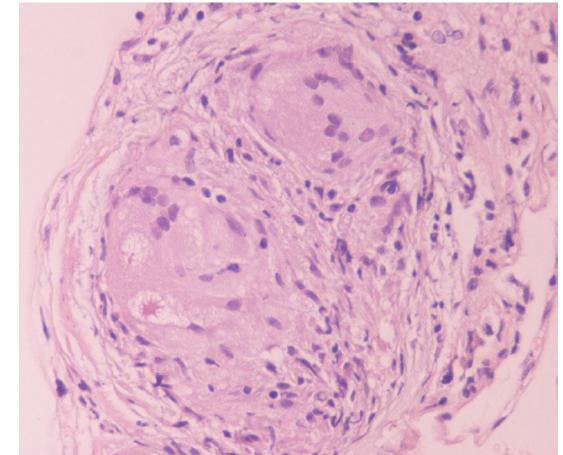
The primary goals of **EARLY TREATMENT** for cardiac sarcoidosis are to:

- **DECREASE INFLAMMATION**
- **PREVENT FIBROSIS** or scarring associated with granuloma onset
- preserve cardiac function
- reduce SCD risk associated with conduction abnormalities

Serial 18 F-FDG-PET/CT may be used to determine corticosteroid treatment option:
intensification vs tapering

Typical approach: Prednisone
40 -> 5 mg daily x 2-3 yrs

Tan J-L et al. Am J Cardiol (2019) 123: 513-22



BRADICARDIA CORTICOSTEROIDEA

Rheumatology International (2018) 38:2337–2343
<https://doi.org/10.1007/s00296-018-4167-1>

Rheumatology
INTERNATIONAL

CASES WITH A MESSAGE



Dose-dependent bradycardia as a rare side effect of corticosteroids: a case report and review of the literature

Döndü Üsküdar Cansu¹ · Erdal Bodakçı¹ · Cengiz Korkmaz¹

- Suggestive symptoms: **DIZZINESS, FATIGUE, unexpected bradycardia**
- supposed pathophysiological **MECHANISM**: suppressed cytokine production and SNS activation
- **UNPREDICTABLE**
- mostly **DOSE-DEPENDENT**
- **EARLY ONSET**: 1 min to 5 days
- **TREATMENT**: steroid withdrawal (vet. sometimes spontaneous recovery)



DUBBI - DOMANDE ?

