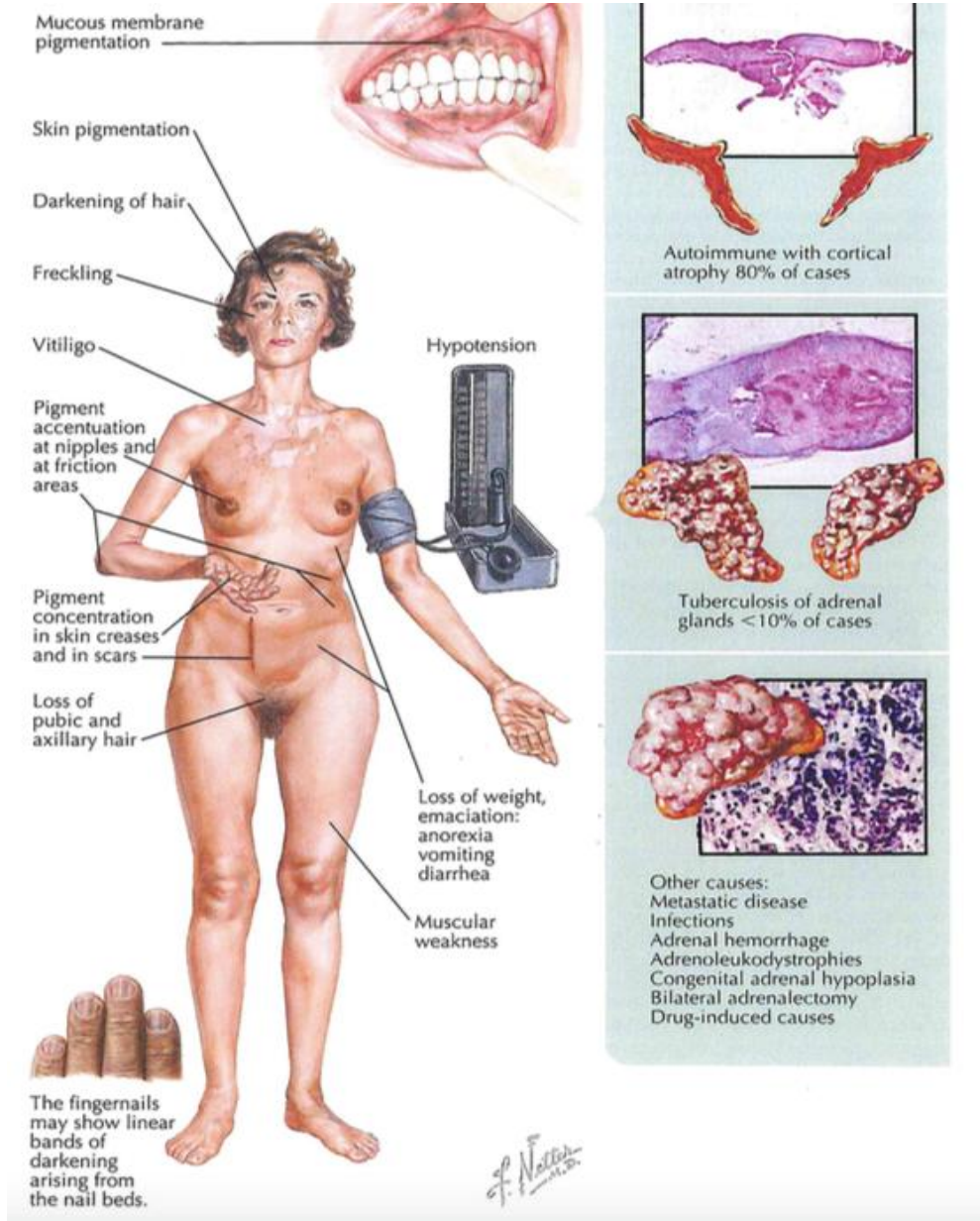
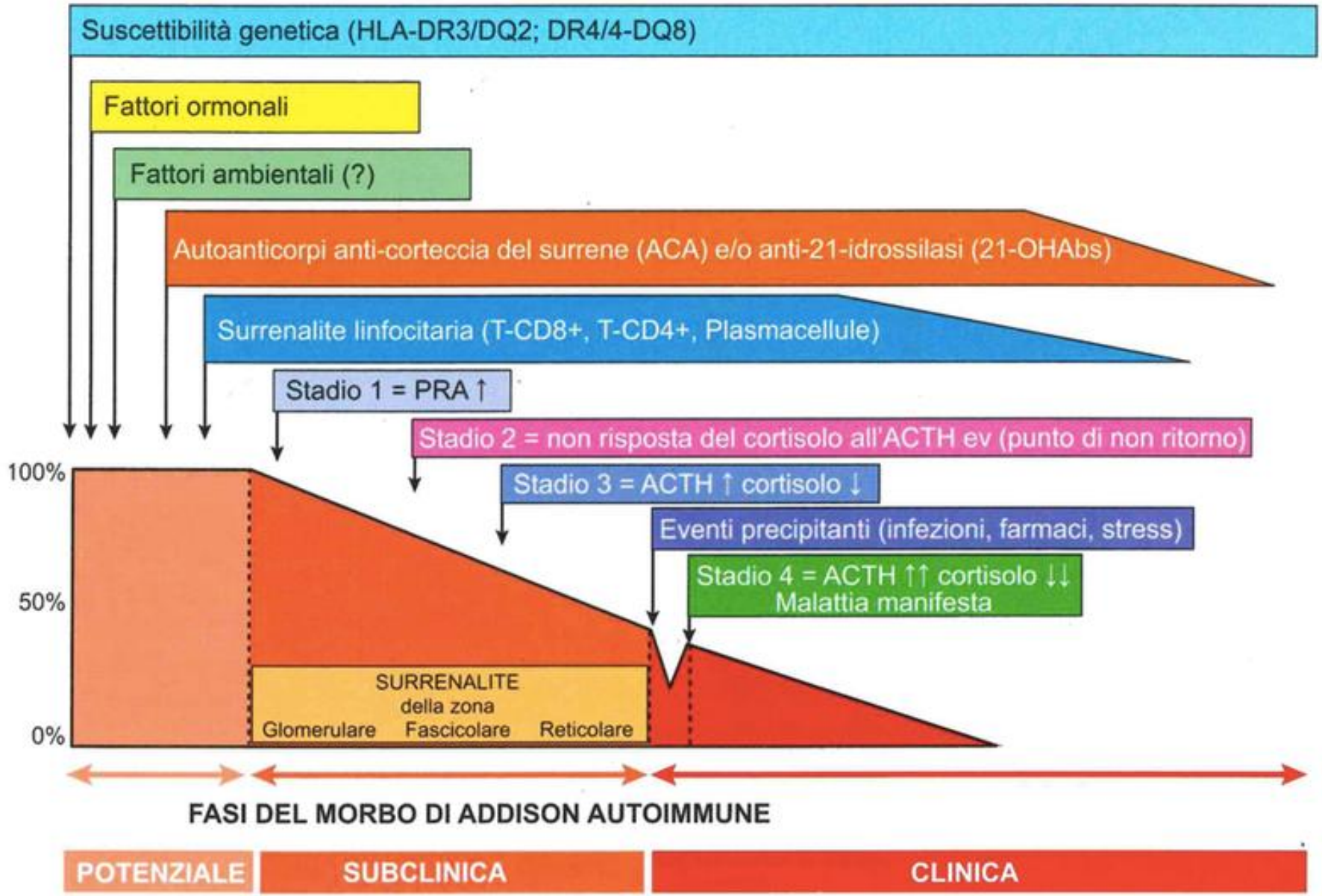
Table 2. Major Etiologies of PAI and Associated Features

Etiology	Associated Features
Autoimmune	
Isolated	Not associated with other autoimmune disorders
APS type 1 (APECED)	Chronic cutaneous candidiasis, hypoparathyroidism
APS type 2	Autoimmune thyroid disease, type 1 diabetes
Adrenal—infiltration/injury	
Adrenal hemorrhage	Associated with sepsis, anticoagulants, anti-cardiolipin/lupus anti-coagulant syndrome
Adrenal metastases	Malignancies: lung, breast, colon, melanoma, lymphoma
Infections: adrenalitis	Tuberculosis, HIV/AIDS, CMV, candidiasis, histoplasmosis, syphilis, African trypanosomiasis, paracoccidioidomycosis (eg, in South America)
Infiltration	Hemochromatosis, primary amyloidosis
Bilateral adrenalectomy	Procedure for intractable Cushing's syndrome or bilateral pheochromocytoma
CAH: most forms can cause salt loss	Commonest cause of PAI in children (80%); may be diagnosed in older individuals
21-Hydroxylase deficiency	Commonest type of CAH is 21-hydroxylase deficiency, with associated hyperandrogenism
11β-hydroxylase deficiency	Hyperandrogenism, hypertension (in older children and adults)
3β-hydroxysteroid dehydrogenase II deficiency	Ambiguous genitalia in boys, hyperandrogenism in girls
P450 side-chain cleavage deficiency (CYP11A1 mutations)	XY sex reversal
P450 oxidoreductase deficiency	Skeletal malformations, abnormal genitalia
Congenital lipoid adrenal hyperplasia (StAR mutations)	XY sex reversal
Adrenal hypoplasia congenita	X-linked NROB1, Xp21 deletion (with Duchenne's muscular deficiency), SF-1 mutations (XY sex reversal), IMAGe syndrome
ACTH insensitivity syndromes	Type 1: ACTH receptor, melanocortin 2 receptor gene MC2R Type 2: MRAP Familial glucocorticoid deficiency (MCM4, NNT, TXNRD2) TripleA (Allgrove's) syndrome, achalasia, Addison's disease, alacrima, AAAS gene mutation
Drug-induced	Adrenal enzyme inhibitors: mitotane, ketoconazole, metyrapone, etomidate, aminoglutethimide, drugs that may accelerate cortisol metabolism and induce adrenal insufficiency T_4 also accelerates cortisol metabolism (at least in part through stimulation of 11β-HSD2) CTLA-4 inhibitors may enhance autoimmunity and cause PAI
Other metabolic disorders	Mitochondrial disease (rare) Adrenoleukodystrophy in males Wolman's disease




Suscettibilità genetica (HLA-DR3/DQ2; DR4/4-DQ8)
Fattori ormonali
Fattori ambientali (?)
Autoanticorpi anti-corteccia del surrene (ACA) e/o anti-21-idrossilasi (21-OHAbs)
Surrenalite linfocitaria (T-CD8+, T-CD4+, Plasmacellule)
Stadio 1 = PRA ↑
Stadio 2 = non risposta del cortisolo all'ACTH ev (punto di non ritorno)
Stadio 3 = ACTH ↑ cortisolo ↓
Eventi precipitanti (infezioni, farmaci, stress)
Stadio 4 = ACTH ↑↑ cortisolo ↓↓
Malattia manifesta
100%
50%
0%
SURRENALITE
della zona
Glomerulare
Fascicolare
Reticolare
FASI DEL MORBO DI ADDISON AUTOIMMUNE
POTENZIALE
SUBCLINICA
CLINICA

NO CORTISOLO (↑ACTH)

NO ALDOSTERONE (↑renina)

Creatinina (metodo enzimatico IFCC-IDMS)	**0.91**		mg/dL
eGFR: filtrato glomerulare stimato (CKD-EPI)	**>60**		ml/min

Stima GFR non applicabile in gravidanza, nelle persone con obesità o grave magrezza e afroamericani il risultato del GFR deve essere moltiplicato per 1.159.

Sodio	**135**		mEq/L
Potassio	**5.10**		mEq/L

Immunometria

ACTH ore 8	**298.8**	>	pg/mL
Cortisolo ore 8	**375**		nmol/L

Creatinina (metodo enzimatico IFCC-IDMS)	**0.79**		mg/dL
Sodio	**125**	<	mEq/L
Potassio	**4.31**		mEq/L
Proteina C reattiva	**10.5**		mg/L

Immunometria

ACTH ore 8	**1497.0**	>	pg/mL
Cortisolo ore 8	**48**	<	nmol/L

Creatinina (metodo enzimatico IFCC-IDMS)	**2.56**	>	mg/dL
Sodio	**126**	<	mEq/L
Potassio	**7.76**	>	mEq/L

invio fax 4009

ACTH ore 8	**2844.0**	>	pg/mL
Cortisolo ore 8	**57**	<	nmol/L

Acute adrenal insufficiency, also known as **adrenal crisis or Addisonian crisis,** is a **life threatening emergency** resulting from a lack of cortisol, the major glucocorticoid. [1] It can affect patients with adrenal insufficiency of any aetiology.

Significance

Patients with established adrenal insufficiency and those receiving chronic exogenous supraphysiological glucocorticoid treatment (eg for asthma or autoimmune disease) and topical or injected steroids, including for joint or back problems, are at possible risk of adrenal crisis. Adrenal insufficiency-related hospital admissions and adrenal crises (with their associated morbidity and mortality) have increased considerably in the last two decades, [2] [3] with one in 200 adrenal crises being fatal. [1] [4]

Recognition of adrenal crisis

Signs and symptoms of adrenal crisis can include:

- Nausea/vomiting
- Abdominal pain
- Low grade fever
- Muscle pain
- Headache
- Hypoglycaemia (especially in children)

Later signs/symptoms include:

- Reduced consciousness
- Confusion
- Hypotension
- Hypovolemic shock
- Cold peripheries

Emergency management of an adrenal crisis

If adrenal crisis is suspected, then treatment must be started immediately. It must not be delayed by investigations.

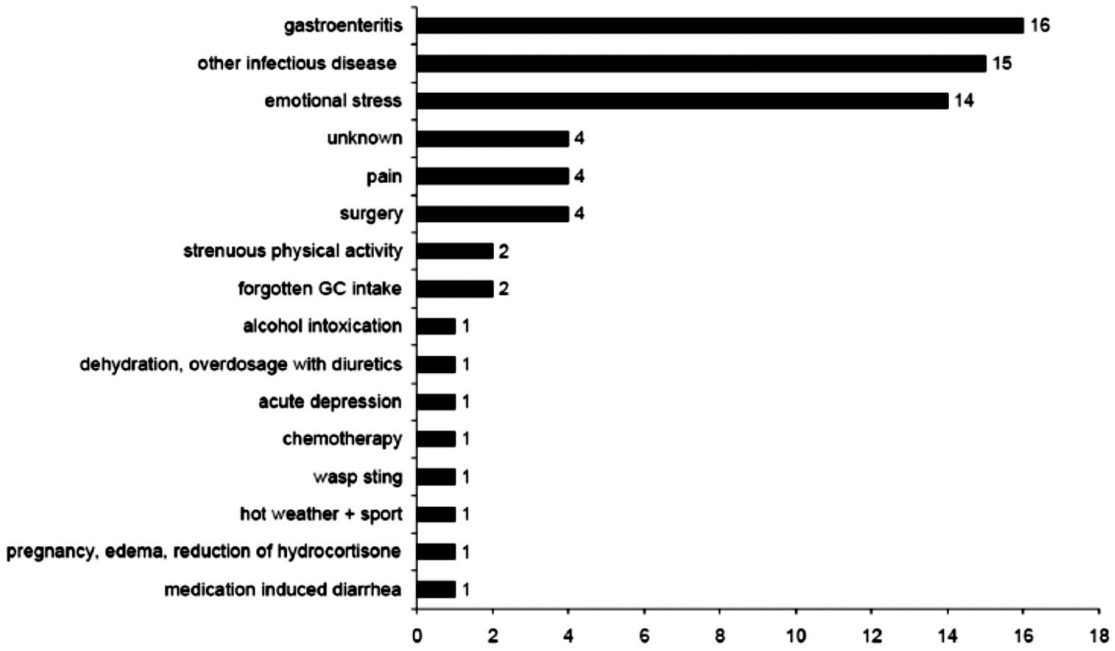
Hydrocortisone injection

- Hydrocortisone sodium phosphate 100 mg 1 ml vial of liquid, **or**
- Hydrocortisone sodium succinate 100 mg (Solu-Cortef powder) plus 2 ml vial of water
- Intramuscular (blue) needles and 2 ml syringes
- Three to five vials of injectable hydrocortisone in case of breakages and for a second emergency injection kit (for administration in case of vomiting, illness, accident, or other severe injury)

Note: Hydrocortisone acetate is slow acting so should not be used.

La crisi surrenalica: il problema è (ri)conoscerla!

EMERGENZA MEDICA
Incidenza 6-8 pazienti/100 all'anno



<u>DETERIORAMENTO dello STATO di SALUTE</u>
con (2 dei seguenti):
IPOTENSIONE
NAUSEA o VOMITO
ASTENIA PROFONDA
FEBBRE
SONNOLENZA/STATO SOPOROSO
IPONATRIEMIA
IPERKALIEMIA
IPOGLICEMIA

↓

CRISI SURRENALICA

↓

IDROCORTISONE 100 mg

Hahner S JCEM 2015; Bornstein SR JCEM 2016; Allolio B EJE 2015