"CORTICOTERAPIA EN NEONATOLOGÍA: UN ENFOQUE BASADO EN LA EVIDENCIA"

DRA. ALEXANDRA VIMOS TIXI
ENDOCRINOLOGA PEDIATRA

CONFLICTO DE INTERES

Declaro que esta información será utilizada solo con fines educativos para estudiantes de medicina, médicos generales, pedíatras medicos de atención primaria.

Es presentación es preparada por mi persona para el grupo de personas antes enunciadas

OBJETIVOS

1. Revisión de embriogénesis de glándula suprarrenal
2. Fisiología de la glándula suprarrenal fetal neonatal y de lactante
3. Valores de referencia
4. Uso o abuso de esteroides: cuales y cuando - evidencia ??

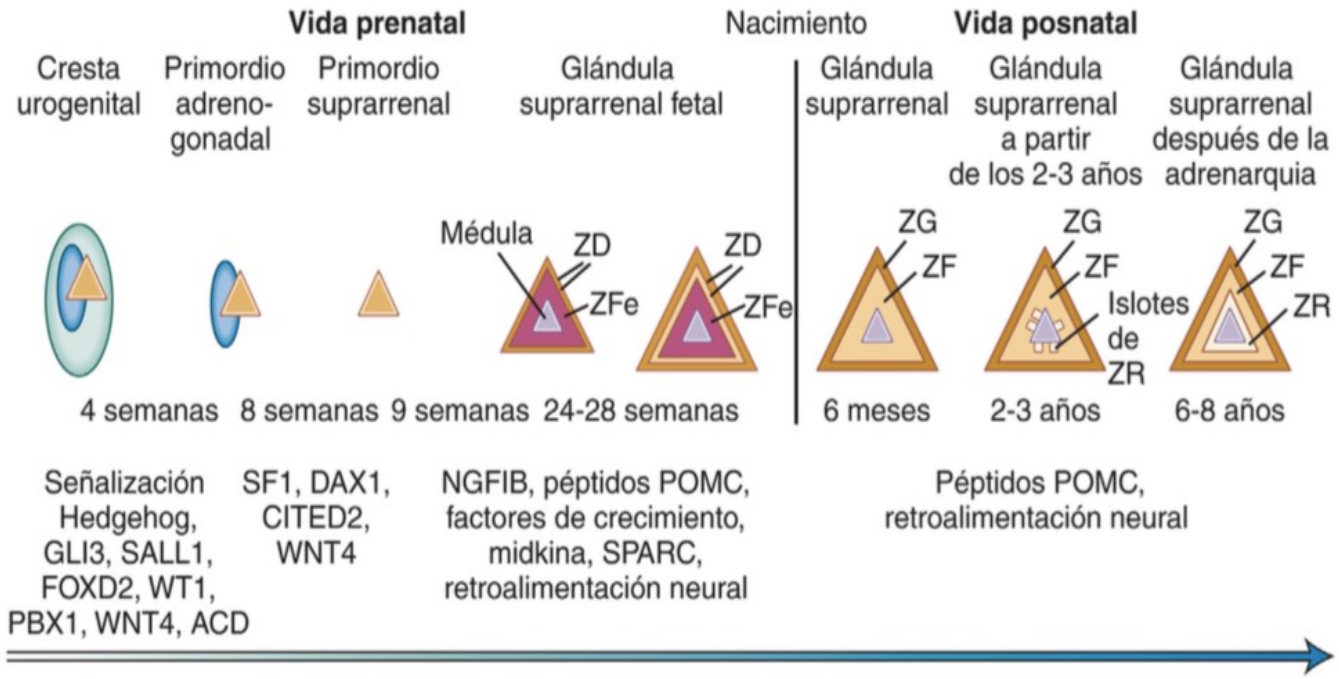
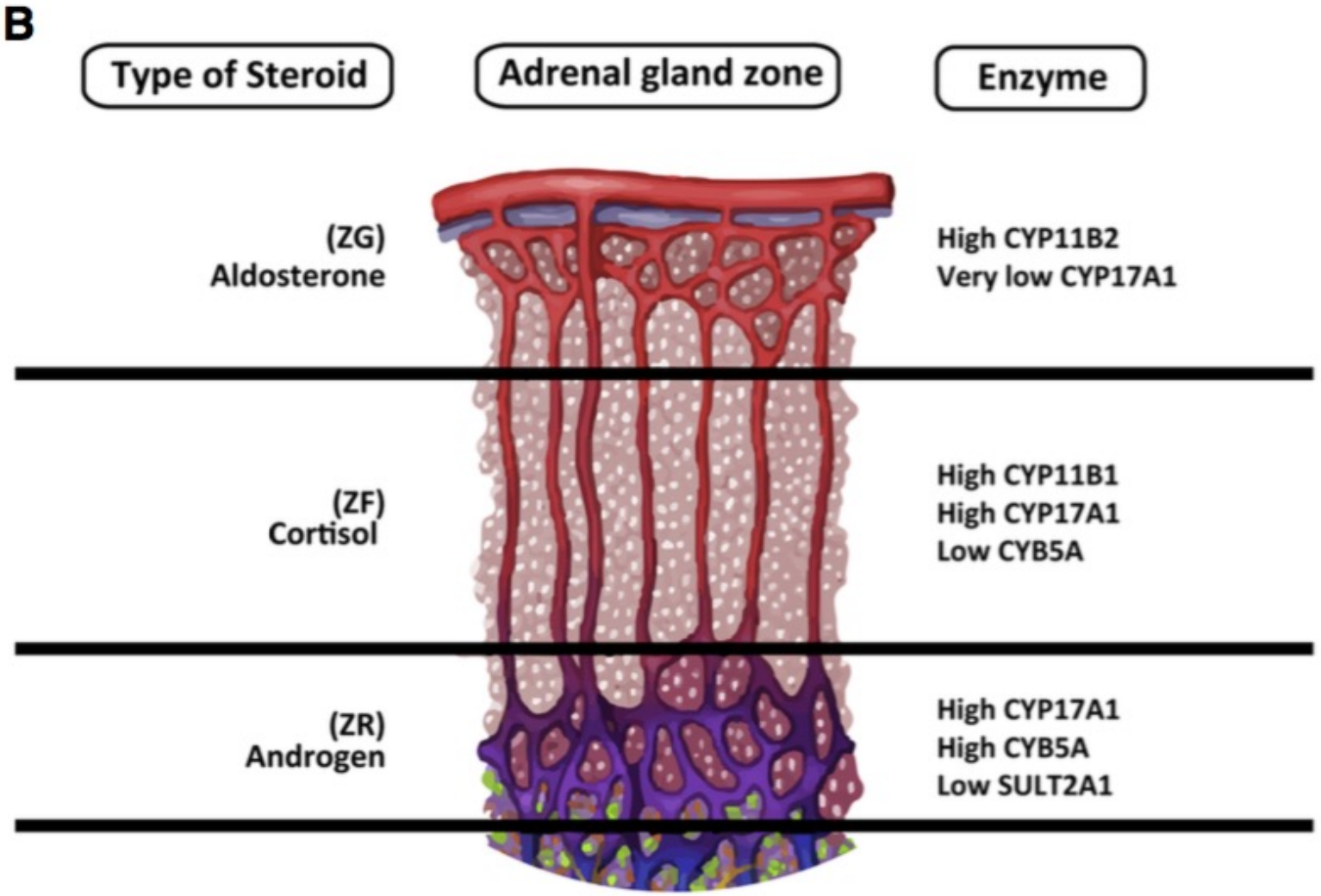


Figura 15-1 Diagrama esquemático del desarrollo de la corteza suprarrenal humana durante la vida prenatal y posnatal; se ilustran los factores de transcripción activos en cada estadio (v. más detalles en el texto). POMC, proopiomelanocortina; SPARC, proteína ácida secretada rica en cisteína (osteonectina); ZD, zona definitiva; ZF, zona fascicular; ZFe, zona fetal; ZG, zona glomerular; ZR, zona reticular.

Endocrine (2019) 63:407–421
https://doi.org/10.1007/s12020-018-01835-3

REVIEW

Clinical perspectives in congenital adrenal hyperplasia due to 3β-hydroxysteroid dehydrogenase type 2 deficiency



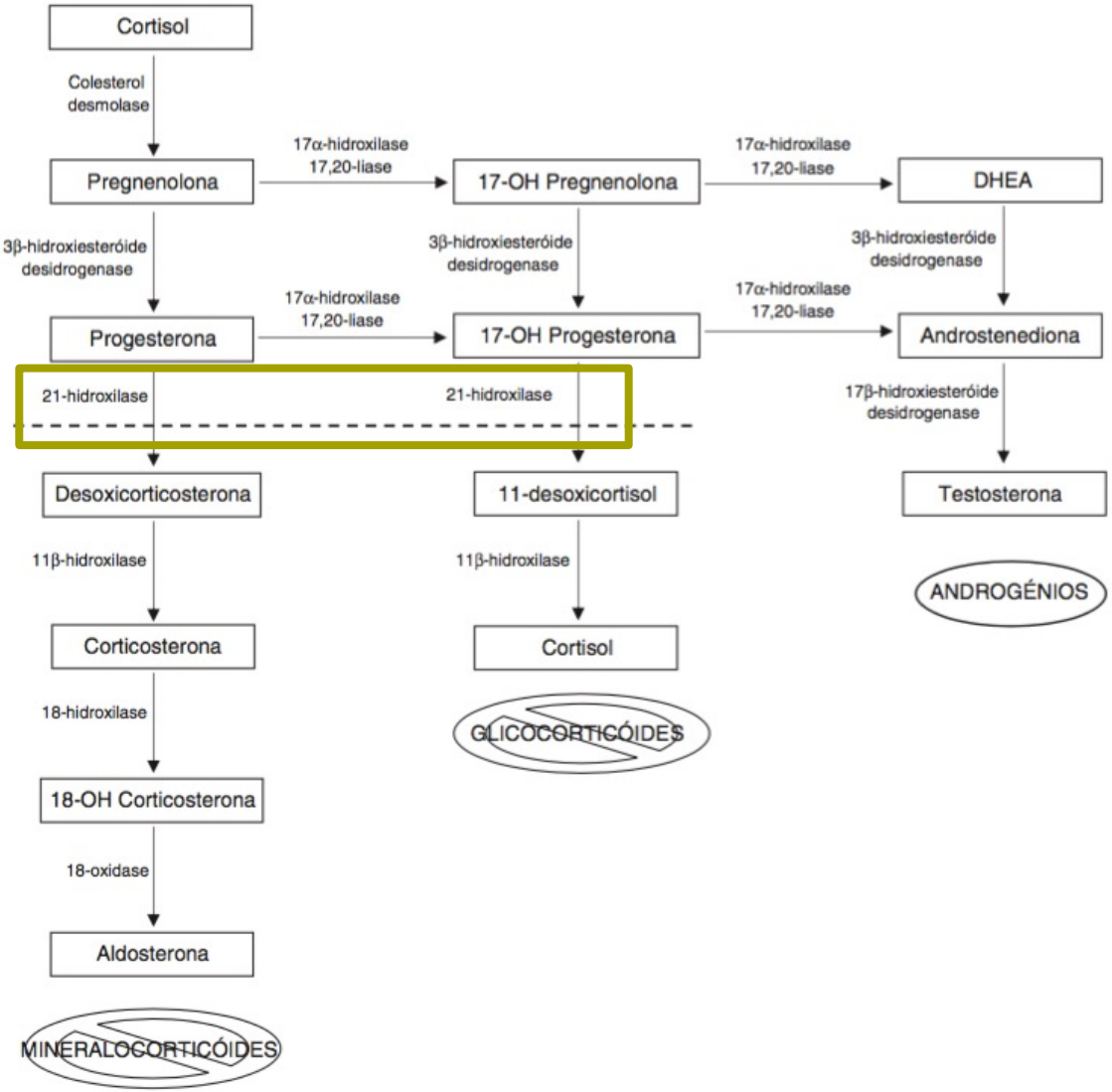
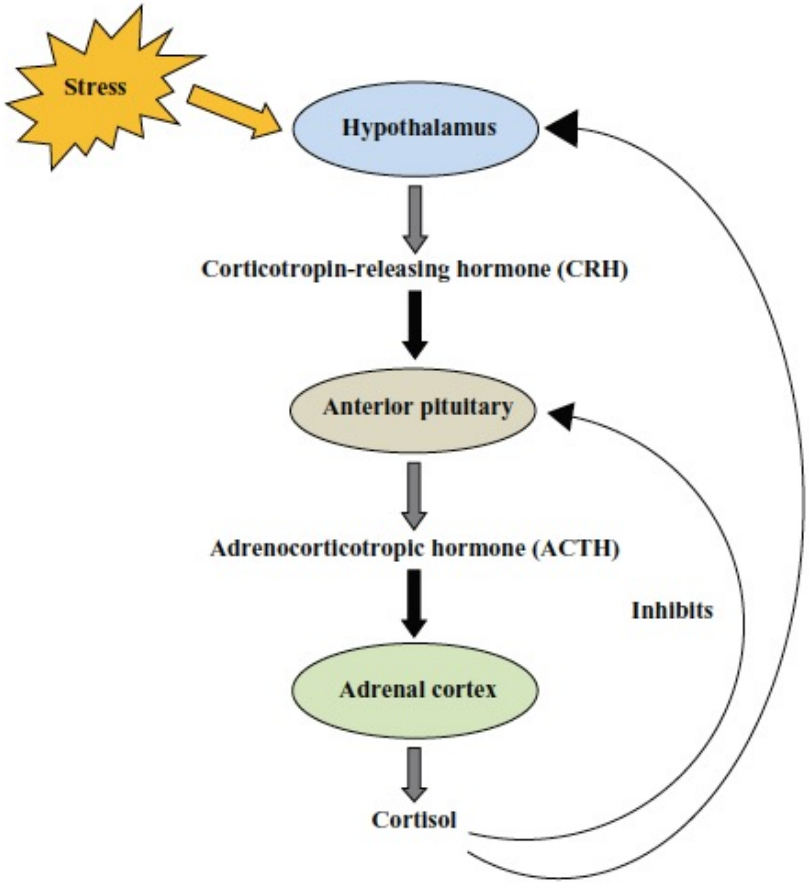

Cortisol
Colesterol desmolase
Pregnenolona
17α-hidroxilase 17,20-liase
17-OH Pregnenolona
17α-hidroxilase 17,20-liase
DHEA
3β-hidroxiesteróide desidrogenase
3β-hidroxiesteróide desidrogenase
3β-hidroxiesteróide desidrogenase
Progesterona
17α-hidroxilase 17,20-liase
17-OH Progesterona
17α-hidroxilase 17,20-liase
Androstenediona
21-hidroxilase
21-hidroxilase
17β-hidroxiesteróide desidrogenase
Desoxicorticosterona
11-desoxicortisol
Testosterona
11β-hidroxilase
11β-hidroxilase
ANDROGÉNIOS
Corticosterona
Cortisol
18-hidroxilase
GLICOCORTICÓIDES
18-OH Corticosterona
18-oxidase
Aldosterona
MINERALOCORTICÓIDES

FIGURE 1 ■ Cortisol feedback system.



Modified from Barrett EJ. The adrenal gland. In: Boron WF, Boulpaep EL, eds. *Medical Physiology*. 2nd ed. Philadelphia, PA: Saunders; 2012:1057-1073.

POINTERS IN PRACTICAL PHARMACOLOGY

Hydrocortisone for Treatment of Hypotension in the Newborn

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TABLE 2 ■ Adrenal Gland Hormones[29]

Structure	Hormone Released	Function
	Adrenal Cortex	
Zona glomerulosa	Mineralocorticoids (mainly aldosterone)	Increase • Urine excretion of K^+ • Reabsorption of Na^+ • Retention of water
Zona fasciculata	Glucocorticoids (mainly cortisol)	Increase • Gluconeogenesis • Blood glucose • Retention of water Anti-inflammatory effects
Zona reticularis	Androgens (mainly DHEA)	Sex hormone precursor
	Adrenal Medulla	
Chromaffin cells (functional postganglionic equivalent cells)	Epinephrine (synthesized solely in adrenal medulla) Dopa Dopamine Norepinephrine	Catecholamine fight or flight responses to stress Increase heart rate and contractility, vasoconstriction, mobilization of fuel stores, pupillary dilation

Abbreviation: DHEA 5 dehydroepiandrosterone.

Modified from Barrett EJ. The adrenal gland. In: Boron WF, Boulpaep EL, eds. *Medical Physiology*. 2nd ed. Philadelphia, PA: Saunders; 2012:1057-1073.

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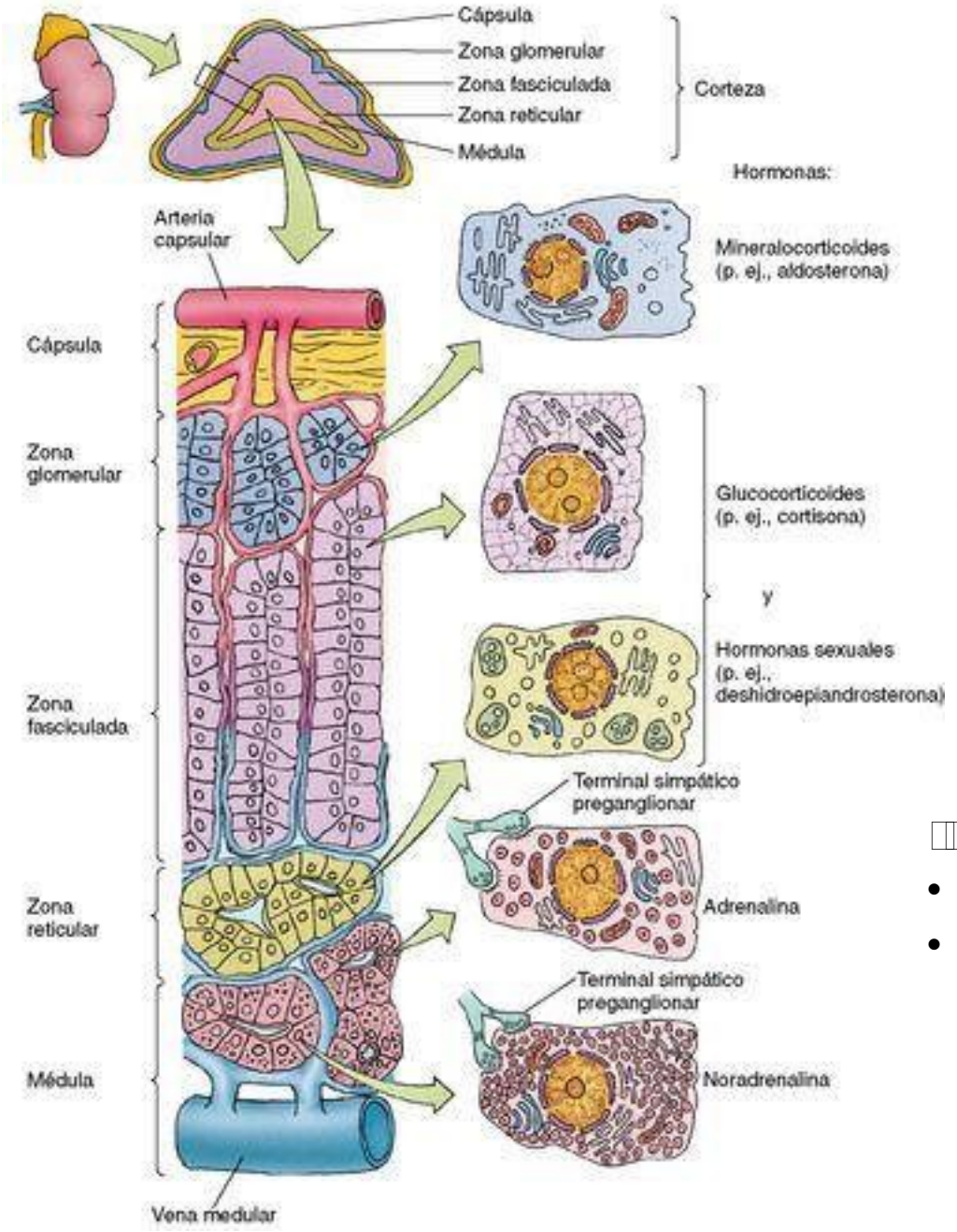
Cápsula
Zona glomerular
Zona fasciculada
Zona reticular
Médula
Corteza
Hormonas:
Arteria capsular
Mineralocorticoides (p. ej., aldosterona)
Cápsula
Zona glomerular
Glucocorticoides (p. ej., cortisona)
y
Hormonas sexuales (p. ej., deshidroepiandrosterona)
Zona fasciculada
Terminal simpático preganglionar
Adrenalina
Zona reticular
Terminal simpático preganglionar
Médula
Noradrenalina
Vena medular

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- [illegible]

RANGOS DE 17 OH PROGESTERONA / DHEAS EDAD – TIEMPO

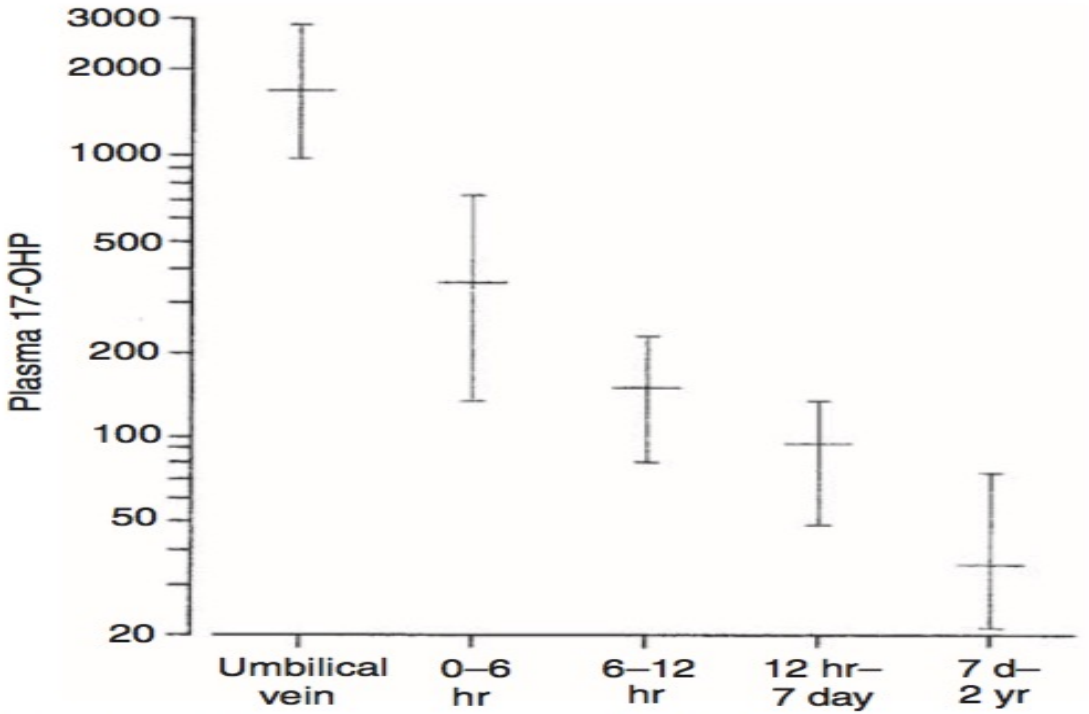

FIGURE 13-14 ■ Means and ranges of 17OHP in normal newborns (data are in ng/100 mL). Note that values can be very high and quite variable for the first 24 hours of life.

RANGOS DE 17 OH PROGESTERONA / DHEAS EDAD – TIEMPO

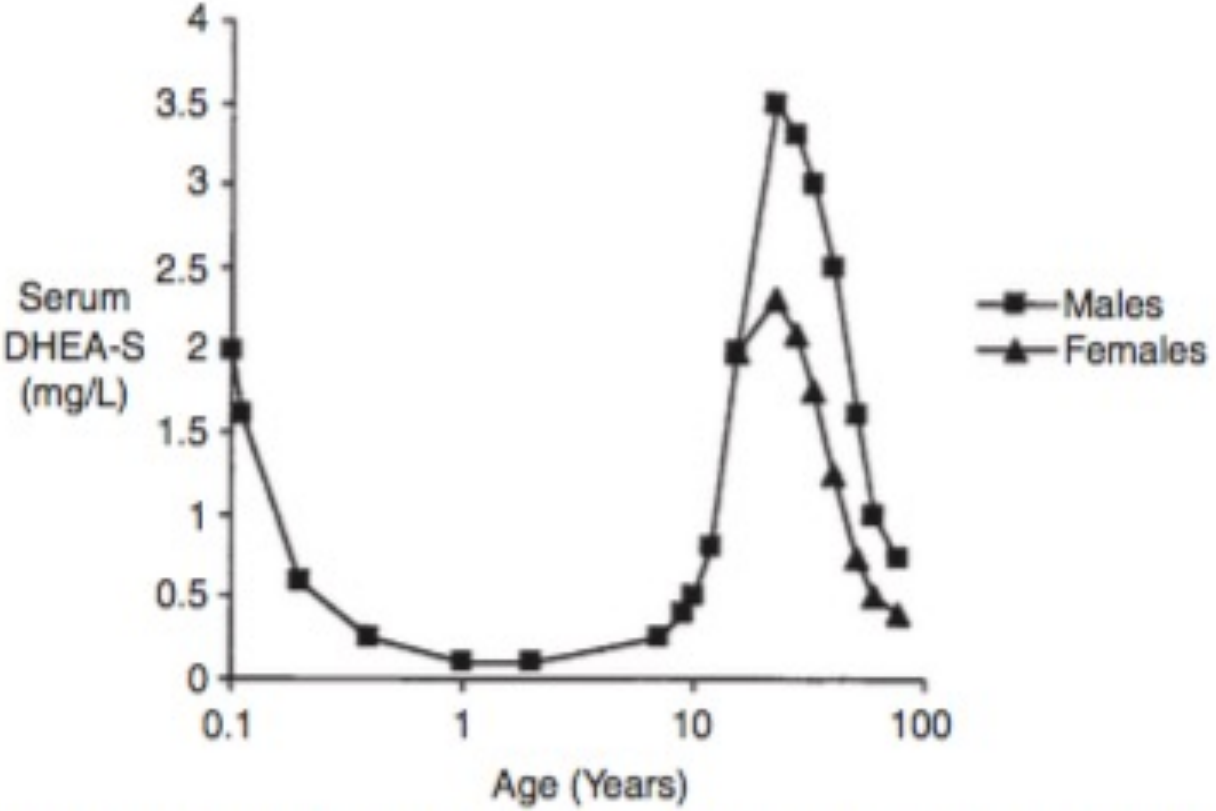

FIGURE 13-9 ■ Concentrations of DHEAS as a function of age. Note that the x-axis is on a log scale.

ADRENAL CORTEX AND ITS DISORDERS WALTER L. MILLER, MD • CHRISTA E. FLÜCK, MD CHAPTER 13

DIAGNÓSTICO BIOQUIMICO HSC NO CLASIFICA

Rev Port Endocrinol Diabetes Metab. 2014;9(1):59–64

ELSEVIER DOYMA

Revista Portuguesa
de Endocrinologia, Diabetes e Metabolismo

www.elsevier.pt/rpedm

Revisão

Hiperplasia congénita da suprarrenal não clássica – aspetos relevantes para a prática clínica

Teresa Azevedo[a,*], Teresa Martins[a], Manuel Carlos Lemos[a,b] e Fernando Rodrigues[a]

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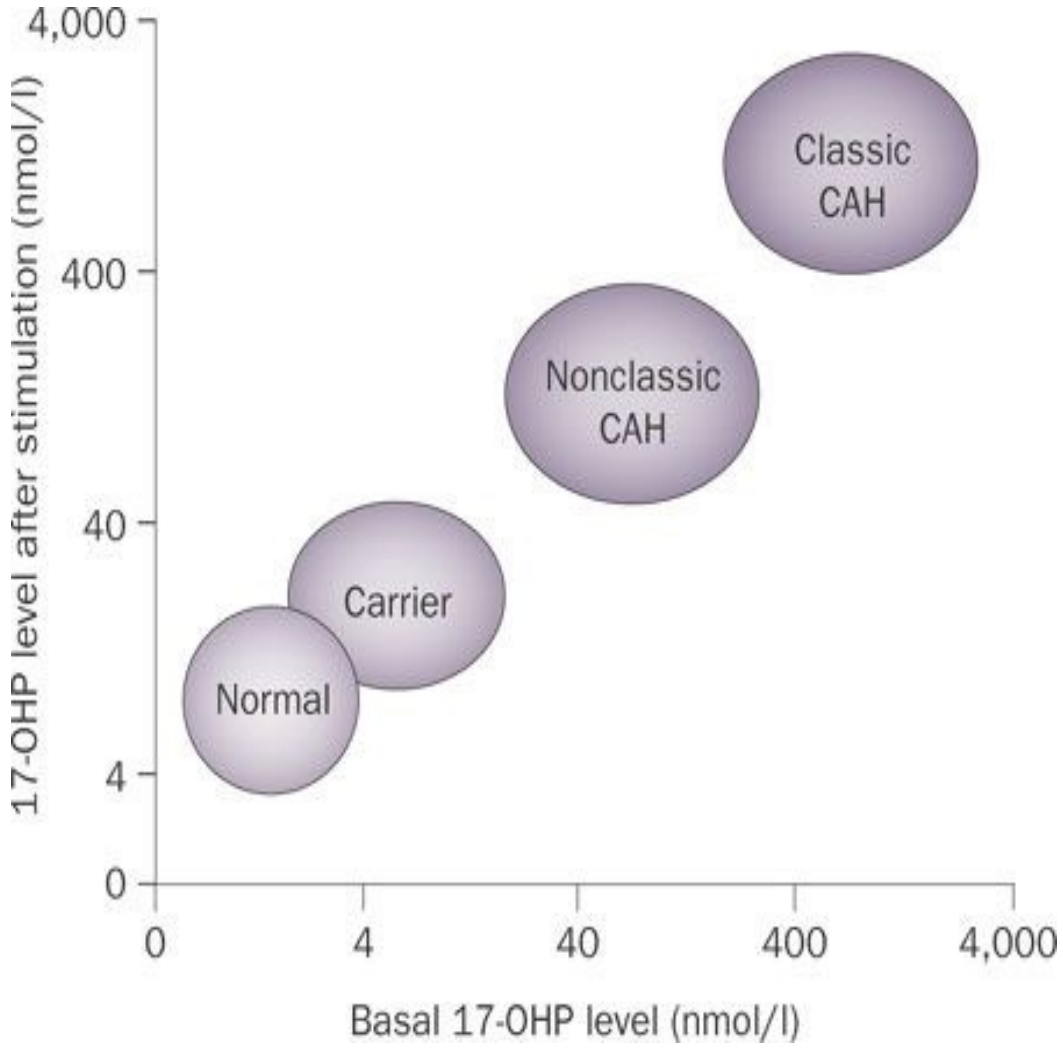
[b] Centro de Investigação em Ciências da Saúde (CICS), Universidade da Beira Interior, Covilhã, Portugal

a 2. Valores de referência para diagnóstico de hiperplasia congénita suprar
través da prova de estimulação com ACTH.

NORMOGRAMA POST ESTIMULO



PERRY WHITE. NEONATAL SCREENING FOR CONGENITAL ADRENAL HIPERPLASIA. NAT REV ENDOCRINOL. 2009 SEP;5(9):490-8

FACTORES QUE INTERVIENEN EN NIVELES DE 17 OH PROGESTERONA

NIVELES POR PESO

Indian J Pediatr (January 2013) 80(1):21–25

Table 1 Comparison of 17OHP levels in various weight ranges

Weight ranges	< 1500 g	1500–2000 g	2000–2500 g	> 2500 g
Median 17OHP ng/ml	45	34	20	14
Interquartile range	30–60	23.5–50	14–30	7.75–32.75

SERUM 17 ALPHA HYDROXYPROGESTERONE IN NORMAL FULL. TERM AND PRETERM VS. SICK PRETERM AND FULL TERM NEWBORNS IN A TERTIARY HOSPITA. INDIAN J PEDIATR (JANUARY 2013) 80(1):21–25

NIVEL POR EDAD GESTACIONAL

Table 2 Comparison of 17OHP levels in various gestational groups

Gestational groups	Number of cases	Median 17 OHP ng/ml	Interquartile range
28–32 wk	8	41.50	22.5 to 71.25
32–36 wk	39	30.00	20 to 58
36–38 wk	13	15.00	9.10 to 21.25
38–40 wk	53	14.00	8.30 to 32.25
40–42 wk	9	29.00	6.35 to 35.50

SERUM 17 ALPHA HYDROXYPROGESTERONE IN NORMAL FULL. TERM AND PRETERM VS. SICK PRETERM AND FULL TERM NEWBORNS IN A TERTIARY HOSPITA. INDIAN J PEDIATR (JANUARY 2013) 80(1):21–25

EDAD GESTACIONAL Y ESTADO DE SALUD

Table 3 Serum 17 OHP levels in normal and sick full term and preterm babies at 3 to 5 d after birth and on follow up at 3 mo

	Serum 17 OHP (ng/ml) at 3 to 5 d [median, interquartile range, no. of cases]	Serum 17 OHP levels (ng/ml) on follow- up at 3 mo) (median and interquartile, no. of cases)	Wilcoxon signed rank test *p* value
FT	8.4 (6–13) (*n*=33)	1.50(0.97–2.02) (*n*=6)	0.02
PT	20 (11–29.5)(*n*=36)	0.9(0.62–2.2) (*n*=27)	0.000
FS	34 (26–45)(*n*=29)	1.3(0.7–4.45) (*n*=21)	0.000
PS	58(40.75–76.5)(*n*=24)	1.3(0.6–3.4) (*n*=19)	0.000

FT Full term healthy newborns; *PT* Preterm healthy newborns; *FS* Full term stressed newborns; *PS* Preterm stressed newborns

SERUM 17 ALPHA HYDROXYPROGESTERONE IN NORMAL FULL. TERM AND PRETERM VS. SICK PRETERM AND FULL TERM NEWBORNS IN A TERTIARY HOSPITA. INDIAN J PEDIATR (JANUARY 2013) 80(1):21–25

FACTORES QUE MODIFICAN

Sex of the baby	−0.110	0.228
Gestational age	−0.299	0.001
Stress factor	0.678	0.000
Birth weight	−0.370	0.000
Maternal antenatal steroids	0.221	0.014
Apgar score	−0.432	0.000
Mode of delivery	0.360	0.000
TSH levels	−0.169	0.06
Presence of maternal illness	0.200	0.027
Admission in NICU	0.659	0.000
Use of ventilation	0.420	0.000

SERUM 17 ALPHA HYDROXYPROGESTERONE IN NORMAL FULL. TERM AND PRETERM VS. SICK PRETERM AND FULL TERM NEWBORNS IN A TERTIARY HOSPITA. INDIAN J PEDIATR (JANUARY 2013) 80(1):21–25

Kopacek et al. BMC Pediatrics (2017) 17:22
DOI 10.1186/s12887-016-0772-x

BMC Pediatrics

RESEARCH ARTICLE Open Access

Neonatal screening for congenital adrenal hyperplasia in Southern Brazil: a population based study with 108,409 infants

Cristiane Kopacek[1,4], Simone Martins de Castro[1,2,5*], Mayara Jorgens Prado[2,3], Claudia Maria Dornelles da Silva[3], Luciana Amorim Beltrão[1] and Poli Mara Spritzer[4]

Table 3 Family history, maternal, perinatal, newborn and laboratory data of newborns diagnosed with congenital adrenal hyperplasia vs. false positive newborns

Variables	CAH cases ($n = 8$)	False positives ($n = 109$)	p
Maternal data			
Caesarean delivery (n [%])	4/8 (50.0)	42/70 (60.0)	0.496
Newborn data			
ICU care (n [%])	4/8 (50.0)	71/98 (72.4)	0.281
Preterm (n [%])	2/8 (25.0)	59/109 (54.1)	0.004
Birth weight (n [%])	2940 ± 570.34 ($n = 8$)	2496 ± 761.63 ($n = 109$)	0.110
Gestational age (week)	38.0 ± 1.9 ($n = 8$)	34.8 ± 3.2 ($n = 72$)	0.007
Dehydration (n [%])	5/8 (62.5)	3/76 (3.9)	<0.001
Na (nmol/L)[a]	122.25 ± 10.15 ($n = 8$)	136.56 ± 2.28 ($n = 54$)	0.005
K (nmol/L)[a]	6.17 ± 1.21 ($n = 8$)	5.31 ± 0.67 ($n = 54$)	0.004
Serum 17-OHP (ng/mL) (Md [P25-P75])	25.6 (12.8–285) ($n = 3$)	12.5 (7.4–17.8) ($n = 45$)	0.006
Family data			
Family history (n [%])	3/8 (37.5)	9/67 (13.4)	0.196
Consanguinity (n [%])	2/8 (25.0)	0/109 (0%)	<0.001

CAH Congenital adrenal hyperplasia, *ICU* Intensive care unit. Data are presented as percentage (Fisher's exact test) or [a]mean ± SD (Student's t test)

Indian J Pediatr (February 2014) 81(2):178–185
DOI 10.1007/s12098-013-1280-8

SYMPOSIUM ON PEDIATRIC ENDOCRINOLOGY

Congenital Adrenal Hyperplasia: Issues in Diagnosis and Treatment in Children

Rajni Sharma · Anju Seth

abnormal [2]. Due to the inherent fallacies in immunoassays, there is a high false positive rate on newborn screening. The positive predictive value of screening is <1 % meaning that for every 100 samples testing positive, only 1 would represent true CAH [4]. To decrease the recall rate, various second-tier tests have been employed to diagnose CAH among the false

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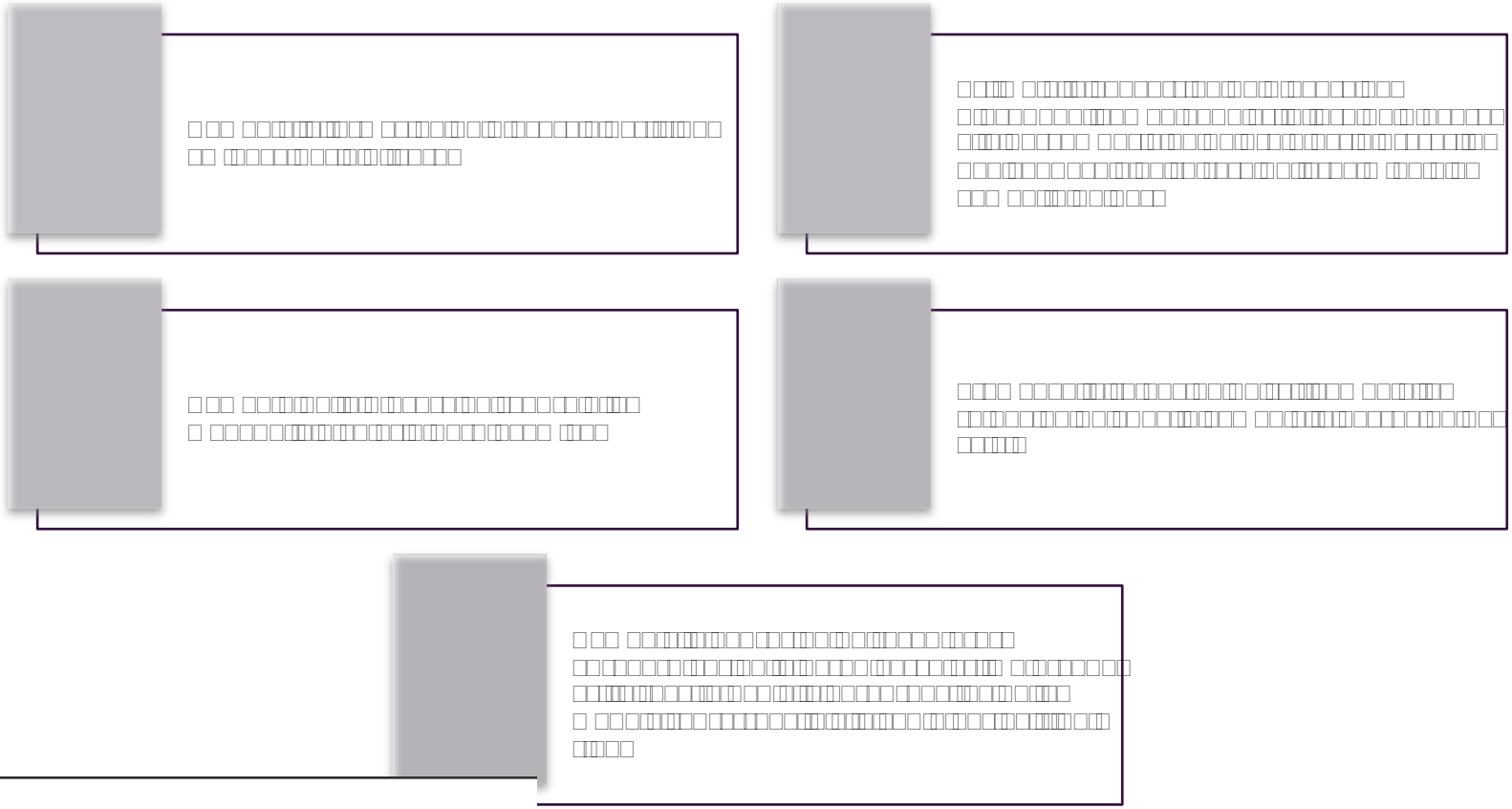

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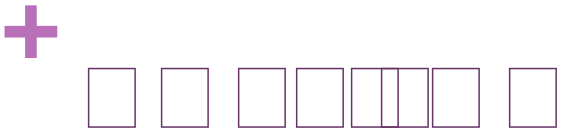

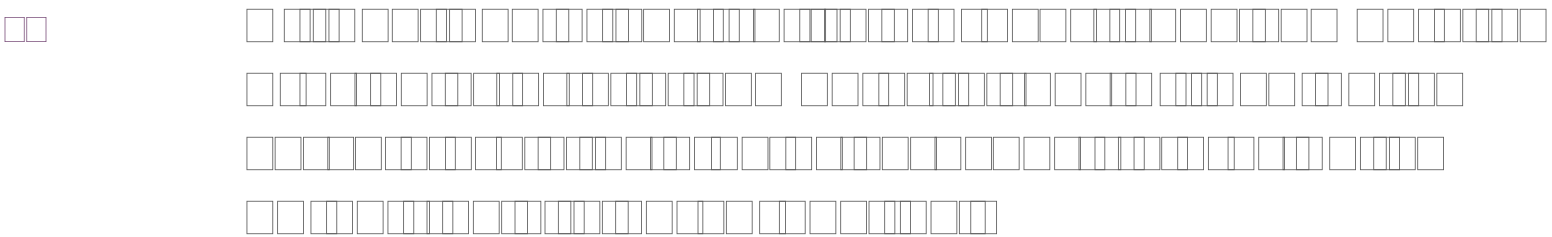

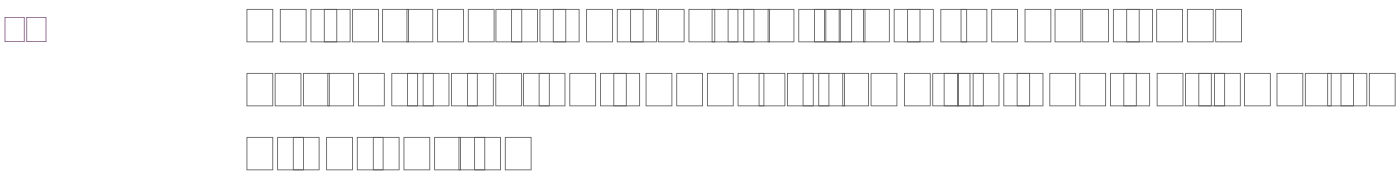

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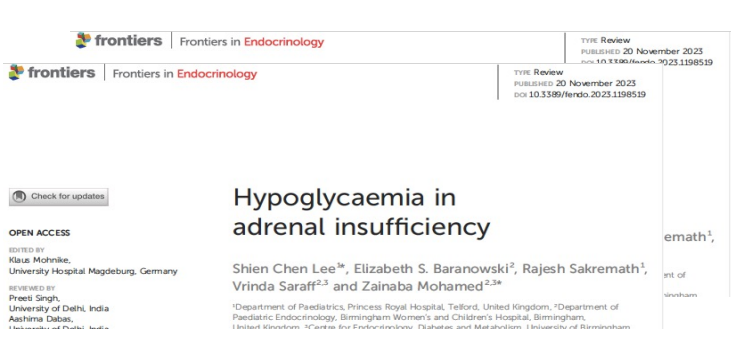

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TYPE Review
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DOI 10.3389/fendo.2023.1198519

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University of Delhi, India
Aashima Dabas,

Hypoglycaemia in adrenal insufficiency

Shien Chen Lee[1*], Elizabeth S. Baranowski[2], Rajesh Sakremath[1], Vrinda Saraff[2,3] and Zainaba Mohamed[2,3*]

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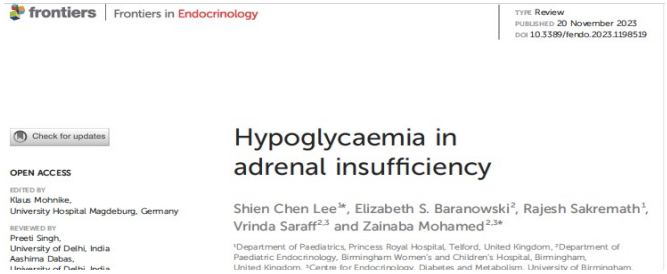

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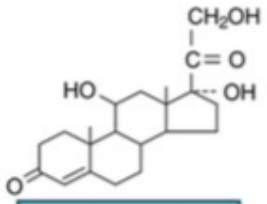
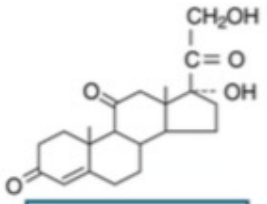
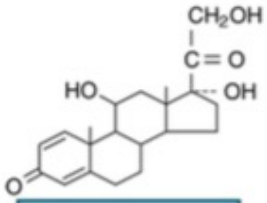


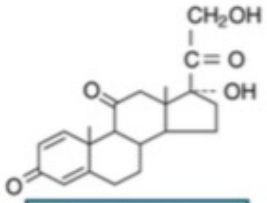
Cortisol



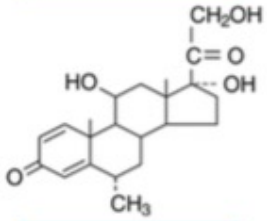
Cortisona



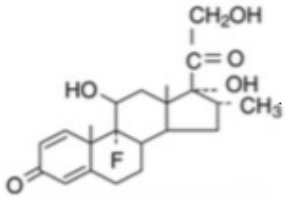
Prednisolona



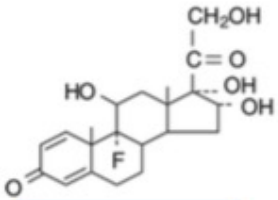
Prednisona



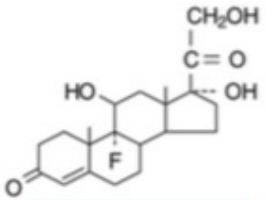
Metilprednisolona



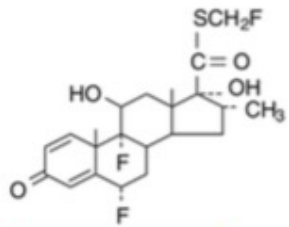
Dexametasona



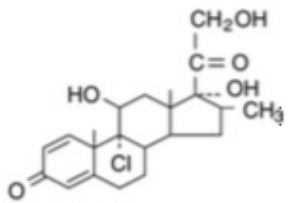
Triamcinolona



Fludrocortisona



Fluticasona



Beclometasona

Esteroide	Glucocorticoides Anti-inflamatorios Efecto esteroide	Efecto de glucocorticoide en el crecimiento (retardando)	Efecto mineralocorticoide que retiene sal	Plasma Vida media (minutos)	Vida media biologica (horas)
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[illegible]	[illegible]		[illegible]		

TABLE 1 Emergency hydrocortisone doses as per BSPED 2023 guidelines.

Age of Child	Community	Hospital
Neonates (< 28 days)	25mg IM dose	4mg/kg IV initially 4–6 hourly Once stable: 2mg/kg IV 4–6 hourly
Children (< 1 year) Children (1–5 years) Children (> 6 years)	25mg IM dose 50mg IM dose 100mg IM dose	2mg/kg (max 100mg) IV initially 4–6 hourly Once stable: 1mg/kg (max 50mg) IV 4–6 hourly

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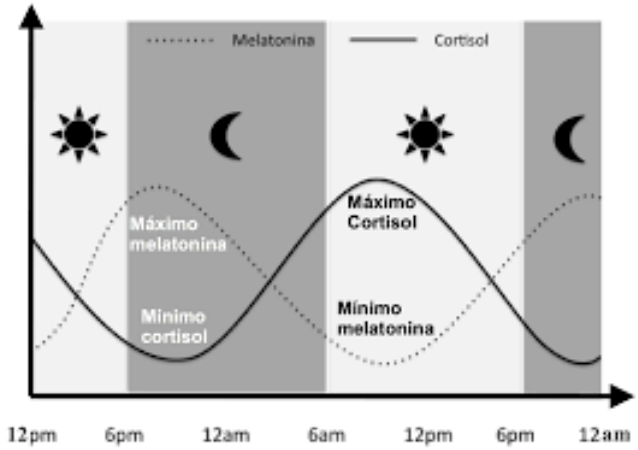

FUTURO

- En los últimos años se ha visto el desarrollo de versiones modificadas. hidrocortisona (MR-HC)
- La versión modificada la preparación tiene un mecanismo de doble liberación; un revestimiento exterior para una liberación inmediata de hidrocortisona y un núcleo interno para una liberación más lenta y sostenida.
- Tanto el tratamiento una vez al día , como el dos veces al día
- Se ha demostrado que las versiones modificadas son más cercanas imitación del ritmo circadiano fisiológico, en comparación con el régimen convencional de dosis múltiples
- Los estudios han reportado una significativa reducción del índice de masa corporal, mejora del perfil lipídico, mejor control glucémico y mejor calidad de vida en aquellos que en el grupo MR-HC