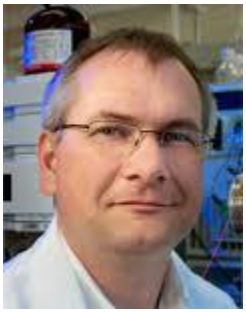
ENDOCRINOLOGY
DIVISION NEWS
Volume 1 | Issue 1 April 2015

AACC Better health through laboratory medicine.

THE RECEPTOR

Greetings and welcome to the first issue of THE RECEPTOR, the AACC Endocrinology Division's newsletter! The newsletter is intended to provide information on division activities from the past and in the future. We hope to include additional content such as Bill Winter's Hormone of the Month featuring 21-deoxycortisol. AACC members interested in contributing content for the newsletter are encouraged to contact Stan Lo. (slo@mcw.edu)

Message from the Chair



Hubert Vesper, PhD,
Centers for Disease Control and Prevention

Dear Endocrinology Division Members,

It is my pleasure to greet all Endocrinology Division members! I hope this letter finds you in good health and high spirits.

After establishing all elements and the necessary infrastructure to ensure successful operation of our Division, we are moving ahead planning the next projects and activities. First, however, I would like to introduce the Division leadership:

Chair-Elect: Ross J. Molinaro, PhD, Siemens Diagnostics

Secretary: William E Winter, MD, University of Florida

Treasurer: Deanna DH Franke, PhD, LipoScience, Inc.

Communication Officer: Stanley F. Lo, PhD, Medical College of Wisconsin

Nominating Committee Officers: Laurence M. Demers, PhD, Penn State University
James F. Faix, MD, Stanford University

It is an honor to work with such a distinguished and motivated team. I would like to thank each of them for their hard work getting this Division off the ground.

The field of endocrinology covers a wide range of diseases and conditions and a constant increase in research activities, technologies, and practice guidelines. One of our objectives is to provide relevant updates and information to our members. As such,

we have conducted last year an AACC session on the diagnosis and treatment of polycystic ovary syndrome. In that session, we informed you about a new Endocrine Society Clinical Practice Guideline and its implications to the clinical laboratory. The session was organized in collaboration with the Endocrine Society and the Partnership for the Accurate Testing of Hormones (PATH). We will continue to collaborate with professional organizations and stakeholders to provide you the latest developments. Thus, we plan to have a presentation at the 2015 Division meeting during the annual AACC meeting to provide updates on diagnostic endocrinology. The Division meeting will be held on July 27, 12noon – 2:00pm (mark your calendar, more details to follow soon). Facilitating and fostering professional development and education is one of our key objectives and thus we aim to offer CME/ACCENT credit for the presentations provided at our Division meeting. We are planning additional educational activities and will provide you with updates through newsletters, email and on our Division website.

Though the field of endocrinology is diverse and broad, one common characteristic is its reliance on the work performed by the clinical laboratory. Thus, it is imperative that we not only update you about the lasted developments in endocrinology but also that we inform the medical and research communities about the latest information generated by us. Last year, our Division in collaboration with NIH/NCI, the Endocrine Society, PATH, and Penn State Hershey College of Medicine conducted a workshop on measuring estrogen exposure and metabolism, where experts discussed how to improve and standardize methods for assessing estrogen exposure and metabolism in epidemiologic and clinical research. As a result of this workshop, several recommendations are being formulated. We will provide them to you as they become available. We will continue advancing the relationship of clinical endocrinology with laboratory medicine, patient care, and research.

The work performed by this Division would not be possible without the help and support from our sponsors and members. I would like to thank Waters Corporation and Siemens Healthcare Diagnostics for their support at last years' AACC meeting. Also, I would like to thank the volunteers, who helped with the poster awards and organization of our annual meeting! It is the help and support (ongoing and occasional) from you and our sponsors that allows this Division to thrive and continue to meet your needs. Please feel free to contact me or our secretary, if you would like to support or participate in our Division and its activities.

I am looking forward to working with you on all the exciting upcoming activities.

Sincerely,
Hubert Vesper

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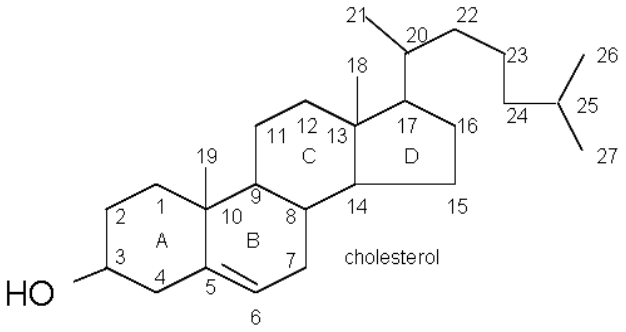
HORMONE OF THE MONTH

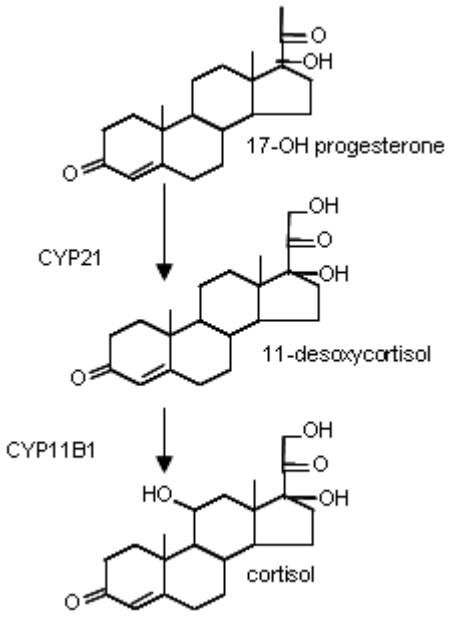
What is 21-deoxycortisol?

William E. Winter, MD, University of Florida

Steroid terminology is complex. In cholesterol, each of the 27 carbons is uniquely numbered.



Most steroid biologists and clinical endocrinologists are familial with 11-desoxycortisol (a.k.a. – 11-deoxycortisol). This is sometimes abbreviated 11-DF [cortisol = compound F, and D = deoxy (a.k.a. – "desoxy," e.g., without oxygen – the hydroxyl group at the 11 position is missing)] or 11-DOF (where "DO" = deoxy or desoxy). 11-DF is an intermediate in the synthesis of cortisol (compound F) from 17-hydroxyprogesterone (17-OHP).



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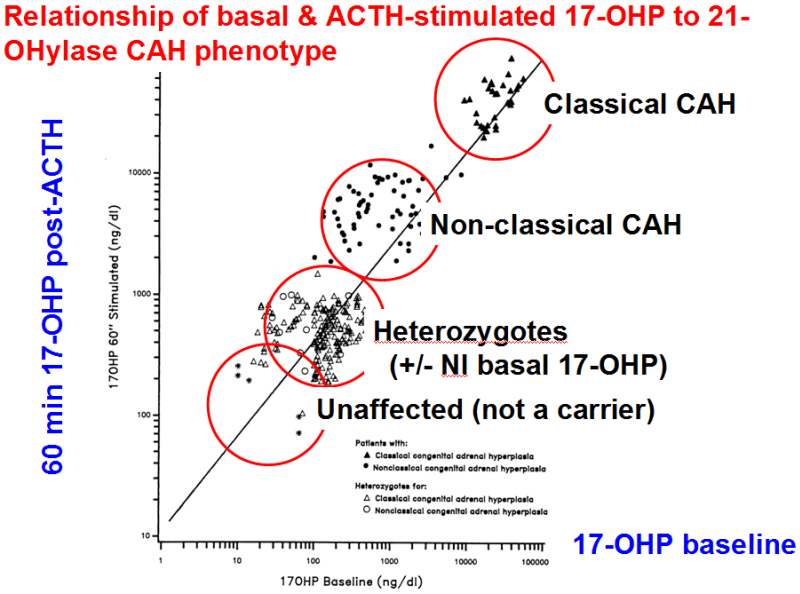
A deficiency of 21-hydroxylase (CYP21) produces various phenotypes of congenital adrenal hyperplasia (CAH). Classical CAH in newborns is manifested as salt-losing

CAH (SLCAH) resulting from cortisol and aldosterone deficiency whereas simple virilizing CAH (SVCAH) is not as severe and manifests as cortisol deficiency without frank aldosterone deficiency.

In untreated SLCAH, vascular collapse from Addisonian crisis in the first weeks of life can be fatal. In girls with SLCAH or SVCAH, exposure to excess fetal adrenal androgens in utero produces virilization of the external genitalia [a form of a "disorder of sexual development" (DSD)]. "Androgenization" of the brain is also influenced by excess fetal adrenal androgens [1,2]. Untreated CAH in children surviving infancy can be manifested as precocious puberty with accelerated growth, hirsutism and virilization.

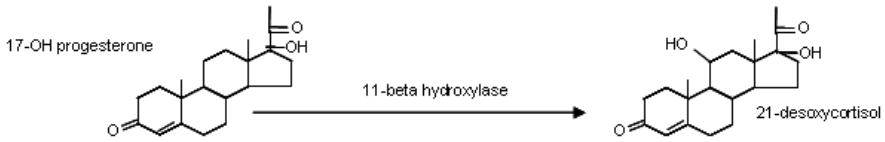
As opposed to SVCAH and SLCAH, there is a late-onset form of CAH (LOCAH; non-classical CAH) that is manifested as hirsutism, virilization and oligomenorrhea or amenorrhea in pubertal girls and adult women. In LOCAH there are no disorders of sexual development (DSD).

The diagnosis of 21-hydroxylase CAH depends upon a compatible clinical history and elevated concentrations of 17-OHP. The classic graph published by Maria New and colleagues [3] differentiates classical CAH (SLCAH and SVCAH) from non-classical CAH (LOCAH), CAH heterozygotes and unaffected subjects. This being said, there is considerable overlap between CAH heterozygotes and unaffected subjects. What measurement might then distinguish these later 2 groups?



An analyte, not as well-known as 11-DF, is 21-deoxycortisol (21-DF). 21-DF is normally in very low concentrations. However in cases of CAH, elevated concentrations of 17-

OHP provide increased substrate for the synthesis of 21-DF catalyzed by 11-beta hydroxylase as illustrated below.



21-DF measurements appear to be able to distinguish CAH heterozygotes from unaffected individuals [4].

How might the measurement of 21-DF be clinically valuable? Suppose that the patient is a sibling of a person affected with CAH. In this person, there is a 67% chance that they will be a CAH carrier. This could persuade this individual to undergo hormonal or genetic testing for CAH heterozygosity prior to planning a family.

If the frequency of classical CAH varies between 1 in 3500 and 1 in 15,000, the higher frequency (1 in 3500) predicts a CAH carrier (heterozygote) frequency of ~1 in 30. When a person has an affected CAH sibling, if their risk of being a CAH carrier is 2 in 3 and the risk of a mate being a CAH carrier is 1 in 30, the risk of having a child affected with CAH is now ~1 in 180. This is ~20 times as likely as the general population risk for CAH. This suggests that prenatal genetic counseling and testing may be useful in family planning.

Whereas genetic testing (with DNA sequencing of the 21-hydroxylase genes) should be definitive for the diagnosis of CAH, at the present time genetic testing would be relatively expensive with a turn-around time of days to weeks. Alternatively, measuring 21-DF in the basal state and 1 hour after a 250 ug infusion or injection of parenteral cosyntropin would be less expensive with a potentially shorter turn-around time [5].

21-DF testing might also assist in (1) newborn screening for CAH where 17-OHP testing is not very specific [4]), (2) the prenatal diagnosis of CAH [6], and (3) the detection of LOCAH [7]). Possibly other uses for 21-DF testing will arise in the future.

References:

[1] Gooren L. The biology of human psychosexual differentiation. Horm Behav. 2006 Nov;50(4):589-601.

[2] Thornton J, Zehr JL, Loose MD. Effects of prenatal androgens on rhesus monkeys: a model system to explore the organizational hypothesis in primates. Horm Behav. 2009 May;55(5):633-45.

[3] New MI, Wilson RC. Steroid disorders in children: Congenital adrenal hyperplasia and apparent mineralocorticoid excess PNAS 1999 96 (22) 12790-12797.

[4] Forest MG. Recent advances in the diagnosis and management of congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Human Reproduction Update, Vol.10, No.6 pp. 469–485, 2004.

[5] Gourmelen M, Gueux B, Pham Huu Trung MT, Fiet J, Raux-Demay MC, Girard F. Detection of heterozygous carriers for 21-hydroxylase deficiency by plasma 21-deoxycortisol measurement. Acta Endocrinol (Copenh). 1987 Dec;116(4):507-12.

[6] Gueux B, Fiet J, Couillin P, Raux-Demay MC, Mornet E, Galons H, Villette JM, Boue J, Dreux C. Prenatal diagnosis of 21-hydroxylase deficiency congenital adrenal hyperplasia by simultaneous radioimmunoassay of 21-deoxycortisol and 17-hydroxyprogesterone in amniotic fluid. J Clin Endocrinol Metab. 1988 Mar;66(3):534-7.

[7] Fiet J, Gueux B, Gourmelen M, Kuttenn F, Vexiau P, Couillin P, Pham-Huu-Trung MT, Villette JM, Raux-Demay MC, Galons H, et al. Comparison of basal and adrenocorticotropin-stimulated plasma 21-deoxycortisol and 17-hydroxyprogesterone values as biological markers of late-onset adrenal hyperplasia. J Clin Endocrinol Metab. 1988 Apr;66(4):659-67.

Upcoming Activities and Events

- AACC Endocrinology Division Annual Luncheon and Mixer:
  Date/Time: July 27, 2015 - 12 noon – 2:00 pm
  Location: Hyatt Regency Atlanta Farlie Room

- AACC Poster Walk:
  Date/Time: July 28, 2015/ time to be determined

Resources/Information/News

- CAP Chemistry Resource Committee educational discussions on survey results:
  http://www.cap.org/web/home/involved/council-committees/chemistry-participant-reports?_afrLoop=260758403591358#%40%3F_afrLoop%3D260758403591358%26_adf.ctrl-state%3Dfwpumenjs_323
  Find the latest discussions on thyroid hormones and vitamin D

If you would like to recommend other interesting resources, news and information, please contact Stan Lo.