CURRICULUM VITAE

DAVID J. MORRIS, D.Phil.

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PERSONAL:

Born -	May 17, 1939; Ramsgate, Kent, England
Citizenship -	United States
Marital Status	- Married, 2 children

EDUCATION:

- D.Phil. Dyson Perrins Organic Chemistry Lab., Oxford Univ., England (1963)
- D.S.I.R. Fellow, Oxford Univ., Stereochemical and Spectroscopic Studies of Steroids (1960-63)
- M.A., B.A. (Honors) Chemistry, St. Catherine's College, Oxford Univ., England (1960); State Scholar (1957-60)

PROFESSIONAL LICENSE AND CERTIFICATION:

National Registry of Clinical Chemists (1971-Present)

ACADEMIC APPOINTMENTS:

Emeritus Professor of Pathology and Laboratory Medicine, Brown University School of Medicine (2014 – present) Professor of Pathology, Brown Univ., Providence, RI (1981-2014) Associate Professor of Pathology, Brown Univ. (1979-81) Associate Professor of Biochemical Pharmacology, Brown Univ. (1975-79) Assistant Professor of Biochemical Pharmacology, Div. of Biology and Medicine, Brown Univ. (1969-75) Research Associate, Medical Sciences Div., Brown Univ. (1963-66)

HOSPITAL APPOINTMENTS:

Director of Clinical Biochemistry, Lifespan AMC Pathology Laboratories (RI Hospital & The Miriam Hospital) (1997-2014) Chief Biochemist, The Miriam Hospital, Providence, RI (1968-1997) Chairman, Section of Biochemistry, BRISMeT School of Medical Technology (1972-73, 1977-80)

Team Leader, Medicinal Chemistry Section, Beecham Research Labs., Betchworth, Surrey, England (1966-68)

OTHER APPOINTMENTS:

Editorial Board, Steroids (1984-present)
Fellow, American Heart Association Council for High Blood Pressure Research (October 1984)
Analytical Chemistry Journal, Manuscript Reviewer (1982-Present)
Member (Ad Hoc), Cardiovascular and Renal Study Section, NIH (June 1977)
Visiting Scientist, Steroid Unit, Karolinska Institute, Stockholm, Sweden (May-June 1976)
Member - Study Section on Continuing Education, RIHSEC (1973-Present)
Member - Genetic Determinants of High Blood Pressure (NHLBI), Study Section (Dec. 1994)
Member - AHA Cardiovascular and Renal Study Section (1993-present)

COMMITTEES:

Board of Trustees, AHA R.I. Affiliate (1993-1999)
AHA R.I. Affiliate Research Committee (Chairman, 1993-1996)
Faculty Executive Committee, Brown Univ. (1992-1995)
Promotions Committee, Dept. of Pathology, Brown Univ. School of Medicine (2005–present)
Promotions Committee, Dept. of Pathology, Brown Univ. (Chairman, 1985-2005)
Promotion's Committee (Ad Hoc), Dept. of Pathology, Brown Univ. (Chairman, 1983-84)
Executive Committee, Section of Pathology, Brown Univ. (1980-84)
Graduate Program Committee, Experimental Pharmacology and Pathology (1976–Present)
Radiation Safety Committee, The Miriam Hospital (1969-Present)

MEMBERSHIPS IN SOCIETIES:

American Association for the Advancement of Science American Association of Clinical Chemists American Heart Association Council for High Blood Pressure Research The Chemical Society, London The Endocrine Society, London National Registry of Clinical Chemists Rhode Island Society for Diabetes Society for Drug Research, London American Society of Hypertension

SELECTED (INVITED) PRESENTATIONS

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Morris D.J, Gong R, Latif S.A., and Brem, A.S., The surprising biological function(s) of 11dehydro- glucocorticoids, the end-products of 11β-HSD2. Congress on Steroid Research, Chicago, March 2011.

Brem, A.S., Morris, D.J., and Gong, R.. Aldosterone Induces Pro- Fibrotic Effects on Vascular Tissue from Normal Mice; Processes Attenuated by 11-Dehydro-Corticosterone. 37th International Aldosterone Symposium, Boston, June 2011

- Brem, A.S, Morris, D.J, Gong, R. Pro-Fibrotic Effects of Aldosterone on Normal Kidney: Processes Attenuated by Renal Metabolites of 11β-Hydroxysteroid Dehydrogenase (11β-HSD). 36th International Aldosterone Conference, San Diego, Calif., June, 2010.
- Morris, D.J, Interactions of mineralocorticoids and glucocorticoids in epithelial target tissues revisited. 6th International Symposium on "Aldosterone and ENaC: from gene to disease. Zermatt, Switzerland, October, 2007.
 - Hardy, M.P, Hu, G-x, Lian, Q-q, Lin, H, Latif, S.A, Morris, D.J, and Ge, R. Rapid mechanisms of glucocorticoid signaling in the Leydig cell. Dublin, Ireland, September, 2007.
 - Morris ,D.J. Experiences in Laboratory Automation. AACC 18th Annual Northeast Region Conference. Boxborough, Mass. April, 2005.
 - Morris D.J. Choosing an Automated Laboratory System: Points to be Considered. Laboratory Management 2004: A Senior Executive Forum. Needham, Mass. February, 2004.
 - Latif, S.A., Hardy,M.P., Brem, A.S., Morris, D.J. Selective Inhibitors of 11b-Hydroxysteroid Dehydrogenase Isoforms 1 and 2; 5 alpha Pathway Reduced Products of Aldosterone, Corticosterone and Endogenous Steroids. 29th International Aldosterone Conference, Philadelphia, Pa., June, 2003.
- Souness,G.W, Brem, A.S, Latif. S.A, and Morris,D. J. 2002. Effect of Chenodeoxycholic Acid on the contractile response or rat aortic rings. . 26th International Aldosterone Conference.

Souness,G.W, Brem, A.S, and Morris, D.J. Antisense to both 11B–HSD1 and 2 Increase Glucocorticoid Activity in Vascular Tissue. AHA Mtg of Council for High Blood Pressure, Washington, D.C., October, 2000.

Wang, G –M, Latif, S.A. Morris, D.J, and Hardy, M.P. Leydig Cells express 11bhydroxylase message and 11b-hydroxlated androgens inhibit 11b-HSD1 enzymatic activity. International Symposium of Endocrinology, Melbourne, Australia, September, 2000.

Morris, DJ. Inhibitors of 11B-HSD and Their Role in Glucocorticoid Na retention Hypertension. Population Council, Rockefeller University, New York. October, 1999 Morris, DJ, Souness, GW, Brem, AS ,and Oblin, ME. Interactions of Mineralocorticoids and Glucocorticoids in Epithelial Target tisssues. International Symposium : News in Aldosterone. Paris, France. August ,1999.

Morris, DJ, and Johnston, JP. The Hormonal Action of 11B-OH-Progesterone on Na transport In Toad Kidney A6 Cells. 24th International Aldosterone Conference. New Orleans,LA. June, 1998.

Morris, D.J., Lo, Y.H., Lichtfield, W.R. and Williams, G.W. Impact of dietary Na+ on glycyrrhetinic acid-like factors (kidney-11 β -HSD2 GALFs) in human essential hypertension. AHA Council for High Blood Pressure Research Meeting, Washington, DC. September 1997.

Lo, Y.H., Sheff, M.F., Latif, S.A., Ribeiro, C., Silver, H., and Morris, D.J. Kidney 11β-HSD2 is inhibited by glycyrrhetinic acid-like factors (GALFs) in human urine. AHA Council for High Blood Pressure Research Meeting, Chicago, IL. September 1996.

Morris, D.J. and Souness, G.W. Progesterone derivatives that inhibit 11β -hydorxysteroid dehydrogenase are also hypertensinogenic in the rat. 22nd Intl. Aldosterone Symp. San Francisco, CA. June 1996.

Morris, D.J. Endogenous 11β -hydroxysteroid dehydrogenase inhibitors and their role in glucocorticoid Na⁺ retention and hypertension. Conference on Adrenal Cortex, Creiff, Scotland, June, 1996.

- Morris, D.J. Endogenous inhibitors of 11β-hydroxysteroid dehydrogenase and their role in glucocorticoid Na⁺ retention. National Institutes of Health. Bethesda, MD (NICHD) Dec. 1994.
- Morris, D.J. Ring-<u>A</u> reduced steroids can confer mineralocorticoid activity upon corticosterone in the ADX rat. 20th Int. Aldosterone Symp. Anaheim, CA, June 1994.
- Morris, D.J. Other physiological considerations of protective mechanisms of mineralocorticoid action. Symp. on Role of 11β-OHSD. Berne, Switzerland, June 1993.
- Morris, D.J. Pharmacology and physiological actions of 11β-OHSD inhibitors. 11β-OHSD Symposium. Int. Congress of Endocrinology. Nice, France, Sept. 1992.
- Morris, D.J., Semafuko, W.E.B., Sheff, M.F., Grimes, C., Latif, S.A., Levinson, P., Walker, B.R., and Edwards, C.R.W.. Measurement of endogenous glycyrrhetinic acid-like factors in urine from patients with essential hypertension. Ann. Mtg. of AHA Council for High Blood Pressure Research. Cleveland, Ohio, Sept. 1992.
- Morris, D.J. Protective and specificity conferring mechanisms of mineralocorticoid action. Univ. of Lausanne. Switzerland, Sept. 1992.
- Morris, D.J. and Souness, G.W. 11-Dehydrocorticosterone in the presence of carbenoxolone is a more potent sodium retainer than its parent steroid, corticosterone. 18th Int. Searle Aldosterone Conf. San Antonio, TX, June 1992.

- Morris, D.J., Souness, G.W., Saccoccio, N.A., and Harnik, M. The effects of infusions of Ring-<u>A</u>-reduced derivatives of aldosterone on the antinatriuretic and kaliuretic actions of aldosterone. 3rd Conf. of the Adrenal Cortex. New Orleans, LA, June, 1988.
- Morris, D.J. The possible biological role of aldosterone metabolites and the effects of dietary sodium on their synthesis. Weitzman Institute for Science, Rehovoth, and Tel-Hashomer Medical Center. Tel Aviv, Israel, September 1987.
- Morris, D.J. Measurement of urinary 19-nor-aldosterone in human hypertension. 13th Aldosterone Conf. Indianapolis, IN, June 1987.
- Morris, D.J. The possible biological role of aldosterone metabolites. Free University of Berlin, Institute of Clinical Physiology. Berlin, September 1986.
- Morris, D.J. The hypertensinogenic properties of 5α- and 5β-reduced metabolites of aldosterone. 11th Annual Aldosterone Conf. Alexandria, VA, June 1985.
- Morris, D.J. Further studies on aldosterone metabolism. Claude P.Brown Memorial Lecture. 74th Meeting of Assoc. of Clinical Scientists. Newport, RI, May 1985.
- Morris, D.J. The effects of antimineralocorticoids on the synthesis of aldosterone metabolites in target tissues. 8th Annual Aldosterone Conf. Montreal, Canada, June 1984.
- Morris, D.J. The possible biological role of aldosterone metabolites. National Institutes of Health. Bethesda, MD, October 1983.
- Morris, D.J. and Kenyon, C.J. Aldosterone and its metabolism in spontaneously hypertensive rats (SHR). Symp. on mineralocorticoids and experimental hypertension. Newport Beach, CA, February 1982.
- Morris, D.J., Kenyon, C.J., Latif, S.A., McDermott, M.J., and Goodfriend, T. The biological significance of aldosterone metabolites. AHA Council for High Blood Pressure Research, 36th Annual Conf. Cleveland, OH, October 1982.
- Morris, D.J., McDermott, M.J., Latif, S.A., Keating, A., and Kenyon, C.J. The metabolism of aldosterone in target tissues. 6th Int. Symp. of Journal of Steroid Biochemistry. Puerto Vallarta, Mexico, July 1981.
- Morris, D.J. Aldosterone, its metabolism and mechanism of action. Amer. Assoc. of Clinical Chemists (Northeast Section). Boston, MA, October 1980.
- Latif, S.A., McEnany, T.E., Reinhold, V., and Morris, D. Isolation and partial identification of several polar metabolites of aldosterone synthesized by male rat, dog, and human liver. Annual Meeting of Endocrine Soc.. Washington, D.C., June 1980.
- Morris, D.J., DeConti, G.A., and Latif, S.A. The mineralocorticoid activity of reduced metabolites of aldosterone in rats. 5th Int. Congress on Hormonal Steroids. New Delhi, India. October 1978.

- Latif, S.A., Tsai, R., Reinhold V., and Morris, D.J. Isolation and partial identification of several polar metabolites of aldosterone synthesized in the liver of male rats. 5th International Congress on Hormonal Steroids. New Delhi, India. October 1978.
- Morris, D.J. and Tsai, R. The effects of the antimineralocorticoid, spironolactone, on the hepatic metabolism of aldosterone in rats. XIth Acta Endocrinological Congress. Lausanne, Switzerland, June 1977.
- Hantoot, M.S., DeConti, G.A., and Morris, D.J. The enterohepatic circulation of aldosterone metabolites in rats. 6th Meeting of New England Pharmacologists. January 1977.
- Morris, D.J., Tsai, R., and DeConti, G.A. Regulation of plasma levels of aldosterone and its metabolites in rats during the latent period of aldosterone. 3rd Int. Symp. of Journal of Steroid Biochemistry. Helsinki, Finland, June 1976.
- DeConti, G.A. and Morris, D.J. The effects of castration on biliary excretion of aldosterone metabolites in rats. 5th Annual Meeting of New England Pharmacologists. January 1976.
- Silverman, J.A. and Morris, D.J. Sex dependence of aldosterone excretion in the bile of rats. 4th Annual Meeting of New England Pharmacologists. February 1975.
- Pfizer Lecturer, Institute of Clinical Research of Montreal Univ. of Montreal, Canada. Mode of action of aldosterone in the kidney. November 1974.
- Drug measurements and monitoring of drug levels. Amer. Soc. of Clinical Pathology Workshop on Toxicology, April 11-12, 1974.
- Aldosterone, its metabolism and mechanisms of action in the kidney. Colloquium: Chemistry Department, Brown Univ. Providence, RI, January 1974.
- Mechanism of action of the antimineralocorticoid aldactone (spironolactone). Colloquium: Department. G.D. Searle and Co. Chicago, IL, March 1973.
- Morris, D.J., Berek, J.S., and Davis, R.P. The physiological response to aldosterone in adrenalectomized and intact rats and its sex dependence. 2nd Annual Meeting of New England Pharmacologists. February 1973.

PUBLICATIONS:

- 1. Morris, D.J. 1963. Stereochemical and spectrographic studies of steroid compounds. D. Phil. Thesis, Oxford Univ..
- 2. Hampson, D.J., Meakins, G.D. and Morris, D.J. 1966. Hydroxysteroids. Part V. Oxidation of 2hydroxymethylene-4, 4-dimethyl-3-ketones with alkaline peroxide. J. Chem. Soc. 1277.
- 3. Meakins, G.D. and Morris, D.J. 1966. Hydroxysteroids. Part X. Preparation and properties of Ahomo-5 cholestan-4-one. J. Chem. Soc. 394.

- 4. McGinnis, E.L., Meakins, and Morris, D.J. 1967. Studies in the steroid group. Derivatives of 22, 23-dihydroneoergosterol. J. Chem. Soc. 1, 1238.
- 5. Morris, D.J. and Barnes, F.W. Jr. 1967. On the intracellular distribution of (4-¹⁴C) cortisol in rat liver. <u>Biochemica et Biophysica Acta 1</u>, 67-68.
- 6. MacMillan, J. and Morris, D.J. 1969 Tricyclic dimers of propenylphenyl ethers N.M.R. and Stereochemistry. <u>Tetrahedron 25</u>, 905.
- 7. Morris, D.J., Sarma, M.H., and Barnes, F.W. Jr. 1970. Labelled complexes in liver cytosol after administration of (4-¹⁴C) corticosterone and (4-¹⁴C) cortisol. <u>Endocrinology 87</u>, 486-493.
- 8. Morris, D.J. and Davis, R.P. 1973. Complex formation by ³H-aldosterone in rat kidney and liver. <u>Steroids 21</u>, 383-396.
- 9. Morris, D.J. and Davis, R.P. 1973. Sex dependence of aldosterone response in rats. <u>Metabolism 22</u>, 923-926.
- 10. Morris, D.J., Berek, J.S., and Davis, R.P. 1973. The physiological response to aldosterone in adrenalectomized and intact rats and its sex dependence. <u>Endocrinology 92</u>, 989-993.
- 11. Morris, D.J., Berek, J.S. and Davis, R.P. 1973. Sex dependence of the metabolism of aldosterone in adrenalectomized and intact rats. <u>Steroids 21</u>, 397-407.
- 12. Morris, D.J. and Davis, R.P. 1974. Progress in endocrinology and metabolism. Aldosterone, concepts. Review on mechanisms of action of aldosterone. <u>Metabolism 23</u>, 473-495.
- 13. Morris, D.J. 1974. Drug metabolism and monitoring of therapeutic drug levels. <u>R.I. Med. J. 57</u>, 461-464.
- Morris, D.J., Graham, W.G., and Davis, R.P. 1975. The metabolism and binding properties of ³Haldosterone in plasma and its sex dependence in adrenalectomized rats. <u>Endocrinology</u> <u>96</u>, 178-184.
- 15. Morris, D.J. and Silverman, J. 1975. Sex dependence of bile secretion of aldosterone in rats. Endocrinology 96, 1360-1365.
- 16. Morris, D.J., Caron, P., Graham, W., DeConti, G., and Silverman, J. 1975. Sex dependence of clearance rats of aldosterone and its metabolites from plasma in intact rats. <u>Steroids 25</u>, 763-771.
- 17. Morris, D.J. and DeConti, G.A. 1976. The effects of castration and treatment with testosterone on the biliary excretion of ³H-aldosterone in rats. <u>Endocrinology 99</u>, 476-480.
- 18. Morris, D.J., Silverman, J.A., and Tsai, R. 1976. Fecal and urinary excretion of ³H-aldosterone and its sex dependence in rats. J. Steroid Biochem. 7, 410-415.

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- 19. Morris, D.J., Tsai, R. and DeConti, G. 1976. Regulation of plasma levels of aldosterone and its metabolites in rats during the latent period of aldosterone. J. Steroid Biochem. 7, 971-978.
- 20. Morris, D.J., Hantoot, M.S., and DeConti, G.A. 1977. The enterohepatic circulation of aldosterone metabolites and its sex dependence in rats. <u>Endocrinology 101</u>, 1776-1784.
- 21. Morris, D.J., Douglis, F., and DeConti, G.A. 1978. Effects of high potassium diet on metabolism of aldosterone in rats. <u>Metabolism 27</u>, 735-742.
- 22. Tsai, R. and Morris, D.J. 1978. The effects of spironolactone on the hepatic metabolism of aldosterone in male rats. <u>Endocrinology 103</u>, 1239-1244.
- 23. Morris, D.J., DeConti, G.A., and Latif, S.A. 1979. The mineralocorticoid properties of reduced metabolites of aldosterone. J. Endocrinology 81, 111P-112P.
- 24. Morris, D.J. 1979. The biological significance of reduced metabolites of aldosterone. <u>Human</u> <u>Pathology 10</u>, 128-131.
- 25. Tsai, R., Davis, R.P., and Morris, D.J. 1980. The effect of the antrimineralocorticoids spironolactone on the hepatic synthesis of polar metabolites of aldosterone male rats. J. Steroid Biochem. 13, 481-487.
- 26. Morris, D.J. and Tsai, R. 1980. Chromatographic separation of aldosterone and its metabolites. In -<u>Advances in Chromatography</u>. Vol. 19, Chap. 6 (Ed. Giddings, J.C.) Marcel Dekker, pp. 261-285.
- 27. DeConti, G.A., Greene, E., and Morris, D.J. 1981. The effect of treatment with estraradiol on the biliary excretion of ³H-aldosterone in male rats. J. Steroid Biochem. 143, 231-233.
- 28. Morris, D.J. and Davis, R.P. 1981. The distribution and metabolism of aldosterone. In <u>Hormones</u> <u>in Normal and Abnormal Tissues</u>. (Ed. Fothersby, K., Pal, S.B., DeGruyter, W.) pp. 71-100.
- 29. Morris, D.J. 1981. Review: The metabolism and mechanisms of action of aldosterone. <u>Endocrine</u> <u>Reviews 2</u>, 234-237.
- 30. Latif, S.A., McDermott, M.J., and Morris, D.J. 1981. The role of cytochrome P-450 in the synthesis of polar metabolites of aldosterone by microsomes of male rat liver. <u>Steroids</u> <u>38</u>, 307-319.
- Kenyon, C.J., DeConti, G.A., Cupulo, N., and Morris, D.J. 1981. The role of aldosterone in the development of hypertension in spontaneously hypertensive rats (SHR). <u>Endocrinology 109</u>, 1841-1845.
- 32. Morris, D.J., McDermott, M.J., Latif, S.A., Keating, A., and Kenyon, C.J. 1982. The metabolism of aldosterone in target tissues. J. Steroid Biochem. 15, 473-477.
- 33. Morris, D.J., and Kenyon, C.J. 1982. Aldosterone and its metabolism in spontaneously hypertensive rats (SHR). <u>Clin. and Exper. Hypertension A4</u> (9&10), 1613-1626.

- 34. Greco, R.G., Carroll, J.E., Morris, D.J., Grekin, R.J., and Melby, J.C. 1982. Familial hyperaldosteronism, not suppressed by dexamethasone. J. Clin. Endocrinology Metab. 55, 1013-1016.
- 35. Morris, D.J., Kenyon, C.J., Latif, S.A. McDermott, M., and Goodfriend, T. 1983. The possible biological significance of aldosterone metabolites. <u>Hypertension (Suppl. I)</u> 135-140.
- 36. Kenyon, C.J., Brem, A.S., McDermott, M.J., DeConti, G.A., Latif, S.A., and Morris, D.J. 1983. Antinatriuretic and kaliuretic activities of the reduced derivatives of aldosterone. <u>Endocrinology</u> <u>112</u>, 1825-1856.
- 37. McDermott, M., Latif, S.A., and Morris, D.J. 1983. The metabolism of aldosterone in kidney. <u>J.</u> <u>Steroid Biochem. 19</u>, 1205-1211.
- 38. Latif, S.A., McDermott, M.J., and Morris, D.J. 1983. The effects of adrenal and gonadal steroids on the <u>in vitro</u> synthesis of aldosterone metabolites by microsomes and cytosol of male rat liver. <u>Steroids 42(3)</u>, 283-297.
- 39. Kenyon, C.J., Sacoccio, N.A., and Morris, D.J. 1984. Aldosterone effects on water and electrolyte metabolism. J. Endocrinology 100, 93-100.
- 40. Kenyon, C.J., Saccoccio, N.A., and Morris, D.J. 1984. Glucocorticoids inhibition of mineralocorticoid action. <u>Clin. Sci. 67</u>, 341-347.
- 41. Harnik, M., Kashman, Y., and Morris, D.J. 1984. Synthesis of 3α, 5α-tetrahydro-aldosterone. J. Steroid Biochem. 20, 1313-1320.
- 42. Kenyon, C.J., Saccoccio, N.A., and Morris, D.J. 1984. Further studies on the mineralocorticoid activity of 19-oxo-deoxycorticosterone. <u>Endocrinology 115</u>, 535-537.
- 43. Kenyon, C.J. and Morris, D.J. 1984. The effects of thyroidectomy on the mineralocorticoid response to aldosterone in male adrenalectomized rats. <u>Ann. N.Y. Acad. Sci. 435</u>, 164-167.
- 44. Trachewsky, D., Oakes, M.L.I., and Morris, D.J. 1985. Induction of flavokinase (EC 2.7.1.2.6) by aldosterone in the rat kidney. <u>Endocrinology 116</u>, 879-888.
- 45. Harnik, M., Kashman, Y., Aharonowitz, and Morris, D.J. 1985. Synthesis of 19-hydroxyaldosterone and the 3α-hydroxy-5-ene-analog of aldosterone, active mineralocorticoids. J. Steroid Biochem. 23, 207-218.
- 46. McDermott, M.J., Freiberger, M., Latif, S.A., and Morris, D.J. 1985. The synthesis of reduced metabolites of aldosterone by subcellular fractions of rat kidney: Effects of antimineralo-corticoids. J. Steroid Biochem. 23, 503-509.
- 47. Gorsline, J. and Morris, D.J. 1985. The hypertensinogenic activity of 19-nor-deoxycorticosterone in the adrenalectomized spontaneously hypertensive rat. J. Steroid Biochem. 23, 535-536.

- 48. Morris, D.J., McDermott, M.J., Freiberger, M., Latif, S.A., Pacholski M., and Brem, A. 1986. Effects of antimineralocorticoids of synthesis of aldosterone metabolites in target tissues. J. Steroid Biochem. 24, 341-344.
- 49. Morris, D.J. 1986. Further studies on aldosterone metabolism. <u>Annals Clin. Lab. Sci.</u> 16, 94-102.
- 50. Gorsline, J., Harnik, M., Tresco, P., and Morris, D.J. 1986. Hypertensinogenic activities of Ring-<u>A</u>-reduced metabolites of aldosterone. <u>Hypertension 8</u> (Suppl I), 1187-1190.
- 51. Morris, D.J., Brem, A.S., Saccccio, N.A. Pacholski, M., and Harnik, M. 1986. Mineralocorticoid activity of 19-hydroxy-aldosterone, 19-nor-aldosterone and 3β-hydroxy-5-aldosterone: Relative potencies measured in two bioassay systems. <u>Endocrinology 118</u>, 2505-2509.
- 52. Harnik, M., Kashman, Y., Cojocaru, M., Rosenthal, T., and Morris, D.J. 1986. Synthesis of 19-noraldosterone: A potent mineralocorticoid. J. Steroid Biochem. 24, 1163-1169.
- 53. Morris, D.J., Gorsline, J., Tresco, P.A., and Harnik, M. 1987. The hypertensinogenic properties of 19-nor-aldosterone in ADX SHR. <u>Steroids 46</u>, 1003-1010.
- 54. Kenyon, C.J., Saccoccio, N.A., Harnik, M., and Morris, D.J. 1986. The effect of long-term infusions of the reduced derivatives of aldosterone on water and electrolyte metabolism. Serono Symposium, Padua, Italy. pp. 209-214.
- 55. Morris, D.J. and Brem, A.S. 1987. Editorial review: reduced analogues for aldosterone. <u>Amer. J.</u> <u>Physiol. 252</u>, F365-F373.
- 56. Latif, S.A., Camara, P., Rosen, M.P., and Morris, D.J. 1987. Enzymatic synthesis of ³H-labelled Ring-<u>A</u>-reduced metabolites of aldosterone and their separation by high pressure liquid chromatography. <u>Steroids 49</u>, 589-600.
- 57. Gorsline, J., Latif, S.A., and Morris, D.J. 1988. Changes in 5α-and 5β-reductase pathways of aldosterone metabolism by dietary sodium. <u>Am. J. Hypertension 1</u>, 272-275.
- 58. Gorsline, J. and Morris, D.J. 1988. Effects of adrenalectomy and spironolactone on urinary metabolites of aldosterone in rats. <u>Steroids 51</u>, 81-99.
- 59. Brem, A.S., Pacholski, M., and Morris, D.J. 1988. Time dependent aldosterone metabolism in the toad urinary bladder. <u>Amer. J. Physiol. 254</u>, F547-F553.
- 60. Morris, D.J., Souness, G.W, Saccoccio, N.A., and Harnik, M. 1988. The effects of infusions of Ring-<u>A</u>-reduced derivatives of aldosterone on the antinatriuretic and kaliuretic actions of aldosterone. <u>Steroids 53</u>, 21-26.
- 61. Gorsline, J., Morris, D.J., and Holmes, W.N. 1988. Metabolism of aldosterone in the colosotomized duck (Anas. Platyrhynchos): Partial characterization of urinary metabolites. <u>J.</u> <u>Comp. Biochem. Physiol. 92</u>, 773-777.

- 62. Kirk, D.N., Burke, P.J., Toms, H.C., Latif, S.A., and Morris, D.J. 1989. 18-Substituted steroids -Part 15. 6B-hydroxylation of aldosterone by rat liver. <u>Steroids 54</u>, 169-184.
- Kirk, D.N., Miller, B.W., Cooley, G., Latif, S.A., and Morris, D.J. 1989. 18-Substituted steroids -Part 16. Synthesis of 6β-hydroxy and 6α-hydroxy-aldosterone and their 17α-isomers. J. Chem. Res. <u>6</u>, 1274-1289.
- 64. Souness, G.W. and Morris, D.J. 1989. The antinatriuretic and kaliuretic effect of the glucocorticoids corticosterone and cortisol following pretreatment with carbenoxolone sodium (a liquorice derivative) in the adrenalectomized rat. Endocrinology 124, 1588-1590.
- 65. Lewicka, S., Koch, S., Harnik, M., Cojocaru, M., Morris, D.J., and Vecsei, P. 1989. Demonstration and quantitative determination of 19-nor-aldosterone in human urine. <u>Serono Symposium: The Adrenal and Hypertension 57</u>, 432-437.
- 66. Brem, A.S., Matheson, K., Conca, T., and Morris, D.J. 1989. Effect of carbenoxolone on glucocorticoid metabolism and Na transport in toad bladder. <u>Amer. J. Physiol. 257</u>, F700-F704.
- Latif, S.A., Morris, D.J., Wei, L., Kirk, D.N., Burke, P.J., Toms, H.C., and Shackleton, C.H.L. 1990. 18-Substituted steroids - Part 17. 2α-hydroxylated liver metabolites of aldosterone identified by high field 'H NMR spectroscopy. <u>J. Steroid Biochem. 33</u>, 1119-1125.
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RESEARCH WORK IN PROGRESS

- 1. We are currently investigating the inter-relationships between mineralocorticoids and glucocorticoids and their role(s) in Na homeostasis, blood pressure control, and the regulation of testicular Leydig cell biosynthesis of testosterone. My research is focussed on the mechanism of action of Mineralocorticoids and Glucocorticoids, not only in the kidney but also in vascular tissue, with particular attention to their effects on Sodium retention and Hypertension. In addition, my lab is engaged in determining the identity of a variety of adrenally- derived steroid metabolites which provide a source of endogenous inhibitors of the 11beta-hydroxysteroid dehydrogenase isoenzymes, 11β HSD1 and 11β -HSD2, which regulate the levels of cortisol and cortisone in their target tissues.
- Recently we are studying the hormonal effects of Aldosterone on pro-fibrotic effects in both kidney and cardiovascular tissues
 Particular attention is being given to the role and mechanisms by which 11-dehydroglucocorticoids, the enzymatic products of 11β-HSD2 dehydrogenase, inhibit these effects.
- 3. <u>Glycyrrhetinic Acid-Like Factors (GALF's)</u> We have recently demonstrated the presence of endogenous substances in human urine which like the licorice ingredient, glycyrrhetinic acid, inhibits 11β-hydroxysteroid dehydrogenase and steroid 5β-reductase and confers mineralocorticoid activity upon the glucocorticoid, cortisol. We are currently in the process of isolating and chemically characterizing these GALF substances present in elevated levels in pregnant human urine and the urine of essential hypertensives. We believe GALF substances are adrenally derived from side-chain cleaved cortisol and/or metabolites of corticosterone and their derivatives formed by 21-dehydroxylation performed by intestinal flora.
- 4. We plan to quantify the levels of several steroid metabolites of adrenal origin identified by my lab as potent GALF substances. These will be measured in individuals with essential hypertension, obesity, and ocular hypertension.

5. Patients with 17α -hydroxylase deficiency secrete large quantities of corticosterone. In a recent review article we have presented supporting evidence that corticosterone and its 5α -pathway metabolites as well as their further metabolized 11-oxygenated progesterone derivatives (produced

by intestinal microflora), may play a role in the increased Na⁺ retention and hypertension observed in this disease. Current experiments are focused on determining the role of bacterial anaerobes in Na⁺ homeostasis and BP, particularly in patients with 17 α -hydroxylase deficiency and essential hypertension

GRANTS:

- NIH Grant HL52972, 1994-97, \$394,251. "Novel Endogenous Regulators of Sodium and Hypertension."
- NIH Grant DK21404, 1990-95, \$662,066. "Regulation of Metabolism and Action of Action of Aldosterone."
- NIH Grant DK 21404, 1987-89, \$198,317. "Regulation of Metabolism and Action of Aldosterone."
- National Dairy Council, 1987-90, \$194,803. "Dietary Factors Affecting the Development of Hypertension in SHR."
- NIH Grant AM 21404, 1983-86, \$285,100. "Regulation of Metabolism and Action of Aldosterone."
- American Heart Association, RI Affiliate, 1983-85, \$35,000. "The Role of Aldosterone and its Metabolites in Hypertension."
- NIH Grant AM19179, 1979-82, \$196,660. "Metabolism and Endocrine Action of Aldosterone."
- NIH Grant AM 21404, 1979-82, \$201,030. "Regulation of Metabolism and Action of and Action of Aldosterone."
- NIH Grant AM 19179, 1976-79, \$84,500 "Metabolism and Endocrine Action of Aldosterone."
- American Heart Association Grant, 1974-1977, \$19,000 per year.

TEACHING INVOLVEMENT:

Medical Interns, Residents, Fellows, and House Staff in fields of Clinical Biochemistry, thyroid, steroids, and endocrine metabolism. Enzymes in cardiology and lipid metabolism and liver function (approximately 6 hr/wk).

House Staff: Walter Limehouse, M.D. (Clinical Pathology - Biochemistry), February-May 1980. Renee Vogel, M.D. (Clinical Pathology - Biochemistry) 4 months, 1978 (Clinical Pathology Residents - Biochemistry training) 1979-present.

School of Medical Technology Teaching, 1974-80.

Chairman, Internal Coordination Committee for the School of Medical Technology, 1980 (Recent students - 1979-80: D.Bernier, M. Johnson, D. Caccicio and D. Bedard).

BROWN UNIVERSITY:

Brown University Integrated Residency Training Program in Pathology Clinical Biochemistry Rotation, 1979-Present, Course Leader 1996-Present Biomed 30 Endocrinology (2003-Biomed 122/30, Course Leader, Endocrinology (1990-2002) - 12 hr Biomed 122, Endocrinology (1988, 1989) - 10.5 hr Biomed 122, Endocrinology (1987) - 10.5 hr Biomed 122, Endocrinology (1986) - 10.5 hr Biomed 195 (1986) J. Selengut Biomed 112, Endocrinology (1985) - 10.5 hr Biomed 196 (1984-85) D. Lustgarten Biomed 112, Endocrinology (1984) - 10.5 hr Biomed 196 (1983-84) K. DeSimone, D. Lustgarten Biomed 112, Endocrinology (1983) - 10.5 hr Biomed 196 (1982-83) K. Harris Biomed 195/196 (1981-82) M. Farwell, P. Vikoren Biomed 195 (1980-81) A. Tager, M. Rosen Ms. Thesis (June 1979) Biochem. Pharm. Biomed 195 (1979-80) M. Wilner, M. Rosen Biomed 196 (1979-80) Second Semester, M. Wilner, M. Rosen Biomed 291 (1978-79) G. DeConti, thesis Biomed 292 (1978-79) Second Semester, G., DeConti thesis Biomed 196 (1978-79) Second Semester, M. Wilner Biomed 128, Biochem. Pharm. (1978) 8 hr lecture, Dr. Parks, Course Leader Biomed 195 (1977-78) R. Homan Biomed 196 (1977-78) Second Semester, T. Homan Biomed 295 (1977-78) S. Steidl Biomed Biomed 295 (1977-78) M. Hantoot, M. LeCompte, S. Steidl and H. Frumpkin Biomed 296 (1976-77) Second Semester, M. Hantoot, S. Steidl Biomed 291 (1976-77) R. Tsai, Thesis Biomed 195 (1975-76), First Semester, M. Hantoot Biomed 196 (1975-76) M. Hantoot, S. Steidl, M. LeCompte, H. Frumpkin Biomed 225, Phys. Pharm. (1975) 4 hr lecture Biomed 125, Pharmacology (1975) 3 hr lecture Biomed 126, Endocrinology (1975) 3 hr (1976), 6 hr (1977), 4 hr - Dr. Czech, Course Leader Biomed 195 (1974-75) J. Silverman, G. DeConti, T. Green Biomed 196 (1974-75) G. DeConti Biomed 292 (1974-75) Second Semester, R. Tsai, thesis Biomed I, Introductory Biology "Perspectives in Hormonal Research" (1969-79) 40 hr/semester, Dr. Quevedo, Course Leader