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Recent Research on Mechanistic Determinants, Biomarkers and Possible Holdup of Geriatrics

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I.INTRODUCTION

Aging is a universal phenomenon which can be either programmed or stochastic. The programmed ageing includes a wide range of genetic determinants while the stochastic process includes mitochondrial and somatic mutations, oxidative stress and protein glycation [1,2]. However, these hypotheses have been unable to link the proximate and ultimate processes of geriatrics. Research does not leave any doubt that ageing is naturally selected and genetically programmed in all animal species [1]. It is considered as a complex multifactorial process that results in progressive morbidity and disability [3]. The hypothalamic, pituitary and adrenal glands are an important hormonal system that determines homeostatic function. Present research findings have proposed that ageing is associated with enhanced cortisol levels in cerebrospinal fluid and particularly ventricular, and concomitant increased cortisol level in blood [4]. Various studies have proposed that life expectance is not always proportional to reduced metabolic rate however; organ metabolic rate and energy expenditure may be a more appropriate determinant of geriatrics [5].

II. OXIDATIVE DAMAGE AND GERIATRICS

Oxidative damage appears to be an early and consistent alteration linked with the aging canine neurological metabolic syndrome, and is considered as important determinant of the lifespan. There are variety of metabolism-related features have an impact on aging processes; nongenetic determinants such as, nutrient deprivation or low temperature and mutations are associated with an increased metabolic efficiency and diminished metabolic rate [6,7]. Geriatric organisms down regulate metabolic rate as an adaptation to the cellular nutrient stress, [8,9].

III. HORMONAL IMBALANCE AND GERIATRICS

Metabolic alterations are closely linked with endocrine function. Chronic hyperglycaemia elicits aging-like alterations in ventromedial hypothalamus and hyperinsulinaemia followed by insulin resistance [10]. Increased insulin exposure results a 'vicious circle' which may also control the rate of mammalian ageing and age related diseases [11]. The neuroendocrine alterations follow a stereotypic pattern in geriatric animals. In general, cytoprotective and proglycolytic hormones like insulin, gonadal steroids, melatonin and thyroid hormones decrease with aging [12]. Aging is routinely associated with insulin insensitivity, glucose intolerance [13] and leptin insensitivity [14] which appears to be common determinants of the metabolic syndrome X [15, 16].

4. METABOLISM AND GERIATRICS

Atherosclerosis and other cardiovascular diseases are main metabolic disorders contributing to premature morbidity and mortality [17,18]. Epidemiological [19] and cell biological evidences [20,21,22]indicate that pathophysiology of geriatrics related diseases such as NIDDM, hypertension, atherosclerosis and cancer unfold at a continuum of shared risk factors. There are reports of vulnerabilities and molecular processes linked to oxidative stress, mutability and insulin/growth factor exposure. The geriatrics -related derangement of hormonal balances [23] further deteriorates and results in metabolic syndrome and associated geriatrics related diseases [24,25]. In contrast, the hypothalamus pituitary axis (HPA) is activated in comparison to healthy age-matched control [1,3,6,26].

5. ENDOCRINE DISEASES AND GERIATRICS

Endocrine diseases are common in the geriatric dog and are mainly represented by insulinoma, hyperadrenocorticism, phaeochromocytoma, hyperparathyroidism, diabetes mellitus and hypothyroidism. An elevated level of parathyroid hormone (PTH) has been described in old humans and rats [27]. Geriatrics predisposes individuals to insulin resistance and prevalence of diabetes increases markedly with advancement of age resistance of peripheral tissues to insulin action is known to contribute to the development of the disease [23]. This insulin resistance is tissue-specific in nondiabetic and insulin-resistant old Wistar rats (24-month-old). Decreased cellular insulin signalling is a potential mechanism responsible for the defects in insulin action characteristic of old age from data it is evident that white adipose tissue (WAT) is extremely insulin resistant in old rats, [23]. However, a decline in insulin receptor (IR) and insulin receptor tyrosine phosphorylation was found after insulin stimulation in vivo in liver and skeletal muscle of aged rats. More importantly, canines show substantial cognitive impairment with increased age in measures of object recognition memory. Earlier findings showed that the hippocampus lose approximately 50% of mineralocorticoid receptors as well as some of the glucocorticoid receptor sites with ageing [28,29,30]. The feedback regulation via hippocampal mineralocorticoid receptors became more susceptible in elderly subjects leading to an elevated responsiveness of HPA axis and increased basal cortisol levels [31,32].

6. BIOMARKERS OF GERIATRICS

The concept of biomarkers of aging and age-related disease began to appear in the gerontology in the early 1980s. In early days, the interest was in eliminating the confounding influence of disease from research on aging so that indicators of underlying processes of aging could be determined [33,34]. An ideal biomarker of Aging

must possess the quality to postulate accurately functional capability of organs at some later age. Presently mtDNA deletions has been detected as most eligible biomarker of aging [35]

7. CONCLUSIONS

There is increased incidence of geriatric related disorders due change in lifestyle and dietary habits. So need of an hour is to address the age related disorders and search for the risk factors associated with ageing and their rectification.

REFERENCE

1. S.N. Austad, Why we Age. John Wiley & Sons, New York, 1997, 6.
2. R. Arking, Biology of Ageing, 2nd Edn. Sinauer Association, Sunderland, 1998, 803-805.
3. J.W. Rowe, K.L. Minaker, J.A. Pallotta, and Flier. J.S, Characterization of the insulin resistance of aging, *Journal of Clinical Investigation, (71),* 1983, 1581–1587.
4. K. Murakami, T. Nakagawa, M. Shozu, K. Uchide, K. Koike and M. Inoue, () Changes with aging of steroidal levels in the cerebrospinal fluid. Maturitas, (33), 1999, 71–80.
5. J.A. Greenberg, H.C. Wie, K. Ward, and C.N. Boozer, () Wholebody metabolic rate appears to determine the rate of DNA oxidative damage and glycation involved in aging. *Mechanism of Ageing and Development, (115),* 2000, 107–117.
6. J.J. Ramsey, M.E. Harper and R. Weindruch, Restriction of energy intake, energy expenditure and aging, *Free Radical Biology and Medicine, (29),* 2000, 946–968.
7. S.M. Jazwinski, Metabolic control and ageing. Trends in *Gerentology, (16),* 2000, 506–511.
8. W.A. Van Voorhies, Production of sperm reduces nematode lifespan, *Nature, (360),* 1992, 456–458.
9. L.S. Piers, M.J. Soares, L.M. McCormack and O'Dea, K, Is there evidence for an age-related reduction in metabolic rate, *Journal of Applied Physiology, (85),* 1998, 2196–2204.
10. J.A. Greenberg, H.C. Wie, K. Ward, and C.N. Boozer, Wholebody metabolic rate appears to determine the rate of DNA oxidative damage and glycation involved in aging, *Mechanism of Ageing Development, (115),* 2000, 107–117.
11. C.V. Mobbs, Genetic influences on glucose neurotoxicity, aging, and diabetes: a possible role for glucose hysteresis, *Gerentology, (91),* 1993, 239–253.
12. F.S. Facchini, N.W. Hua, G.M. Reaven, and R.A. Stoohs, Hyperinsulinemia: the missing link among oxidative stress and age-related diseases, *Free Radical in Biological Medicine, (29)* 2000, 1302–1306.
13. K. Heininger, A unifying hypothesis of Alzheimer's disease. I. Ageing sets the stage, *Psychopharmacology and Clinical Experiments, (14),* 1999, 363–414.
14. J.D. Veldhuis, Network-like facets of neuroendocrine aging: Specific disruption of feedback and feed forward linkages within the aging somatotropic, gonadotropic, and corticotropic axis, and corticotropic axis, *Journal of Anti-Aging Medicine. (3),* 2000, 269–301.
15. J.W.Rowe, K.L. Minaker, J.A. Pallotta and J.S Flier, Characterization of the insulin resistance of aging, *Journal of Clinical Investigation, (71),* 1983, 1581–1587.

16. P.J. Scarpace, M. Matheny, R.L. Moore, and N. Tumer, Impaired leptin responsiveness in aged rats, *Diabetes, (49),* 2000, 431–435.

17. G. Reaven, P. Johnston, C. Hollenbeck, R. Skowronski, J. Zhang, and Y.D. Chen, Combined metformin-sulfonylurea treatment of patients with noninsulin dependent diabetes in fair to poor glycemic control, *The Journal of Clinical Endocrinology and Metabolism, (74)* 1992, 1020– 1026,

18. P. Zimmet, E.J. Boyko, G.R. Collier, and M. de Courten, Etiology of the metabolic syndrome: potential role of insulin resistance, leptin resistance, and other players. Ann. New York. Acad. Sci. (892), 1999, 25–44.

19. B.C. Hansen, The metabolic syndrome X: A work in progress. Ann. New York Acad. Sci. 892: 1–24. Ginsberg, H.N (2000) Insulin resistance and cardiovascular disease. *Journal of Clinical Investigation (106),* 1999, 453–458.

20. M.A. Moore, C.B. Park, and H. Tsuda, Implications of the hyperinsulinaemia–diabetes–cancer link for preventive efforts. *European Journal of Cancer Prevention, (7),* 1998, 89–107.

21. J.E. Trosko, and C.C. Chang, () An integrative hypothesis linking cancer, diabetes, and atherosclerosis: the role of mutations and epigenetic changes. *Medical. Hypotheses, (6),* 1980, 455–468.

22. P. Hamet, Cancer and hypertension: A potential for crosstalk. *Journal of Hypertension, (15),* 1997, 1573–1577.

23. N. Volkers, Diabetes and cancer: scientists search for a possible link. J. Natl. Cancer. Inst. 92: 192–194. Heininger, K. (1999) A unifying hypothesis of Alzheimer's disease. I. Ageing sets the stage. *Psychopharmacology and Clinical Experiments, (14),* 2000, 363–414.

24. I.A. O'Brien, I.G. Lewin, J.P. O'Hare, J. Arendt, and R.J. Corrall, Abnormal circadian rhythm of melatonin in diabetic autonomic neuropathy. *Clinical Endocrinology, (24),* 2002, 359–364.

25. R.G. Troxler, Sprague, E.A., Albanese, R.A., Fuchs, R. and Thompson, A.J. The association of elevated plasma cortisol and early atherosclerosis as demonstrated by coronary angiography. *Atherosclerosis, (26),* 1977, 151–162.

26. R.P. Dullaart, F.L. Ubels, K. Hoogenberg, A.J. Smit, J.J. Pratt, J.H. Muntinga, Sluiter and Wolthers, B.G. Alterations in cortisol metabolism in insulin-dependent diabetes mellitus: relationship with metabolic control and estimated blood volume and effect of angiotensin-converting enzyme inhibition. *Journal of Clinical Endocrinology and Metabolism, (80)* 1995, 3002–3008.

27. D.F. Kelly, V.M. Leckie, and C.J. Gasket, Note on pathology for small Animal Clinician. John Wright and Sons Ltd; England, 1982.

28. Björntorp, P. and Rosmond, R. Hypothalamic origin of the metabolic syndrome X. Ann. New York. Acad. Sci, (892) 1999, 297–307.

29. K. Heininger, A unifying hypothesis of Alzheimer's disease. I. Ageing sets the stage. *Psychopharmacology and Clinical Experiments,* (14), 1999, 363–414.

30. R. Marcus, P. Madvig, and G. Young, Age-related changes in paratbyraid hormone and pamthyroid hormone action in normal humans, *Journal of Clinical Endocrinology Metabolism,* (58) 1984, 223-230.

31. E. Orwoll, and D. Meier, Alterations in calcium, vitamin D and pamthyroid hormone physiology in normal men with aging: relationship to the development of senile osteopenia, *Journal of Clinical Endocrinology Metabolism, (63),* 1986, 1262-1269.

32. P. R. Ebeling, M. E. Sangren, E. P. Dimagno, A. W. Lane, H. F. Deluca and B. L. Riggs, Evidence of an age-related decrease in intestinal responsiveness to vitamin D: relationship between serum 1,2% dihydroxyvitamin D3 and intestinal vitamin D receptor concentrations in normal women, *Journal of Clinical Endocrinology Metabolism,* (*5),* 1992, 176-182.

33. J.M. Reul, J. Rothuizen, and de Kloet, E.R, Age-related changes in the dog hypothalamic–pituitary–adrenocortical system: neuroendocrine activity and corticosteroid receptors. *Journal of Steroid Biochemistry and Molucular. Biology, (40),* 1991, 63–70.

34. S.S.C. Yen, and G.A. Laughlin, Aging and the adrenal cortex, Exp. Gerontol, (33) 1998, 897–910.

35. E. Ferrari, D. Casarotti, B. Muzzoni, N. Albertelli, L. Cravello, M. Fioravanti, S.B. Solerte, and Magri. F, Age-related changes of adrenal secretory pattern: possible role in pathological brain aging, *British Research Review, (37),* 2001, 294–300.

36. G.W. Miller, Mineral and bone metabolism. In : Tietz textbook of clinical chemistry, C.A.burtis and E.R.Ashwood, (Eds.) W.B.Saunders, Philadelphia, 1994, 395-1457.

37. M. Heuser, Deuschle, A. Weber, A. Kniest, C. Ziegler, B. Weber, and M. Colla, The role of mineralocorticoid receptors in the circadian activity of the human hypothalamus–pituitary–adrenal system: effect of age, *Neurobiological Aging. (21),* 2000, 585–589.

38. R.L Sprott, and E.L. Schneider, Biomarkers of aging. In: Hart, S. (Ed.), Proceedings of the International Conference on Nutrition and Aging. A.R. Liss, New York, 1985, pp.43–52.

39. A. Eshaghian, R.A. Vleugels, J.A. Canter, M.A. McDonald T., Stasko, and , J.E Sligh, Mitochondrial DNA deletions serve as biomarkers of aging in the skin, but are typically absent in nonmelanoma skin cancers. *Journal of Investigative Dermatology, (126),* 2006, 336–344.