40th Inaugural Lecture

PHYSIOLOGY:

Influence of Environmental Factors, Diet and Herbs

by

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<u>PHYSIOLOGY: Influence of Environmental</u> <u>Factors, Diet and Herbs</u>

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Ladies and Gentlemen

This inaugural lecture is the third from the College of Medicine and my area of specialization is Endocrine and Reproductive Physiology. In order to get a clear picture of what we are to learn about today, we must first define the term, "Physiology".

What is physiology? The new <u>Lexicon Webster Dictionary</u> defines physiology as the branch of biology concerned with the functions of living organisms; it is also the functions, collectively, of an organism or its parts. <u>Longman Dictionary of</u> <u>Contemporary English</u> defines Physiology as a science concerned with the study of how the bodies of living things work. It also defines it as the way the body of a person or an animal works and looks. From these definitions, one can say generally that physiology is the study of the normal functions of the human or animal body. The functional systems studied in physiology are:

- {1} Body fluids and blood;
- {2} Cardiovascular system;
- {3} Respiratory system
- {4} Renal system;
- {5} Gastrointestinal system;
- {6} Nervous system; and
- {7} Reproductive and endocrine systems

In physiology, observation may be made and experiment performed on man and animals. Without animal experiment, modern physiology and, for that matter modern medicine could never have progressed. Fortunately, the basic behaviour of living matter is the same in microscopic unicellular creatures as in the cells of the human body.

Objectives of the Lecture

At the end of this lecture, you are expected to have been informed on:

{1} how some environmental factors like changing lighting rhythm, climatic or temperature variations and cigarette smoke can affect the functional

systems of the body.

{2} The effects of certain diets on some functional systems;

{3} The effects of some medicinal plants and herbs on the physiological systems.

<u>Responses of the Body to Heat</u>

When core temperature rises due to heat gained from thermogenesis or from heat gained from the environment, a number of responses occur. These are reflex cutaneous vasodilation and sweating due to decreased sympathetic activity leading to heat loss by evaporation, conduction, convection and radiation. Adrenaline and thyroxine secretions are inhibited, while adrenocorticoid secretions are markedly increased.

In order to elucidate the effect of long term exposure, we studied the effect of prolonged (i.e., 6 weeks or more) exposure of mature rats to heat or warmth (34°C) on the thyroid gland function. The result showed a non-significant increase in serum thyrotropin (TSH) level and a non-significant decrease in level of thyroxine (T_4). Radioactive iodine uptake by the thyroid gland was not affected, while the histological examination of the thyroid gland was suggestive of unaltered thyroid function. This, we reported, may be due to temperature used in this study, which was 34°C, lower than body temperature. This was unable to raise the core temperature above 37°C. The mean arterial blood pressure and heart rates were also maintained.

Table 1

Rectal temperatures, Mean Arterial Blood Pressure and Heart Rates

	Normal	Cold	Heat
Rectal			
temperature (°C)	37.1 <u>+</u> 0.24	33.4 <u>+</u> 0.26	37 <u>+</u> 0.18
Mean Arterial BP			
(mm Hg)	125.32 <u>+</u> 243	73.66 <u>+</u> 2.85	120.66 <u>+</u> 2.57
Heart Rate		288 <u>+</u> 20.1	
Beats/min	396 <u>+</u> 13.1 beats/min	beats/min	384 <u>+</u> 13.15

- Effect of Cold and Heat

Responses of the Body to Cold

In most homoeothermic animals, core temperature is higher than environmental temperatures. Therefore, there must be active thermogenic processes that maintain a constant body temperature or the body has a highly regulated system that reduces heat loss from the core. Thus, cold results in heat conservations by two main mechanisms.

{i} Reduction in heat loss as a result of cutaneous vasoconstriction

{ii} Thermogenesis resulting in shivering which increases the metabolic rate Our study on the effect of prolonged exposure of mature rats to lower ambient temperature ($18 - 19^{o^{c}}$) on thyroid function showed that serum thyrotropin (TSH) was elevated, while thyroxine (T_4) level as well as the radioactive iodine uptake by the thyroid gland was significantly reduced. This result suggested that the observed high level of serum TSH could be as a result of the lower level of serum T_4 . This lower level of T_4 will lead to a decrease in the negative feedback of the hormone at the level of the pituitary gland, thereby causing more TSH secretions. The results appeared to be valid as they were substantiated by the various confirmatory tests performed on the cold-exposed rats, i.e the larger colloid size in the thyroid follicle of the cold-exposed rats (Fig 1a & 1b) and the flattening of the epithelia of the thyroid follicles and lower resting heart rate and blood pressure (see table 1; Figures 1a & 1b).

Histological Sections of Thyroid Glands of Normal and Cold-exposed Rats



Figure 1a Control rat: Note larger spaces between follicles and smaller colloid size

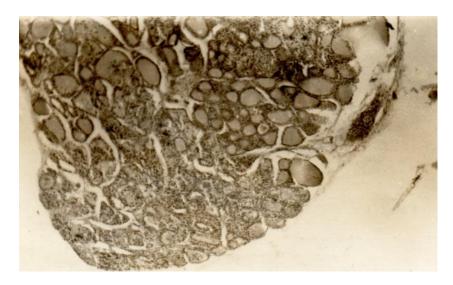


Figure 1b Cold-exposed rat: Follicles are completely filled with colloid with the epithelial flattened

The lower core temperature was probably an adaptation to the cold environment. Lower body temperature will reduce thermogenesis in the rats and so reduced the basal metabolic rate and heat production in the body. The lower core temperature in addition will lead to a reduction in enzymatic activities in the body. These will include that of adenyl cyclase which causes formation of cyclic AMP which acts as a second messenger to mediate the effects of TSH. The activities of other thyroidal enzymes involved in thyroid hormone synthesis and release like the proteases and the deiodinases, are expectedly depressed by the fall in core temperature. This is bound to affect the rate of thyroid hormone synthesis.

From our results, we infer that during chronic or prolonged exposure of rats to cold, there is an elevated TSH level while the levels of T_4 and I^{131} uptake are depressed. These observations strongly suggest that the elevated serum level of TSH is secondary to a reduced serum level of T_4 rather than being a primary response. This is so since I^{131} – uptake was not increased and the thyroid gland was not being stimulated.

<u>Effect of Varying Lighting Rhythm on Gonadal Function and Thyroid Activity</u> <u>in Rats</u>

Some researchers (Reiter and Sorrentino, 1971) elucidated the role of environmental lighting in modulating pineal gland activity. Until then, the physiological potential of the pineal gland was not clear.

Darkness is known to exaggerate the gonad-inhibiting capability of the pineal gland. The constraining effects of this organ on reproduction have been routinely demonstrated.

The most widely accepted mechanism whereby melatonin is believed to alter the function of the hypothalamo-adenohypophyseal-gonadal axis is through its ability to modify the firing frequency of the hypothalamic-gonadotropin-releasing hormone pulse generator (figure 2).

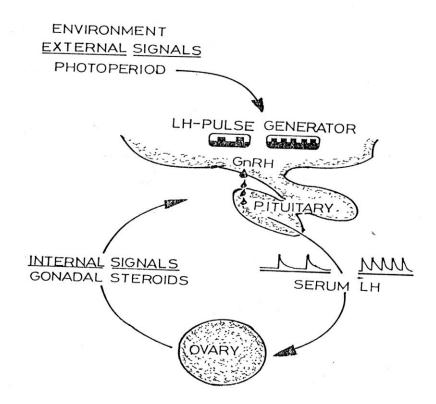


Figure 2: Presumed association between the environment, the hypothalamic gonadotropin-releasing hormone (GnRH), pulse generator, the secretion of LH from the anterior pituitary gland, and the ovarian function in mammals.

The mediator of the photoperiodic effects on the pulse generator is the pineal hormone, Melatonin. Melatonin is generally believed to modify the firing rate of the pulse generator thereby regulating reproductive physiology (Reiter, 1991).

Effect of Constant Light on Thyroid Activity in Rats

The effects of constant light exposure of pubertal male rats were studied. The result showed that the size of the thyroid gland was significantly increased. The level of the thyroid hormone, T_4 was also significantly raised. The histological examination showed that the thyroid gland had an increased activity as evidenced by the presence of little or no colloid in the thyroid follicles.

Normally, during the day, light inhibits the production of melatonin by means of the neural pathway. Conversely, at night during darkness, pineal melatonin production proceeds unabated. The almost exclusive production of melatonin at night has given rise to the concept that melatonin is the chemical expression of darkness. Based on the above statement, constant light exposure literally means melatonin production at night is suppressed; hence the antithyroidic effect of melatonin is absent.

Effect of Constant Light on the Pituitary Gonadal Axis in Rats

The result of our study on pubertal rats showed an increase in the size of the gonads, i.e., testes, epididymides, and ovaries. LH and FSH were also elevated, since the production of melatonin is inhibited by light. It is therefore logical that at night, the level of these hormones would be elevated. The observations were expected. In summary, the exposure to constant light has been shown to lead to a progonadotropic effect in the rat.

Effect of Constant Darkness on the Thyroid Activity in Rats

From our study, constant darkness resulted in reduction of the size of the thyroid gland, serum levels of T_4 remained unchanged. The histological

examination of the thyroid gland showed smaller but more numerous follicles than in the control. The follicles contained less colloid and larger epithelial cells than the control ones. Constant darkness would ensure that melatonin production proceeded unabated. The antithyroidic effect of melatonin would be expected.

Effect of Constant Darkness on the Pituitary Gonadal Axis in Rats

Our study showed that the sizes of the gonads were significantly reduced. The LH level in blood was also reduced significantly, while the FSH level was slightly reduced. The histological examination of the testes and the ovaries of the constantly dark-exposed rats further confirmed the anti-gonadic effect of melatonin in rats, since constant darkness means continuous production of melatonin by the pineal gland.

In summary, exposure of rats to constant darkness for a period of six weeks would result in gonadal regression and anti-gonad tropic effect in the rat as well as other specie particularly the hamster.

Effect of Cigarette Smoke on Tissues

Smoke from the average cigarette contains chemicals which are highly toxic, causing chronic airway diseases in smokers as well as non-smokers exposed to environmental tobacco smoke (ETS). It is associated with an increased risk of developing asthma, pneumonia bronchitis and cancer.

We investigated the effect of ascorbic acid on the degenerative effect of passive cigarette smoke on some vital organs of the rabbits. The result showed that cigarette smoke had deleterious effect on the lungs, testes and kidneys, but no significant effects were seen in the liver, brain and heart. Ascorbic acid appeared to have some attenuating effect on inflammatory processes as observed in the lungs, varying degrees of hypo spermatogenesis were observed in the seminiferous tubules. Although ascorbic acid had some attenuating effect on the inflammatory processes, it neither stopped inflammation nor declining function. Therefore, it is doubtful that the long-term effects of cigarette smoke could be prevented by ascorbic acid.

PHYSIOLOGY AND DIET

There is a correlation between diet and normal physiological processes. This leads to a saying 'you are what you eat'. We shall discuss some of the works we did on the effects of different types of diet on some physiological systems.

Relationships Between Low Calorie Diet, Aging and Peroxidative Damage

Our study on 18 months old male rats which had 60% of the calorie intake of the ad-libitum fed rats since six weeks of age showed that lipid peroxidation was markedly lower in the plasma, lungs and brain of the calorie restricted group while it was higher in the kidney when compared to the control. The activity of the enzyme glutathione peroxidase was higher in the lungs and brain, whereas it was lower in the kidneys when compared to the control and libitum fed rats. The result suggested that aging of the rats had been decelerated by calorie restrictions due to the decrease in the peroxidative damage in the lungs and brain.

We were able to elucidate a mechanism for reduction of lung aging during calorie restriction. That is the antioxidant capacity of the lung is increased, the

generation of free radicals is prevented by the Glutathione peroxidase (GPx) and thus lipid peroxidative damage is reduced. The mechanism for deceleration of brain aging process is similar to that of the lung, except that it is not due to an increase in the antioxidant capacity because the concentration of the glutathione system remained unchanged in the brain but rather due to prevention of free radical generation by the GPx which increase the uptake of peroxides, thus preventing peroxidative damage. Although it is generally accepted that calorie restriction increases longevity in rats, it is important to know that it could be <u>detrimental</u> to the kidneys because our result showed there was higher peroxidative damage on the kidneys of the calorie restricted rats compared to its control counterpart.

More on Low Calorie Diet

Calorie restriction has been shown to reduce the level of free radical generation in the tissue. Vitamin C supplements is also known to reduce blood pressure. We therefore examined whether low carbohydrate diet with slightly high protein and fat would reduce blood pressure and if ascorbic acid would enhance the effect. The study was on rats and we found out that there was a significant fall in the Mean Arterial Pressure in the group (Tables 2 and 3). Vitamin C was added to supplement the low carbohydrate diet. The blood pressure was even lower than the low carbohydrate fed rats. The salt content of the diet was the same, so the result had no relationship with the salt content.

TABLE 2

Body Weights, Ages, Pulse Pressure, Systolic and Diastolic Blood Pressure in the Control, LCHO-fed and LCHO + Vitamin C Rats

Rats	Weights	Age	Pulse	Systolic	Diastolic
	(g)	(Weeks)	Pressure	Pressure	Pressure
			(mmHg)	(mmHg)	(mmHg)
Control	202.5 <u>+</u> 45.2	10.13 <u>+</u> 1.6	16.63 <u>+</u> 3.7	96.13 <u>+</u> 16.1	79.50 <u>+</u> 12.9
(n=8)					
LCHO	208.8 <u>+</u> 26.7	10.50 <u>+</u> 1.3	16.00 <u>+</u> 5.9	76.30 <u>+</u> 25.9	60.30 <u>+</u> 5.9
(n=8)					
LCHO-Vit.C	235.0±34.2	11.75±1.5	13.50±4.0	67.00±15.5	53.50±12.3
(n=8)					
F value	1.82	2.9	1.00	4.52	4.16
P value	0.19	0.08	0.40	0.02	0.03
				Control	Control
				versus	versus
				LCHO-Vit.C	LCHO-Vit.C

TABLE 3 Mean Arterial Pressure and Heart Rate of the Control, LCHO and LCHO + Vit.C rats

Measured Variable	Control (n=8)	LCHO $(n = 8)$	LCHO-Vit. C (n=8)	P value
Mean Arterial Pressure (mmHg)	85.03±13.91	65.56±26.45	58.01±13.36	0.026 Control versus LCHO- Vit.C
Heart Rate (beats/min)	425.25±48.15	352.00±67.00	395.50±53.98	0.055

There was actually no significant reduction in the weight of the test rats. This implies that the attenuation of blood pressure was actually due to the low carbohydrate diet and ascorbic acid and not as a result of weight loss.

Reduced energy intake leads to the reduction in free radical generation. This would lead to the reduction in the oxidant levels in the cells. Vitamin C or ascorbic acid is water soluble and can directly react with the generated oxidants like super oxides and hydroxyl radicals. This means that there is a further reduction in the oxidant level in the cells. We suggested from the result of our study that low carbohydrate diet, by reducing the generation of free radicals, may allow the synthesis of more nitric oxide for smooth muscle relaxation, which leads to the observed fall in blood pressure. Ascorbic acid supplementation by its antioxidant effect, would further reduce the free radicals, enhance nitric oxide synthesis and, by this, reduce blood pressure even further.

Effect of Garri on Fertility and Pregnancy Outcome

Garri (roasted fermented cassava mash) is the staple food of most of the West African countries, including Nigeria. Cassava was reported to be high in dietary energy or carbohydrate and low in protein. Also, residual cyanogen in garri is implicated in the causation of tropical ataxic neuropathy. It has been shown that when garri is made into eba it reduces dietary cyanide load in consumers.

Diet during pregnancy should provide adequate energy and nutrients to support maternal and foetal needs. As a result, nutrients from all basic food groups – carbohydrate, protein, fats, vitamins and minerals are included in quantities to meet increased nutrient needs of pregnancy, thus promoting health and optimal pregnancy outcome.

In a region where garri is the staple food and mostly eaten by the majority of poor people leading to maternal malnutrition, one wondered how a high carbohydrate diet would affect the fertility and pregnancy outcome in a woman who eats this food throughout pregnancy. In order to answer this question, we designed an experiment using the female Sprague–Dawley rats. The index of fertility employed was the duration before conception (DBC) by monitoring the presence of spermatozoa in the vaginal smear after introducing a male rat into

the cage of the female rats. For pregnancy outcome, the parameters studied are foetal weights, number of live fetuses, number of implantation and resorption sites.

In this study, a total of 36 Sprague-Dawley rats (28 female and 8 male rats) with ages ranging from 18-20 weeks were randomly selected. The rats were divided into control and garri-fed groups. The control group received normal rat pellets and drinking water ad-libiturm and were mated in the 4th week of the experiment. The garri-fed group had garri plus ground rat pellets in the ratio of 1:1 and normal drinking water. They were also mated in the 4th week of the study. Each rat was weighed weekly and blood glucose levels were measured at the start and end of the experiment. Vaginal smear was performed on each rat.

TABLE 4

	MEAN BODY WEIGHT (Before Conception) (g)	BLOOD GLUCOSE LEVEL (Before Conception (mg/dl)	MEAN BODY WEIGHT (g)	WEIGHT GAIN (g)	BLOOD GLUCOSE LEVEL (mg/dI)	DURATION BEFORE CONCEPTION (Days)
Garri-fed	188 ± 7	62.8 ± 1.4	238 ± 17	50 ± 9	119.8 ± 2.4	11.8 ± 0.8
rats (n =						
14)						
Control	189 ± 6	60.2 ± 1.6	232 ± 15	43 ± 10	96.7 ± 2.7	5.4 ± 0.4
rats (N =						
14)						
P value	NS	NS	NS	NS	0.000	0.000

<u>Effect of Garri Intake on Mean Body Weight, Blood Glucose Level and Duration</u> <u>before Conception in Pregnant Rats</u>

<u>TABLE 5</u> <u>Effect of High Garri Intake on Pregnancy Outcome</u>

	MEAN FOETAL WEIGHT (g)	NUMBER OF LIVE FOETUSES	NUMBER OF IMPLANTATION SITES	NUMBER OF RESORPTION SITES
Garri-fed rats $(n = 14)$	30.8 ± 1.5	5.6 ± 0.7	7.8 ± 0.4	2.2 ± 0.6
Control Rats	23.4 ± 1.4	8.0 ± 0.5	8.6 ± 0.2	0.6 ± 0.4

(N = 14)				
P value	0.001	0.010	0.085	0.035

The result above shows that garri consumption might reduce fertility by delaying conception and reducing the number of live fetuses. However, there is need to take caution in extrapolating these findings to humans!!!

HERBS AND PHYSIOLOGY

The use of medicinal plants in preventive and curative disease conditions is not new. In view of this more plants are being investigated for their possible beneficial effects with the aim of bringing hope of adequate and affordable healthcare delivery to mankind. However, there is a need for proper scientific investigation of the effects (beneficial and harmful) of these plants on the physiology of man. We shall attempt to discuss the effects of some medicinal plants on physiology of man using experimental animals.

Tocolytic Effect of Cajanus cajan(Pigeonpea)

Cajanus cajan seeds are known to be widely used in the management of sickle cell anemia probably, because of their anti-sickling properties in vitro. Traditional herbalists claimed that the leaves of this leguminous plant are effective in the prevention of premature parturition. This was the reason that led to its crude extract being tested on the isolated rat uterus by our team. We observed that there was a significant reduction in the force and frequency of contraction. Low concentration of 2mg/ml of the aqueous extract of leaves of *Cajanus cajan* caused this significant reduction. At higher doses, the inhibition

was maintained. Thus, from our results, the traditional birth attendant's use of the leaves and seeds of *Cajanus cajan* as a preventive measure against premature parturition or miscarriage may be scientifically justified.

Effects of Methanolic Seed Extract of Piper Guineense (IYERE) on Fertility

The effects of methanolic seed extract of *Piper guineense* on fertility were studied using forty-two pubertal Sprague-Dawley female rats.

The results showed that there was a statistically significant increase in the occurrence of diestrous phase and a significant reduction in the proestrous and estrous phases in the treated rats compared to the control. The relative weights of the liver, kidney and heart were also significantly higher than those of the control. However, significantly lower mean relative weight of the uterus was recorded in the treated rats as compared to the control rats, while the length of the uterine horn was more than the control. Furthermore, there was a fewer number of developing follicles in the treated rats, as compared with the control group. Serum FSH was also lower in the treated group, while serum estrogen and progesterone levels were significantly higher when compared to the control group. There was no significant change in body weight in both treated and control rats. There was no pregnancy recorded in the treated group but mating was successful in the control group where all the rats were pregnant. Some of the rats in the treated group were able to get pregnant only after recovering from the effect of the extract for 3 weeks.

We concluded, therefore that, methanolic seed extract of *Piper guineense* could have a negative effect on female fertility in rats.

Effects of Aqueous Extract of Magnifera Indica on Reproductive Function

The effect of aqueous leaf extract of *Magnifera indica* (500mg/kg-body weight, orally) on the oestrous cycle, serum level of gonadotropic and female sex hormones, pregnancy, body weight and in-vitro uterine contractions were investigated in adult female Sprague-Dawley rats.

All these results revealed that the aqueous extract of *Magnifera indica* causes disruption of the oestrous cycle, reduces weight gain, reduces fetal weight, has no significant effect on implantation activities and prevents spontaneous contraction of the uterus effect

Effects of *Abelmoschus Esculentus* (Okra) On Reproductive Functions in Male Rats

The effects of *Abelmoschus esculentus* (Okra) extract on the male fertility parameters were investigated. Furthermore, it was investigated if the rats would recover from these effects (if any). The effect of *Abelmoschus esculentus* was also investigated on some reproductive and vital organs, hormone serum level and body weight.

A. esculentus significantly reduced (P < 0.05) sperm motility, sperm count, live/dead ratio (viability) and it increased percent abnormality. *A esculentus* had no effect on epididymal volume, neither did it have any significant effect on both testosterone and luteinizing hormone serum levels (p > 0.05). *A. esculentus* did not affect the weight of some vital organs like the heart, liver, and kidney. However, it reduced the mean weight of testes, this is supported by the

histological studies which showed testicular atrophy. There was significant reduction in the weight of the prostate gland. On the other hand, *A. esculentus* significantly increased body weight (P< 0.05). These effects were reversed after 2 weeks recovery period.

We therefore conclude that *A. esculentus* may reduce fertility of male rats as a result of the testicular atrophy seen, which is reversible while causing weight gain.

CONCLUSION

In conclusion, Vice Chancellor, Sir, normal body function could be altered when one is exposed to different environmental temperatures and lightings. Also, one needs to take caution especially on the type of diet or herbal medicine one takes, because of some adverse effects we have just discussed. Low calorie diet should be encouraged, but only in moderation, because of the adverse effect it has on the kidneys as reported earlier.

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To the Almighty God, my Redeemer, Saviour, lifter up of my head, my High Tower, my Rock, my Light, and my Buckler, I give all the glory.

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