***ADEBAYO ADETUTU MERCY***

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***MEDICINE AND SURGERY***

***300 LEVEL***

**ETIOLOGY OF CANCER**

All cancers are multifactorial in origin. They include genetic, hormonal, metabolic,physical, chemical and environmental factors .Most human cancers are spontaneous.

All cancers originate usually from one aberrant cell, which goes on to multiply and produce a tumor mass. One mutation occurs out of 1010 cell divisions. By the time a person reaches adulthood, about 1026 cell divisions have occurred. Through surveillance by the immune system, these aberrant cells are usually destroyed. As age advances, the number of mutations accumulate, hence the statistical probability of the incidence of cancer is increased. No wonder cancer is a disease of old age

* MUTAGENS: any substance which increases the rate of mutation can also enhance the rate of incidence of cancer. Therefore all carcinogens are mutagens. Examples of physical carcinogens are X-rays, gamma –rays and ultraviolet rays. Some human cancers are caused by chemicals. These may be introduced into the body by means of occupation (aniline, asbestos), diet (aflatoxins) orlifestyle (smoking). Chemical carcinogens act cumulatively. Tobacco, food additives, coloring agents and aflatoxins are common carcinogens in our environment.
* HEREDITARY: mutated gene causing cancer has 50% chance of being passed to offspring e.g. Xeroderma pigmentoza, familial adenomatous polypscoli.These 2 cancers are known to be highly hereditary.
* ONCOGENIC VIRUS/ONCOVIRUS: these viruses get integrated into the host DNAleading to multiplication of viral gene overtaking the normal host causing uncontrollable multiplication of cells.

MOLECULAR BIOLOGY OF CANCER

Normal cells tend to replicate normally and when they get older, they are remove by apoptosis (programmed cell death). The molecular basis of this is seen in the shortening of telomeres on the chromosomes of normal cells. Cancer cells are able to escapeapoptosis of the normal cell cycle. They accomplish this by production of the enzyme telomere polymerase which lengthens telomeres on chromosomes, through this apoptosis is prevented and cancer cells are immortalized. All normal cells receive signals for apoptosis, chemicals that cause cancer destroy these signals, and hence cells continue to multiply uncontrollably.

2. Simple obesity is characterized by a normal or increased growth rate with an acceleration of bone age maturation. It is characterized by a reduced growth hormone secretion evaluated by standard provocative test. The administration of GH releasing hormone or spontaneous 24-hour secretion.

Primary obesity is a medical condition in which excess body fat has accumulated to an extent that it may have negative effect on health. Commonly caused by a combination of excessive food intake, lack of physical activity and genetic susceptibility.

3. EFFECT OF CONGENITAL SYNDROME AND DRUG THERAPY ON OBESITY

**CONGENITAL SYNDROMES**

While the rising epidemic of obesity is primarily attributed to sedentary lifestyle, poor dietary habits and the aging of the population, secondary causes of obesity generally go undetected and untreated. These include endocrinological disorders, such as Cushing’s syndrome, polycystic ovary syndrome, hypogonadism and hypothyroidism, as well as genetic, syndromic and drug-related obesity.

Syndromic obesity:

• Prader–Willi syndrome • Bardet–Biedl syndromes • Beckwith–Wiedemann syndrome • Alstrom–Hallgren syndrome • Carpenter syndrome • Cohen syndrome

Syndromic obesity : Severe obesity is a characteristic feature of many congenital and genetic disorders, such as AHO, Alstrom–Hallgren syndrome, Bardet–Biedl syndrome, Beckwith–Wiedeman syndrome, Carpenter syndrome, Cohen syndrome and Prader–Willi syndrome (PWS), the latter being one of the most common syndromic forms of obesity in children . In addition to being overweight, children with genetic syndromes associated with obesity typically have characteristic physical findings, including dysmorphic features, developmental delay and mental retardation.

Prader–Willi syndrome PWS is a congenital neurodegenerative disorder caused by genetic abnormalities of the long arm of chromosome 15(q11–13), usually secondary to the deletion of paternal DNA, leading to the lack of the SNRP gene, which occurs sporadically. Clinically, PWS results in hypotonic infants and later in insatiable obese, mildly retarded, behaviorally disturbed adolescents and adults. Most patients have reduced GH secretion and hypogonadotropic hypogonadism, suggesting hypothalamic–pituitary dysfunction. Genetic testing usually confirms the clinical diagnosis. There is no effective treatment for most of the problems associated with PWS. Nevertheless, encouraging results have been observed with the early administration of GH, resulting in accelerated growth and decreased body fat; sex hormone replacement may also be beneficial. Obesity management is crucial in the care of the patients with PWS; limiting access to food through close supervision and physical barriers is usually recommended.

**DRUG THERAPY ON OBESITY**

Several drugs are known to be associated with weight gain.

Anti-diabetic medications: treatment of diabetic patients with insulin and sulfonylureas, and not metfomrin, results in an average weight gain of 4.8 kg in 3 years . The effect of insulin is usually associated with increased hunger and appears to be dose-dependent. A potential explanation of the weight gain with insulin is the improved utilization of calories through a decrease in glycosuria. Thiazolidinediones use is also classically associated with modest weight gain, with preferential distribution of fat in the subcutaneous areas and around the hips. Diabetic patients treated with insulin or sulfonylureas or thiazolidinedione should be counseled regarding lifestyle changes necessary to avoid weight gain.

Centrally acting medications: Antipsychotics, antidepressants and antiepileptic can increase body weight, probably through their effect on the monoamines in the CNS. Among newer neuroleptic medications, clozapine and olanzapine have been associated with an average weight gain ranging between 3–4.4 kg and an increased risk of diabetes and dyslipidemia. Moreover, schizophrenia has been associated with an increased risk of metabolic disturbances and diabetes; this link is poorly understood, with a low attribution to the role of antipsychotic medication. The antidepressants amiryptilin and paroxetine have specifically been implicated in weight gain. Carbamazepine, gabapentin and valproates are anticonvulsants that can cause weight gain as well. Weight-reducing or weight-neutral alternatives should always be considered when possible in overweight or obese subjects.

Smoking cessation: Smoking cessation has been traditionally linked to a 3–5 kg average weight gain, which is thought to be at least in part due to nicotine withdrawal. The potential mechanisms of weight gain include increased caloric intake, decreased resting metabolic rate, decreased physical activity and increased lipoprotein lipase activity. Therefore, close monitoring of body weight and promoting lifestyle changes should be part of smoking cessation programs. The use of bupropion and nicotine replacement, particularly nicotine gum, might be helpful in preventing weight gain in this vulnerable population.