The salt tax and cardiac health

Controlling intake would have snowballing benefits, says s ananthanarayanan

THE first results of a study by the Harvard School of Medicine conclude that cutting salt in diet could reduce deaths from cardiovascular disease (CVD) in developing countries by three per cent. CVD is the world's biggest killer, claiming 17.3 million lives each year. More than 80 per cent of these deaths are in low and middle-income countries. CVD is likely to keep its first place as the single biggest cause of death, and by 2030 would account for 23.6 million deaths each year. There are, thus, huge costs of productive hours lost and on medicare, and there is a rising emphasis on prevention by healthy eating, exercise and avoiding smoking.

The study is based on a reduced consumption of salt through voluntary and tax induced control of salt content of processed foods in the UK. As both the use and the regulation of processed foods are negligible in developing countries, the percentages arrived at may be off the mark. But there has been an alarming increase in the incidence of CVD in developing countries and the study — whose results were presented at the World Congress of Cardiology, 2012, in Dubai — underscores the importance of reducing salt intake.

The word signifies disease of the heart, veins and arteries and includes a thickening of artery walls and high blood pressure. The causes and treatment are inter-related and each cause or medication impacts the others. The disease is usually advanced by the time it is detected — and brings with it drastic life-style change and medical costs, hence the crying importance of prevention. While treatment has become sophisticated — mechanical widening of arteries, bypass surgery and even heart transplant — management by careful monitoring and drugs and medicine is also well developed.

A major cause of CVD is considered to be the imbalance of cholesterol, a fatty substance that causes a narrowing of the arteries and increases the load on the heart, apart from sometimes starving the heart muscle itself of oxygen and nutrients. The other major risk factor is hypertension or high blood pressure.

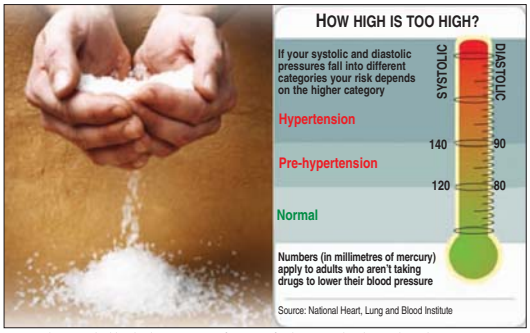
Apart from increasing the load on the heart, hypertension also leads to multi-organ failure, particularly that of the kidneys. Indeed, hypertension is an important cause of CVD and is responsible for 50 per cent of the cases. And the risk of developing CVD doubles for every 10-point increase in the lower of the BP readings. Treating raised blood pressure has been associated with a 35-40 per cent reduction in the risk of a stroke and at least a 16 per cent reduction in the risk of a heart attack.

Dr Thomas Gaziano, assistant professor at the Harvard School of Medicine, says, "These results show that strategies to reduce sodium consumption, even by modest amounts, could lead to significant reductions in CVD mortality in developing countries and potentially save overall healthcare costs associated with these diseases... In developing countries, where the burden of CVD is highest, these simple steps could deliver a significant long-term impact and must be something that governments trying to manage rising healthcare costs should consider."

Salt and BP

In simple terms, the blood requires a controlled level of salinity for its functions. When there is too much salt because of content in the diet, the kidneys move in to eliminate salt via the urine. But when this is not fast enough or efficient, the artery walls take in water, by osmosis, to dilute the blood and reduce salinity. The increased volume of the artery contents is the first, mechanical reason for an increase in BP. Elevated BP need not, of course, be the immediate result, as the arteries and veins do have some elasticity, but higher levels of salt are also found to induce a secretion of adrenaline, which causes constriction of the arteries. And sustained high levels of salt intake can result in chronic hypertension.

As common salt is sodium chloride, salt in solution in the blood splits into a pair of ions, sodium$^+$ and chlorine$^-$. This reduces a value called "water potential" of the water in the bloodstream, as compared to the water content of the body cells and in the intracellular fluids. Water, hence, flows in to balance the water potential. The osmotic pressure can be kept down by using a mixture of salts, like potassium chloride or other mineral salts along with ordinary salt. A higher potassium intake in primitive societies, as opposed to higher sodium levels in processed foods, is considered to explain a lesser incidence of hypertension in primitive cultures.



The quantity of salt a person normally needs is about 500 mg a day. Most people consume many times this level, even 10 times as much. It is a marvel that the body gets rid of the excess salt and keeps working for years and years. But with increasing age or other factors, the symptoms of hypertension set in, with its impact on CVD. Reduction of salt intake is found to be immediately effective and the low level advised is about 1,500 mg a day. The study by the Harvard Medical School collected data of the effect on BP of different factors and has concluded that the control of salt intake, through the twin strategies of voluntary reduction through norms set for industry and enforced reduction through a tax on products that contain salt, could lead to about a three per cent drop in the number of deaths caused by CVD in 19 developing countries. These 19 countries represent half the population of the world.

The base for the study was the UK Food Standards Agency experience which assessed the net intake reduction in Britain at 9.5 per cent as a result of a series of targets that have been set for individual food products. An independent study has also shown that a taxation increase of 40 per cent on industry prices leads to a six per cent reduction in consumption. Based on this model, the study calculated that the same measures could reduce the incidence of myocardial infarctions (heart attacks) by up to about 1.7 per cent in China and 1.47 per cent in India. The reductions in the incidence of stroke are calculated to be about 4.7 per cent in China and four per cent in India.

It is evident that other factors operate in China and India, but Dr Thomas Gaziano, assistant professor at the Harvard School of Medicine, does say, "These results show that strategies to reduce sodium consumption, even by modest amounts, could lead to significant reductions in CVD mortality in developing countries and potentially save overall healthcare costs associated with these diseases… In developing countries, where the burden of CVD is highest, these simple steps could deliver a significant long-term impact and must be something that governments trying to manage rising healthcare costs should consider."

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The secret of lines we never forget

Researchers, says nick clark, have hit on a formula to work out why certain quotes stay with us

'HASTA la vista, baby" may have been uttered by a murderous cyborg played by Arnold Schwarzenegger, but could a computer recognise it as one of cinema's most memorable lines? Yes, according to a group of American researchers at Cornell University that has created a computer programme to break down the formula behind some of cinema's most enduring lines, from *Dirty Harry's* "Do you feel lucky, punk?" to *Casablanca's* "Here's looking at you, kid."

In its current form, the algorithm may not be a huge help for budding screenwriters looking for their first hit, but its creators believe that in the future it may well be able to come out with a few classic quotes, or at least a successful advertising slogan, on its own. Computer scientist Cristian Danescu-Niculescu-Mizil initially wanted to scrutinise political speeches and news bulletins to pick out the best lines, but when these turned out to be too problematic the team turned its attention to films to analyse what drove certain lines into popular culture. For its research paper — entitled "You had me at hello: How phrasing affects memorability" — they scoured the Internet for film scripts and studied 1,000 films, highlighting memorable quotes selected by users of the film website imdb.com.

Errol Flynn and Vivien Leigh in Gone With The Wind.

The team then asked people to judge between two quotes from films they had not seen, with one line memorable and the other less so. In about 78 per cent of cases, people could detect the more memorable quote.

The researchers found that the more memorable quotes were made up of word combinations unlikely to appear elsewhere in the film. Yet the grammatical structures of the quotes tended to be ordinary.

Other interesting quirks of the memorable quotes included more of a use of the indefinite article rather than the definite article, verbs in the past tense and the use of pronouns other than "you". The best quote, according to Danescu-Niculescu-Mizil, was, "Frankly, my dear, I don't give a damn," uttered by Clark Gable as Rhett Butler in *Gone with the Wind*. He said, "That quote ticks a number of boxes. It has the general aspect but also it has an unusual combination of 'my dear' and 'damn'." He also pointed to other general quotes such as the opening of *Star Wars*: "A long time ago, in a galaxy far, far away."

"There are some trends you can pick out of the language. It is no silver bullet; for example, a [common] phrase like 'I'll be back' isn't easily categorized," he added.

Generating lines of its own, he said, would be "the next step. You know what you want to say, but how do you make it more memorable? No computer can tell you that at the moment."

The Independent, London

Lateral differentiation of chromosome

Is there a comparable difference and, if so, how consistent is it with the genetic needs of the cell and with the requirements of the cell in division? tapan kumar maitra explains

THE linear morphological variation evident in somatic, meiotic, lampbrush and salivary gland chromosomes is consistent with, but not demanded by, the fact that chromosomes are similarly differentiated in a genetic sense; that is, the genes that differ among themselves in phenotypic expression are organised along the length of the chromosome in linear fashion. This is established from recombinational evidence. The chromosome, or linkage group, in a bacteriophage has its individual genes organised into a continuous DNA molecule. A small amount of protein is associated with this DNA, but the organisational relationships are unknown.

The bacterial chromosome is similar to that in bacteriophage, but its length is much greater. By way of contrast, the DNA of higher organisms is arranged in the form of microscopically visible chromosomes and its length per chromosome is to be thought of in terms of centimetres rather than microns. Whether this is a continuous strand of DNA is a question that remains to be solved, but the manner in which this is packaged into manoeuvrable chromosomes that can replicate, segregate and manufacture transportable RNA still eludes definition.

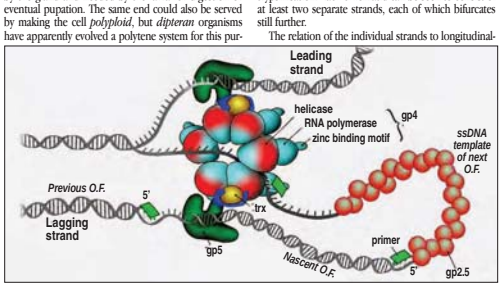
Is there a comparable lateral differentiation of the chromosome (that is, the number of subdivisions) and, if so, how consistent is it with the genetic needs of the cell and with the requirements of the cell in division? That kind of chromosome about which there is little disagreement is the salivary gland chromosome; it is generally agreed that it is a multi-stranded, or polytene, structure. This, of course, is suggested by its very large diameter, and is supported by visual observations, particularly of puffs. Additional support is also provided by chemical evidence because the DNA content continues to increase during development of the cells of the salivary gland in a manner that indicates successive DNA doublings.

As far as we know, every doubling of the DNA content of a nucleus means another replication of all DNA double helices. The meaning of *polyteny* as it relates to division is of little concern, because these cells will undergo no further change before they die. It is, however, of interest to know what genetic purpose is served by the polytene condition of these chromosomes. One possible answer is that it increases the genetic "horsepower" of the cell, particularly of those loci, or puffs, which are actively concerned with the elaboration of products furnished by the gland and needed by the larva for digestion or eventual pupation. The same end could also be served by making the cell *polyploid*, but *dipteran* organisms have apparently evolved a polytene system for this purpose.

Cytologists are divided over whether other chromosomes are multi-stranded or whether, in interphase prior to DNA synthesis, the chromosome contains the minimal number possible, a single DNA helix plus its associated proteins. The multi-stranded concept is derived largely from electron-microscope sections. Numerous very fine fibrils about 40 Å in diameter are repeatedly encountered and have been considered to be the basic longitudinal unit of the chromosome.

Construction of three-dimensional models from consecutive thin slices of nuclei leads to the kind of chromosome depicted. Each chromatid is quadripartite, each chromosome octipartite, from G_2 (after DNA replication) through metaphase. A similar structural view is obtained from the metaphase chromosome of Vicia, isolated from ruptured cells and enzymatically relaxed by trypsinisation. Each chromatid can be seen to consist of at least two separate strands, each of which bifurcates still further.

The relation of the individual strands to longitudinally oriented molecules of nucleoprotein remains to be determined, but clearly each chromatid at metaphase is subdivided laterally at least once, and possibly several times. This point of view is supported, in part, by both X-ray and chemical evidence. If chromosomes are irradiated by X-rays prior to DNA synthesis, the aberrations produced are of the chromosomal type: they involve the entire chromosome across its full diameter rather than some finer longitudinal subdivision of it. If irradiated during or after DNA synthesis, the aberrations are of the chromatid type: the chromatid rather than the entire chromosome is the unit of breakage. However, if chromosomes are irradiated in late prophase, half-chromatid aberrations can be induced.



A depiction of the replication of the chromosome of bacteriophage T7: on the leading strand, T7 DNA polymerase (gp5) undergoes multiple conformational changes as it moves from one template position to another and senses the correct fit of an incoming deoxyribonucleoside triphosphate. E. coli thioredoxin (trx) binds tightly to the thumb subdomain of gp5 and increases its processivity hundreffold. The interaction with gp5 also creates docking sites for the other T7 replication proteins. Unwinding of the DNA to create a ssDNA template for gp5/trx is accomplished by the helicase located in the C-terminal half of T7 gene 4 protein (gp4). Gp4 assembles as a hexamer on the lagging strand and uses the energy of hydrolysis of dTTP to translocate 5'-3' on ssDNA; it unwinds duplex DNA that it encounters.

As no additional period of DNA synthesis has occurred, the induction of aberrations during this stage would suggest that either the chromosome in late prophase is at least quadripartite or that these aberrations result from a rupture of only one of the two polynucleotide chains of a single DNA helix. The chemical evidence, obtained by autoradiographic techniques, supports the former possibility. H^3-thymidine, which is quickly and selectively incorporated into DNA, is given to root tips just prior to DNA synthesis. The newly formed DNA, therefore, can be distinguished from the old DNA by its radioactivity, assuming that DNA replication chromosomes at the first metaphase should show labelling in both chromatids. However, if these same chromosomes are allowed to replicate again in a non-radioactive medium, they have the following appearance: about two-thirds to three-fourths of the chromosomes have chromatid labels, the others unlabelled. This result would suggest that prior to DNA synthesis the chromosome consists of a single double helix of DNA. The remaining chromosomes, however, show both chromatids labelled. Neither genetic phenomena nor the demands of cell division seemingly require that the chromosome, prior to DNA synthesis, be subdivided in the manner suggested by the evidence presented. A single double helix of DNA should suffice. Cell division is an extraordinarily precise process and genes in single dose (double dose in a diploid cell) would seem sufficient to take care of the metabolic needs of the ill. Furthermore, one might expect nature to be economical in this case, with multistrandedness apparently being redundant. It is these moderations that suggest that the lateral differentiation, as observed, is genetic insurance.

The information does not permit us to present a final picture of a chromosome at the molecular level. There are, however, some reasons for drawing tentative conclusions. DNA and histone comprise the bulk of a chromosome and it is thought that the histone may occupy the grooves of the DNA helix, spiralling in the same manner as does the DNA, or it may exist as a sheet-like structure uniting adjacent strands or adjacent coils of DNA. This hypothesis, based on the synthetic capacity of isolated chromatin to make RNA, requires further confirmation. Some mechanism must be present to determine whether DNA is synthesising RNA, is forming more DNA in the process of replication or is metabolically inactive. This control system has no been identified.

The several RNAs of the chromosome appear to be of a transient sort, destined for transfer to the cytoplasm. The role the non-histone protein plays is unknown. It exhibits a turnover rate comparable to RNA, but its amount appears to be related to the metabolic state of the cell. Its place in the functional organisation of the chromosome is unknown but it may well be concerned with the control of chromosome compaction or as a competitor with histone for attachment to DNA.

Whether DNA extends continuously throughout the length of the chromosome or is tied in blocks to link molecules is also undetermined. Enzyme studies would suggest that DNA is continuous from end to end, because only DNase can rupture the chromosome into smaller units. Proteases fail to do this, indicating that there are no protein regions in the chromosome which, if ruptured, lead to breakage of the chromosome. However, if the chromosome were one continuous DNA molecule it would be logical to assume that it would progressively replicate, beginning at one end and progressing to the other.

This it does not do. Replication, as indicated by the incorporation of radioactive DNA precursor molecules, can begin simultaneously at a number of discrete points along the chromosome. A minimum of 50 such beginning points have been found in the X chromosome of *Drosophila melanogaster*, and such a chromosome can be thought of as consisting of a number of replicons, each representing functionally related sets of genes and each being capable of the initiation of DNA synthesis.

It is, furthermore, difficult to conceive of the replication of a continuous DNA molecule, which may reach several centimeters in length when stretched out and possess a complete turn every 34 Å of length. Unwinding of the replicated helices must occur, and the unwinding line is a function of the square of the molecular weight. It has been estimated that a human chromosome of average length should take 400 hours to unwind during replication, but autoradiography indicates that it does so in six hours. Data of this sort would suggest that the DNA of a chromosome cannot be a continuous strand, at least during the replication period, but our lack of information about chromosome structure does not permit the design of a model that satisfies all the requirements demanded of it. Parenthetically, it might be pointed out that unwinding time, calculated on the basis of molecular weight, might well be a misleading estimate, because the line required to melt DNA (melting also involves unwinding of the polynucleotide strands) is considerably shorter.

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