SUMMARY
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1. Various DNA-repair parameters like unscheduled DNA synthesis (UDS), two putative DNA-repair deoxyriboendonucleases - UV DNase and AP DNase, and DNA-polymerase β were studied in the peripheral lymphocytes of humans under various conditions.

2. Subjects of Indian population, living under their natural conditions were divided into three age groups - young (8-14 years), adult (20-35 years) and old (> 55 years).

3. Each of the above three age groups were further subdivided into 2 sub groups - Normal, with a body mass index of 20 or more (NBMI) and undernourished with a body mass index of 18 or less (LBMI).

4. All the subjects were examined for various biochemical and clinical parameters to make sure that they did not suffer from any apparent deficiencies. Thus the LBMI group is considered as a population which has been chronically restricted in its dietary-calorie consumption and therefore regarded as mildly undernourished without any apparent malnutrition.

5. The LBMI group (undernourished) showed higher DNA-repair potential, in terms of above parameters, particularly at 'adult' and 'old' ages. Also, the LBMI group exhibited reduced decline in DNA-repair potential.

6. A similar pattern of results was seen when the lymphocytes were challenged with UV light or stimulated to proliferate with phytoheamagglutinin.

7. These results were taken to indicated a beneficial effect on DNA-repair capacity by reduced calorie consumption in humans also.
8. Down syndrome, with chromosomal aberration of trisomy of chromosome 21, displays maximum number of accelerated aging symptoms. Therefore a study was taken to examine the DNA-repair parameters, mentioned above, in the peripheral lymphocytes of the patients alongwith age and sex matched normals.

9. Here also, the patients were divided into three age groups - Group A upto 12 years; Group B - 13-25 years and Group C beyond 25 years to represent the young, adult and old ages in the accelerated aging scenario.

10. Unscheduled DNA synthesis (UDS) was tow in Down patients at all the ages compared to age- and sex matched controls. Also, the decline in the UDS with advancing age was more precipitous in Down patients.

11. A similar pattern of results was obtained even after the lymphocytes were challenged with either UV (at 2 doses - 20J/m² and 40J/m²) or with MNNG (50µM for 30 minutes).

12. While some induction in UDS was seen with the UV dose of 20J/m² in Down lymphocytes, 40J/m² dose failed to show any further induction, in contrast to that in normals, indicating that the capacity of Down patients to raise their level of DNA-repair against higher doses of UV is limited.

13. When the lymphocytes were treated with the methylating mutagen, MNNG, the induction in Down patients is quite comparable to that in controls suggesting that repair of the MNNG induced DNA-damage is spared in this syndrome.

14. A similar pattern of results was found in the case of activities UV and AP DNases, total DNA-polymerases and polymerase (3 with respect to UV and MNNG induction.
15. In the case of DNA-polymerase s, a recently discovered enzyme with a distinct role in short-patch DNA-repair, activity, both before and after induction with either UV or MNNG, was higher in Down subjects than in normals. Although there was a decline in this activity with age, the values in Down patients were always higher. Furthermore, the percentage of ε activity out of total DNA polymerase activity was about 17% in Down syndrome subjects while it was only about 5% in normals.

16. Since both (3 and ε polymerases are known to participate in short patch DNA-repair (e.g. MNNG induced repair), it is concluded that in Down syndrome, repair involving a short patch synthesis is not very adversely affected while the repair involving long patch synthesis (e.g. UV induced repair) is distinctly reduced.

17. Decreased DNA-repair potential, particularly involving long patch synthesis may be an important causative factor for the accelerated aging symptoms seen in Down patients.

18. Preliminary studies on the Average Telomeric Length (ATL) showed that in aging humans, there is a reduction of ATL with age.

19. When the subjects were grouped as LBMI and NBMI (3 in each group), the LBMI group showed slightly longer ATL as compared to NBMI indicating a delayed aging process.

20. Preliminary studies with Down syndrome subjects, showed that the ATL is shorter as compared to the age- and sex-matched controls - once again showing that Down syndrome patients are in a biologically advanced aging state.