IJGC

INDIAN JOURNAL OF GERIATRIC CARE
MAY-AUGUST 2020, VOL. 9 NO 2

HIGHLIGHTS

- Immunomodulators in Geriatrics
- Geriatric TB: An Area of Concern
- Insurance Policies In Elderly
- Drugs to be Avoided in Liver Diseases

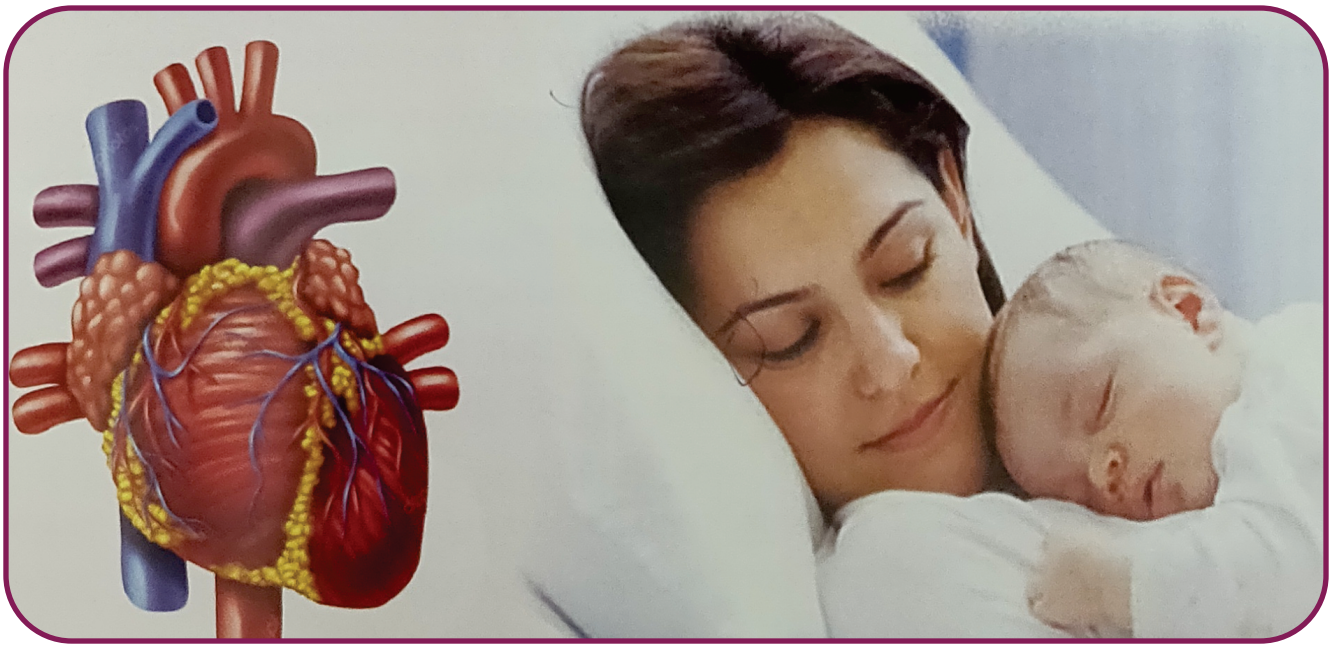
With Best Compliments From

Dr. Satish Gulati
M.D.F.I.C.P., F.I.A.M.S., F.G.S.I.
Consultant Physician & Geriatrician
Cell: +91-9812026168

Dr. (Mrs.) Rita Gulati
M.D., D.G.O., F.I.A.M.S.
Consultant Obstetrician & Gynaecologist
Cell: +91-9896342097

Dr. Dishant Gulati
M.B.B.S. M.D. (Medicine)
Consultant Physician
(Former Assistant Professor SGT Medical College, Budera (Gurgaon)
Cell:+ 91-8930198124

Ms. Divya Gulati
Computer & Administration In-Charge
Cell: +91-9996233397



Bharat Nursing Home

Sonipat Road, Rohtak-124001, Haryana

Equipped with Gynae, Internal Medicine, Pediatric,

Sonography, Biochemistry, I.C.U. & Psysiotherapy Services

Ph: 01262-256955, 01262-313955, 09315507729

Editorial Board

IJGC
Indian Journal of Geriatric Care

Subscription Information:
Indian Journal of Geriatric Care is published three times a year.

DELENG/2012/42798 Dt. 12 June 2012, Price Rs. 20 Per Copy

Annual subscription for Journal, all flyers and circulars Rs: 1000.00 (One Thousand Only) for India; for other countries US $ 40.The journal is dispatched within India by surface mail and to other countries by sea mail.

Business Correspondence:
Enquires concerning subscription, advertisement, etc, should by addressed to Dr.O.P.Sharma, Editor-in- Chief , IJGC, K-49 Green Park Main New Delhi 110016.
Tel: 9810627346. Email : opsharma.gsi@gmail.com

Edited, printed and published by:
Dr. O.P. Sharma, for The Geriatric Society of India, K-49 Green Park Main, New Delhi-110016.
The Editor disclaims any responsibility or liability for statements made and opinion expressed by authors or claims made by advertisers.

Advertorial Enquiry:
Dr. O.P. Sharma, Editor-in- Chief, IJGC, K-49 Green Park Main, New Delhi-110016. Tel: 9810627346. Email : opsharma.gsi@gmail.com

Printed at Modest Graphics (P) Ltd, C-53, DDA Sheds, Okhla Phase-I, New Delhi, India.

CONTENT

IJGC
INDIAN JOURNAL OF GERIATRIC CARE

GUEST EDITORIAL

REVIEW ARTICLES

CLINICAL TIPS

GSI NEWS

Editorial

Dr. P S Shankar
Emeritus Professor of Medicine,
Senior CEO, KBN Teaching & General
Hospital, Kalaburagi, Karnataka

GUEST EDITORIAL

Relevance of Updation in Geriatric Medicine

There is an urgency to address the health issues of this growing mass of population as a separate segment. In advancing years many age-related disabilities begin to appear. Mobility suffers, hearing gets impaired; there is gradual loss of eye sight and loss of memory. The immunity declines making elderly persons more vulnerable to infections. Diabetes, heart diseases, cancer, enlarged prostate, Parkinson's disease, and Alzheimer's disease make their appearance. Often there is fall making them bed-ridden. Hence the aged require special medical attention. At the same time, we must remember that 'there are no diseases of the aged, but simply disease among the aged'.

The grey population which accounted for 6.7% of total population in 1991 in India is expected to increase its share to more than 10% by year 2021. The size of the elderly population has risen from 12.1 million in 1901 to approximately 77 million in Census 2001. According to official population projections, the number of elderly persons will rise to approximately 140 million by 2021. The southern states are the front runners in population ageing along with Himachal Pradesh, Maharashtra, Odisha and Punjab. The central and northern states such as Uttar Pradesh, Rajasthan, Madhya Pradesh, Bihar, Jharkhand, Chhattisgarh and Uttarakhand have much lower proportions of aged population.

With ageing population there is an increase in number of elderlies with disease burden; they suffer from impairment in cognition, vision and hearing, and show reduced physiological reserve becoming susceptible for any minor change in day-to-day life.

There is a great need to focus our attention towards their medical and health needs. The big number of geriatric populations is increasing day by day; year after year. Goethe has said, 'no skill or art is needed to grow old, the trick is to endure it'. The physician has to strive not to put more wrinkles in their minds than their faces.

The elderly exhibit a decline in functions of various organs and systems, along with alteration in the anatomical structure. In advancing years many age-related disabilities begin to appear. Mobility suffers, hearing gets impaired; there is gradual loss of eye sight and loss of memory. The nerve conduction becomes less rapid and the reflexes become slow. The immunity declines making elderly persons more vulnerable to infections. The elderly are susceptible to same diseases to

which middle-aged suffer. Diabetes mellitus, ischaemic heart disease, cerebrovascular disease, cancer, enlarged prostate, Parkinson's disease, and Alzheimer's disease make their appearance. Often there are falls with fractures making them disabled and bed-ridden. The care of elderly has become complex. They have 'to live' rather than 'die from' chronic disorders of advancing age. This has necessitated for care by a comprehensive multidisciplinary approach.

In the background of this, there is an urgent to strengthen the teaching and training of Geriatric Medicine. The number of health care providers with specialized training in geriatrics is not commensurate with the growing population of elderly persons. In a study by Bardach and Rowles, it was found the older patients have unique needs and it is not being fulfilled due to shortage of time in packed curricula, lack of geriatrics-trained educators, absence of financial incentive, and low student demand. They found they formed the barriers to improving geriatric training.[1]

Age Friendly University has taken a new-initiatives in Higher Education Institutions (HEIs), to apply guiding principles to health professions education in healthy gerontology, and to provide specific geriatrics/gerontology competencies for health professions programs to integrate into the program's curriculum. It will give the opportunity to prepare future health professions providers with improved older adult health care skills that also benefits older adults.[2]

Health professionals specializing in geriatrics play a very important role in shaping the care of older adults. Mezey and colleagues have found an interdisciplinary didactic and clinical training *milieu* would have the potential to maximize training opportunities for geriatric health care professionals.[3]

Hitherto the undergraduate curriculum in our country did not have any separate chapters on Geriatrics and the students were not trained. Now with the revision of the curriculum, Geriatrics has found a place. The students are trained on General principles of Gerontology, Evaluation of older persons, ageing brain, cardio-respiratory, musculoskeletal disorders, metabolism, prescribing, management, health promotion and terminal care.

Since the practitioners had no formal training in Geriatrics, they are finding difficulty in the evaluation of the conditions commonly encountered in aged population. The ageing population will suffer from the diseases encountered in adult life and the degenerative conditions make their appearance in old age. They need to be trained in the Geriatric issues which will give confidence to treat Geriatric population.

Geriatric Society of India has initiated an on-line training program to sensitize the Medical Practitioners. This is a 3-months program which covers the disorders encountered in old age and their management. The updating of their knowledge through these programs will go a long way in improving the Geriatric training and education.

REFERENCES

1. Bardach SH, Rowles GD Geriatric Education in the Health Professions: Are we making progress? Gerontol 2012: 52(5); 607-618
2. Gugliucci MR, O'Neill D Health professions education: Advancing geriatrics and gerontology competencies through Age-Friendly University (AFU) principles Gerontol Geriatr Educ 2019: 40(2); 194-202
3. Mezey M, Mitty E, Burger SG, McCallion P. Healthcare professional training: a comparison of geriatric competencies J Amer Geriatr Soc 2008: 56(9); 1724-9

Immunomodulators in Geriatrics

SHIKHAR GARG*, A.K. SINGH**

Our immune system is a network of special cells, tissues, proteins and organs which work in harmony to protect us from damaging foreign invaders and diseases. If our body comes in contact with foreign invaders like bacteria, viruses or parasites then it triggers an immune response against them. The first work of the immune response is to discriminate between self and non-self and if it is non-self then it destroy them. Immunity is of two types, innate or natural and adaptive or learned. Innate immunity is that with which we are born with and is the first line of our defense against infections. Adaptive immunity is that which we learn or acquire throughout our life after getting exposed to various diseases or after getting vaccination against them. Adaptive immunity takes 5-10 days for its proper action and before that innate immunity fights against invaders. Immunosenescence is the senescence of the immune system or decline in the immune system or dysregulation of the immune system with increasing age.[1,2] As actions of the immune system is invisible hence it is very difficult to quantify them. The clinical manifestations of declining immune system are progressive and take decades and may also be mingled with other manifestation of aging. Biomarkers of immunosenescence are unreliable which makes monitoring of immunosenescence and interventions against it very difficult. The overwhelming decrease in T-cell functions is the hallmark of immunosenescence.[3] Declining immunity in elderly make them more susceptible to diseases, more prone to infections and there is also a poor response to treatment with vaccination in them.[4]

CHANGES IN IMMUNE SYSTEM WITH AGEING

Aging is associated with the gradual decrease in lean body mass combined with gradual increase in fatty tissue at various parts of the body. Increased fat accumulation in bone marrow and thymus causes reduction in effective bone marrow and thymic tissue respectively which further results in decreased production of B-cells from bone marrow and naive T-cells from thymus.[5,6] Adipose tissue expansion with aging is also a major source of inflammation in elderly(inflammaging) which has a marked influence on systemic metabolism and may results in increased incidence of insulin resistance, type-2 DM and various cardiovascular disorders in them.[7] Innate immunity declines with aging. In elderly dendritic cells became less effective and functions of neutrophils also declines eg. slow response to chemotaxis, phagocytosis, superoxide generation and alteration in signal transduction and membrane lipid rafts.[8] Aging is also associated with decreased ability of the peripheral lymphoid cells to undergo clonal expansion or regeneration which leads to decreased cell mediated immune response, phagocytic activity and reduced effectiveness of functions of monocytes and macrophages. There is reduced thymopoiesis in elderly which results in reduced number and frequency of naïve T-cells and increased number and frequency of memory T-cells in them. In the presence of persistent infectious agents like CMV, expansion of the memory T-cell pool occurs. It is good for control of CMV but it fills the immunological space with clones specific for CMV and reduces the space for naïve T-cells and memory T-cells against other infectious agents and effectively reduces T-cell repertoire diversity. So knowing immunological history (number and frequency of antigens encounter during life) is very informative and is also a strong determinant of immunological aging. The immunological aging is the extent of senescence seeing at the immunological level. This mostly involve T-cells but B-cells can also be senescent. Reduced thymopoiesis may occur due to age related thymic involution or due to fat deposition in thymus or due to both. As naïve T-cells are the main cells which fight against new infections hence its reduction strongly correlates with reduced efficiency of the elderly to fight against infections. Thymic involution also occurs in stress and in pregnancy but unlike age related thymic involution, they are completely reversible[9] Studies have shown that the involuted thymus of most elderly persons are still able to produce some naïve T-cells though it

*Junior Resident, M.L.B. Medical College, Jhansi & **DNB Course Director & H.O.D. Medicine, S.S.P.G. Divisional District Hospital, Varanasi

is very less as compared to their younger counterparts.[10] Both the production and functions of B-cells decline with aging which may be responsible for increased susceptibility to diseases, reduced response to vaccination and increased cancer incidence in them.[11] Number of naïve B-cells are much less in elderly as compared to their younger counterpart with increase in antigen experienced memory cells in cell pool of elderly, some of which may be exhausted B-cells. The overall antibody affinity in elderly is also reduced due to a general isotype switching from I_gG to I_gM antibodies.[11,12]

Here two questions arise, first if modulation of this immunosenescence is possible? And second If it is possible then what are the interventions against it?. The answer is yes, it is possible. For immunomodulation there are certain objectives which must be kept in mind. First- antigenic load reduction both acute and chronic types, second- thymic restoration and third- modulation of T-cell functions. Interventions may be preventive i.e. nutrition, exercise etc. or curative or supportive i.e. therapy for the damage already occurred.

NUTRITION

The efficiency of immune system declines with nutritional deficiency. A number of factors may be responsible for undernutrition in elderly eg. Loss of denture, atrophy of taste buds, poor absorption from gut, poor diet etc. The nutritional interventions may be beneficial for prevention or retardation of progression of immunosenescence and in some cases it can even reverse the established immunosenescence. The immune system needs adequate energy, macro and micro nutrients for its proper functioning. Normally naive T-cells remain in a quiescent state and after encountering an antigen they change their metabolism and become an activated T-cell. This successful activation is followed by an increased uptake of nutrients, increased mitochondrial oxidative phosphorylation and the cell metabolism become predominantly glycolytic and energy demand is increased[13]. Prolong fasting has been linked with stem cell regeneration of older and damaged immune cells. Calorie restriction has been seen to prolong the life span in experimental animals. So, calorie restriction without undernutrition is the very important nutritional intervention in elderly. Macronutrients like antioxidants, dietary fiber, omega-3 poly unsaturated fatty acids (PUFAs), micronutrients like vitamin-E (200mg/day), Zinc (20mg/day), Selenium (100mcg/day), Iron, copper, folic acid, vitamin B-12, vitamin-C, fish oil (DHA) etc. have proven immune boosting properties in elderly.[14,15,16] Soluble fiber switches immune system from pro-inflammatory to anti-inflammatory which helps in faster healing from infections. Vitamin-E restores depressed Th1 response, down regulates prostaglandin E2 synthesis, enhances response to influenza vaccination, reduces oxidative stress and also increases NK cell activity.[17,18] Zinc supplementation leads to normalization of thymic architecture and functions, enhances T cell and NK cell activity, increases T lymphocyte proliferation and also increases neutrophil functions.[16,19,20] Selenium also increases T lymphocyte proliferation in elderly.[20] Daily zinc and selenium supplementation decreased infection rates in elderly.[21] Vitamin C (200mg/day) was effective as an adjunctive therapy for respiratory tract infections in elderly patients[22]. Fish oil rich in DHA enhances B cell activity.

Lipids like conjugated linoleic acid (CLA) and omega-3 Poly-unsaturated fatty acids (PUFAs) have proven anti-inflammatory properties. CLA increases lymphocyte proliferation and decreases pro-inflammatory cytokine secretion and also increases the response to Hepatitis B vaccination in elderly and has been shown to have anticarcinogenic, antiatherogenic and antidiabetic properties.[23,24] PUFAs have potent anti-inflammatory effects when used against autoimmune diseases, osteoporosis and cognitive decline[25]. Their most important anti-inflammatory effect is to reduce the risk and severity of atherosclerosis induced cardiovascular diseases. As immunosenescence is also a lwo grade inflammatory state hence the anti-inflammatory effect of these lipids (CLA and PUFAs) can be used for prevention or retardation of established immunosenescence. Lipids also have immunomodulatory properties. With increasing age membrane lipid rafts of T cells become less functional. Human high density lipoprotein (HDL) can extract accumulated cholesterol from membrane lipid rafts of T cells and increases signal transduction via TCR.[26] Statins reduces LDL cholesterol and correspondingly increases HDL cholesterol. Futher studies are needed to establish if this increased HDL could also have similar results on T cell membrane lipid rafts. For proper nutrition optimal diet from very beginning and throughout the life is the fundamental rule.

EXERCISE

Exercise relaxes body and mind, improves heart health, promotes blood circulation and is a potential mean to modulate dysregulated immune system with aging. Long term, moderate intensity aerobic exercises are best suited for elderly. Exercise have some immunorestorative properties on the decreased immune response with aging and the main benefits are on T cell functions, anti-body production and

macrophage responses with improvement in imbalance between Th1 and Th2 responses as well as in between naïve and memory T cell imbalance.[27,28,29]

Chronic sleep deprivation has negative impact on immune system by reducing immune response and WBC circulation where as adequate and deep sleep has positive impact by strengthening immune system's memory to previously encountered pathogens. Sun light energizes infection fighting T cells. The blue light present in sun ray makes T cells more faster so that they can reach quickly to infection site for their action. Chronic stress suppresses the immune system and its ability to fight against infections.

Hormones: - Many hormones have immunomodulatory properties. Estrogen modulates innate immune system especially during stress.[30] Insulin directly influences innate immunity,[31] hence insulin resistance with aging can also be an important contributor of immunosenescence. Thus drugs like glitazones, which restore insulin sensitivity, may have immunorestorative effects in elderly.[32] Insulin like growth factor-1(IGF-1) promotes the survival and function of peripheral T cells and also increases the functions of B cells, NK cells and macrophages. Dehydroepiandrosterone (DHEA) increases IL-2 production and NK Cell activity and decreases IL-6 levels.[33, 34] Growth hormone and melatonin also have some immunoregulatory properties but there effect on elderly is not well established. Hormone like vitamin, vitamin D modulates T cell activation.[35]

ANTIGENIC LOAD DECREASING INTERVENTIONS

As previously stated bad immunological history or chronic antigenic load exhausts immunological cell repertoire and is also an important contributor of immunosenescence, hence, every effort should be made to either eliminate or reduce both acute and chronic types of antigenic load from the body. Tumors present in the body also behaves in the same way and need same type of treatment.

1. **Vaccination:** Vaccination is an important tool to reduce infections and antigenic load in elderly. It is effective not only against acute but also against chronic latent infections. Vaccination against pneumococcal pneumonia, influenza and tetanus are rewarding in elderly. Some level of antibody response after vaccination is seen even in immunocompromised elderly.[36] Re-vaccination, as in cases of tetanus, is also an important way to boost immunity.[36] If we would become able to develop effective vaccine against chronic infectious agents like CMV, HSV, EBV etc. then probably we can halt or reduce declining immunity in elderly.

2. **Viral load reduction:** Viral load reduction by appropriate anti viral drugs as in HIV is another way to reduce antigenic load.

3. **Antibiotics:** Appropriate antibiotics are effective in treating bacterial infections and subsequently reducing antigenic load. Subclinical bacterial infections like UTI must be treated to reduce antigenic load. Though these subclinical infections are not causing any problem to the patient but they are constantly increasing antigenic load which has an harmful effect on declining immunity in elderly.

THYMIC RESTORATION

Restoration of declining efficiency of thymus with increasing age is an important way to prevent development of immunosenescence. There are many possibilities for it. First is the physical graft of functionally intact thymus to the older person, but ethical and logistic issues are there with it. Second is stem cell therapy for thymus. Third is the use of IL-7. IL-7 is a cytokine having a crucial role in the development and maintenance of the peripheral T cell pool. IL-7 induces some degree of thymic rejuvenation in mice.[37] Zinc supplementation normalizes thymic architecture and functions in zinc deficient persons.

MODULATION OF T CEL FUNCTION

Antiinflammatory agents-As inflammaging is an important cause of declining immunity in elderly, hence, antiinflammatory drugs are useful in retarding declining immunity in them. Here anti TNF alfa, anti IL-1, anti IL-6 and anti IL-15 monoclonal antibodies are useful. They should be used with caution in persons having cardiac diseases and infections. Non steroidal anti inflammatory drugs (NSAIDs) and statins also have anti inflammatory properties and are safe even in very old persons and can also prevent atherosclerosis, dementia, sarcopenia etc. in elderly.[38]

MODULATING TELOMERE LOSS

Antioxidants are capable of modulating telomere loss by retarding or preventing erosion of telomeres even after several cell division cycles.[39] Decreasing chronic viral load by appropriate vaccination is another way to maintain telomere length.

INJECTION OF AUTOLOGUS T CELL

This is a promising therapy for immunological restoration in elderly but further researches are needed for its

confirmation. Here from healthy young person, ideal T cells for in vitro expansion are obtained and stored in liquid nitrogen. These T cells can be expanded and transfused in his latter life when he needs immunocompetent T cells due to declining immunity.

CONCLUSION

Both innate and adaptive immunity decreases in elderly which causes increased susceptibility to diseases and infection and also poor response to treatment with vaccination. The preventive and promotive interventions for immunomodulation are well balanced diet, caloric restriction without under nutrition, antioxidents, soluble fibers, PUFA, vitamin E, zinc, selenium, vitamin D, vitamin A, vitamin B12, folic acid, copper, vitamin C etc. Long term moderate aerobic exercises are also among good preventive and promotive interventions. Certain hormones like estrogen, insulin, IGF1, DHEA, melatonin, vitamin D etc. also have immunosupportive properties. The main objectives and interventions for immunomodulation are to reduce antigenic load either by vaccination and cytokine (IL-2, IL-7) therapy or by antiviral antibiotics, restore thymic output and modulate T cell functions by antiinflammatory drugs like NSAIDs and statins and by anti inflammatory monoclonal antibodies. Telomere loss modulation can be done by antioxidents and vaccination against chronic diseases. Autologus T cell injection is a promising therapy.

REFERENCES

1. Miller RA. The aging immune system: Primers and prospectus. Science. 1996; 273: 70-74 [Pub Med] [Google Scholar].
2. Pawelec G, Solana R. Immunosenescence. Trend Immunol. 1997; 11: 514-16. [Pub Med] [Google Scholar].
3 Vasto S, Malavolta M, Pawelec G. Age and immunity. Immune Ageing. 2006; 3: 2 [PMC free article] [Pub Med] [Google Scholar].
4. Pawelec G. Immunosenescence comes of age. Symposium on aging research in immunology: the impact of genomics. EMBO Rep. 8(3), 220-223 (2007).
5. Siegrist CA, Aspinall R. B- cell responses to vaccination at the extremes of age. Nat Rev Immunol. 2009; 9: 185-94 [Pub Med] [Google Scholar].
6. Dixit VD. Thymic fatness and approaches to enhance thymopoietic fitness in aging. Curr Opin Immunol. 2010; 22: 521-28 [PMC free article] [Pub Med] [Google Scholar].
7. Bharath LP. Ip BC, Nikolajczyk BS. Adaptive immunity and metabolic health: harmony becomes dissonant in obesity and aging. Compr Physiol. 2017; 7: 1307-37 [Pub Med] [Google Scholar].
8. Fulop T, Larbi A, Douziech N, et al. Signal transduction and functional changes in neutrophils with aging. Aging Cell. 3(4), 217-26 (2004).
9. Rijhsinghani AG, Thopson K, Bhatia SK, et al. Estrogen blocks early T- cell development in the thymus. Am J. Reprod Immunol. 1996; 36: 269-77. [Pub Med] [Google Scholar].
10. Berzins SP, Boyd RL, Miller JF. The role of the thymus and recent thymic migrants in the maintenance of the adult peripheral lymphocyte pool. J Exp. Med. 1998; 187: 1839-48. [PMC free article] [Pub Med] [Google Scholar].
11. Signer RA, Montecino-Rodriguez E, Dorshkind K. Aging, B lymphopoiesis, and patterns of leukemogenesis. Exp. Gerontol. 42(5), 391-95(2007).
12. Kogut I, Scholz JL, Cancro MP, Cambier JC. B- Cell maintenance and function in aging. Semin Immunol. 24(5), 342-349 (2012).
13. Johnson MO, Siska PJ, Contreras DC, Rathmell JC. Nutrients and the microenvironment to feed a T cell army. Semin Immunol. 2016; 28: 505-13 [PMC free article] [Pub Med] [Google Scholar].
14. Ahluwalia N. Aging, nutrition and immune function. J Nutr Health Aging. 2004; 8: 2-6 [Pub Med] [Google Scholar].
15. Reinhold U, Pawelec G, Enczmann J, et al. Class specific effect of selenium on PWM- driven human antibody synthesis in vitro. Biol Trace Elem Res. 1989; 20: 45-58 [Pub Med] [Google Scholar].
16. Mocchegiani E, Muzzioli M, Giacconi R. Zinc and immunoresistance to infection in aging: new biological tools. Trends Pharmacol Sci. 2000b; 21: 205-8 [Pub Med] [Google Scholar].
17. Meydani SN, Meydani M, Blumberg JB, et al. Vitamin E supplementation and in vivo immune response in healthy elderly subjects. A randomized controlled trial. JAMA. 1997; 277: 1380-6 [Pub Med] [Google Scholar].
18. Meydani SN, Han SN, Wu D. Vitamin E and immune response in the aged: molecular mechanisms and clinical implications. Immunol Rev. 2005; 205: 269-84 [Pub Med] [Google Scholar].
19. Mocchegiani E, Giacconi R, Cipriano C, et al. Are zinc-bound metallothionein isoforms (I+II&III) involve in impaired thymulin production and thymic involution during aging? Immun Aging. 2004; 1: 5 [PMC free article] [Pub Med] [Google Scholar].
20. Santos-Neto L, Tosta CE, Dorea JC. Zinc reverses the increased sensitivity of lymphocytes from aged subjects to the antiproliferative effect of prostaglandin E2. Clin Immunol Immunopathol. 1992; 64: 184-7 [Pub Med] [Google Scholar].
21. Girodon E, Lombard M, Galan P, et al. Effect of micronutrient supplementation on infection in institutionalized elderly subjects: a controlled trail. Ann Nutr Metab. 1997; 41: 98-107.
22. Hunt C, Charkravorty NK, Annan G, Habibzadeh N, Schorah CJ. The clinical effects of vitamin C supplementation in elderly hospitalized patients with acute respiratory infections. Int J Vitam Nutr Res. 1994; 64: 212-19.
23. Tricon S, Burdge GC, Williams CM, et al. The effects of conjugated linoleic acid on human health-related outcomes. Proc Nutr Soc. 2005; 64: 171-82 [Pub Med] [Google Scholar].
24. Albers R, van der Wielen RP, Brink EJ, et al. Effects of cis-9 trans-11 and trans-10, cis-12 conjugated linoleic acid (CLA) isomers on immune function in healthy men. Eur J Clin Nutr. 2003; 57: 595-603 [Pub Med] [Google Scholar].
25. Kelley DS, Hubbard NE, Erickson KL. Regulation of human immune and inflammatory responses by dietary fatty acids. Adv Food Nutr Res. 2005; 50: 101-38 [Pub Med] [Google Scholar].
26. Duffy D, Rader DJ. Drugs in development: targeting high-density lipoprotein metabolism and reverse cholesterol transport. Curr Opin Cardiol. 2005; 20: 301-6 [Pub Med] [Google Scholar].
27. Kohut ML, Senchina DS. Reversing age-associated immunosenescence via exercise. Exerc Immunol Rev. 2004; 10: 6-41 [Pub Med] [Google Scholar].
28. Smith TP, Kennedy SL, Fleshner M. Influence of age and physical activity on the primary in vivo antibody and T cell- mediated responses in men. J Appl Physiol. 2004; 97: 491-8 [Pub Med] [Google Scholar].
29. Karanfilov CI, Liu B, Fox CC, et al. Age- related defects in Th1 and Th2 cytokine production by human T cells can be dissociated from altered frequencies of $CD45RA^+$ and $CD45RO^+$ T cell subsets. Mech Ageing Dev. 1999; 109: 97-112 [Pub Med] [Google Scholar].
30. Kovacs JE. Aging, traumatic injury, and estrogen treatment. Exp Gerontol. 2005; 40: 549-55 [Pub Med] [Google Scholar].
31. De Veale B, Brummer T, Seroude L. Immunity and aging: the enemy within? Aging Cell. 2004; 3: 195-208 [Pub Med] [Google Scholar].
32. Berstein LM, Tsyrlina EV, Vasilyev DA, et al. The phenomenon of the swithching of estrogen effects and joker function of glucose: similarities and relation to age-associated pathology and approaches to correction. Ann N Y Acad Sci. 2005; 1057: 235-46 [Pub Med] [Google Scholar].
33. Suzuki T, Suzuki N, Daynes RA, et al. Dehydroepiandrosterone enhances IL-2 production and cytotoxic effector function of human T cells. Clin Immunol Immunopathol. 1991; 61: 202-11 [Pub Med] [Google Scholar].
34. Gordon CM, LeBoff MS, Glowacki J. Adrenal and gonadal steroids inhibit IL-6 secretion by human marrow cells. Cytokine. 2001; 16: 178-86[Pub Med] [Google Scholar].
35. Hewison M, Freeman L, Hughes SV, et al. Differential regulation of vitamin D receptor and its ligand in human monocyte-derived dendritic cells. J Immunol. 2003; 170: 5382-90 [Pub Med] [Google Scholar].
36. Mc Elhaney JE. The unmet need in the elderly: Designing new influenza vaccines for older adults. Vaccine. 2005; 2381: 10-25 [Pub Med] [Google Scholar].
37. Aspinall R. T cell development, ageing and interleukin-7. Mech Ageing Dev. 2006; 127:572-78 [Pub Med] [Google Scholar].
38. Foody JM, Rathore SS, Galusha D, et.al. Hydroxymethylglutaryl-CoA reductase inhibitors in older persons with acute myocardial infarction : evidence for an age – statin interaction. J Am Geriatr Soc. 2006; 54:421-30 [PMC free article] [Pub Med] [Google Scholar].
39. Zhang F, Jia Z, Deng Z, et.al. In vitro modulation of telomerase activity, telomere length and cell cycle in MKN45 cells by verbascoside. Planta Med. 2002; 68 : 115-18 [Pub Med] [Google Scholar].

Geriatric TB: An Area of Concern

VK ARORA*, S RAJPAL**

INTRODUCTION

The Government of India's "National policy on older persons" defines ELDERLY as a person who is of age 60 years and above.[1] The World Health Organization estimates that 19–43% of the world's population is infected with *M. tuberculosis* and about 18 million new cases and 12 million deaths from tuberculosis occur each year.[2] The 2010 Global Burden of Disease estimates show that 57% of all tuberculosis deaths globally occurred among people older than 50, with more than half of these deaths in those aged 65 and above.[3] According to a study ninety-five percent of tuberculosis cases occur in developing countries, as a result of limitations in resources that would ensure adequate treatment[2,4]. *To achieve "TB Elimination by 2025" in India, all age groups of patients especially the elderly need to be covered comprehensively under RTNCP for both early diagnosis and standardized treatment.*

EPIDEMIOLOGY AND UNIQUE FEATURES OF GERIATRIC TB

New smear positive TB case notification in India among those aged 55 and above showed an increase from the year 2000 to 2012 highlighting the fact that it is an area of concern[5,6]. Geriatric population has certain peculiar features and unique challenges in their diagnosis and treatment. Symptoms are non specific among the elderly. *Very often there is delayed diagnosis due to lack of symptoms, which further leads to disease advancement.*

According to studies India has 14% of elderly TB patients. When compared with younger adults, they are more affected in terms of unfavourable outcomes due to drug related effects increased co-morbidity and poverty.[3,7,8] Increased number of deaths were observed in the late 80's among the elderly since they constituted a large group of patients suffering from active TB[9]. This may be attributed to factors like increased life expectancy and better healthcare facilities over the years. NTI estimated that in 2001 the proportion of elderly was about 7.4% of the population which increased to 8.3% in 2011.[4,5] According to a study TB case notification for smear positive patients aged 55 years and above has shown an increasing trend. Figures increased from 31133 in the year 2000 to 132938 in the year 2012[6]. *Hence by 2011 there was an increase in both the proportion as well as increased TB diagnosis among the elderly.*

Another area of concern in the elderly is the presence of co-morbidities like cardiovascular diseases, diabetes mellitus, airway obstructive disease, chronic renal failure and chronic institutionalization[2,5]. TB disease among the elderly may progress due to various other factors like malnutrition, malignancy, immunosuppressants, alcohol consumption which can impair the cell-mediated immunity[5]. *These unique features present in the geriatric population pose a challenge to both TB diagnosis and treatment.*

PATHOGENESIS AND PREDISPOSING FACTORS

TB pathogenesis is determined by the virulence of infecting strain as well as the immune response of the host.[9,10] With increasing age there is a decline in immunity which can lead to various communicable diseases in the elderly[5].

The immune response in TB may be active, sub-optimal or minimal:

- ***Active immune response***: Infection is localized and forms granulomatous tubercles.
- ***Sub-optimal response***: Results in lesions which are exudative in nature.
- ***No immune response***: Non reactive response leading to miliary TB is very common among the elderly whereby there is a high concentration of bacilli.
- ***Chronic TB***: Patients present with prolonged fever withno other focal signs. In 90% of cases among the

*Vice Chairman (P&R), TB Association of India, Executive Editor, Indian Journal of Tuberculosis, Formerly - Additional DGHS, Govt of India, Director, NITRD Delhi
** Chest Physician, New Delhi Tuberculosis Centre, New Delhi, Assistant Associate Executive Editor, Indian Journal of Tuberculosis

elderly it has been observed that there is re-activation of dormant infection foci in the lungs and elsewhere.

Origin of the disease may be attributed to various factors which may be as follows:

I. ***Cell mediated immunity***: Age related decline in the cell mediated immunity may reactivate the latent infection among the elderly.[9]

II. ***Use of immunosuppressive drugs such as corticosteroids*** may activate the dormant infection.

III. ***Conditions like diabetes mellitus, Alcohol abuse, smoking***[5], ***malnutrition***, etc.may result in breakdown of active disease.

IV. ***Other factors like social isolation*** in old age add to the risk of delayed diagnosis. Other contributory factors like ***physical weakness, immobility, poverty, and health-seeking behavior*** hamper the elderly in gaining timely access to medical care.[11] ***Economic and physical dependence*** on their children also played a vital role in the outcome.

CLINICAL FEATURES

Clinical characteristics can be unusual and may be confused with age-related illnesses[2]. Many cases are seen in adults residing in medical institutions like nursing homes and hospitals for some other condition.[12]

TB disease in the elderly may present as:

Pleurisy with effusion:

This is due to the rupture of sub pleural caseous focus into pleural space. It is a common phenomenon among the elderly and has an insidious onset. Pleural biopsy is the most accurate means of diagnosis.[9]

Post-primary form of pulmonary tuberculosis (reactivation):

This is the most common form of tuberculosis among the elderly and usually presents with non-specific complaints. There is often a delay in diagnosis and the elderly patients present at an advanced stage of the disease along with other medical problems. Even after initiating anti tuberculosis therapy, the mortality is high.

Rajagopalan et al have highlighted that 75% of elderly TB patients manifest lung involvement[2] either in form of disseminated or miliary tuberculosis followed by tuberculosis meningitis, skeletal & genitourinary tuberculosis increase in frequency with advancing age. They may not exhibit the classic 4 symptom complex (4S). Tuberculosis in this group may present clinically with changes in functional capacity (e.g. activities of daily living), chronic fatigue, cognitive impairment, anorexia, or unexplained low-grade fever[13,14]. Nonspecific symptoms and signs that range in severity from sub acute to chronic and that persist for a period of weeks to months raise suspicion for Tuberculosis.[2] Abnormal mentation was more common in the elderly. When compared with younger adults, TB symptoms like fever, night sweats, weight loss, sputum production and haemoptysis were noted in a significantly lower proportion in the elderly group.

Radiographic findings were very much similar in both groups. As per a study older TB patients had more frequent dyspnea and less frequent active TB findings on CT.[15] Another study quoted that[16] when compared to 18-59 year old adult patients, geriatric patients had a higher occurrence of cough, dyspnoea, chest pain and night sweats. Treatment success and adverse drug reaction rates were similar in both the groups. Elderly were less likely to present with haemoptysis or cavitary lesions and were more likely to present with complaints of dyspnoea with right lower lobe infiltrates. Atypical presentation observed in the geriatric patients was consistent with the results reported in other studies. Studies from Hong Kong and Jordan emphasize that these atypical presentation may delay the diagnosis of pulmonary TB in geriatric patients[17,18] but, there were no age-related differences in the mortality. *Some other authors concluded that elderly were 6 times more likely to die from TB when compared with younger adults.*[9,15]

The chest radiographs in the elderly patients were less likely to have upper lobe infiltration.[19] Elderly patients had more extensive disease involving both lungs. Cavitation was found to be common in the younger adults hence among PTB patients, culture and smear positivity were seen less frequently in the elderly (76.2 versus 79.1%, OR 0.84 (95% CI 0.79–0.90), p, 0.001 and 38.5% versus 44.7%, OR 0.78 (95% CI 0.73–0.83), p, 0.001).[14]

Other medical illnesses and past history of tuberculosis were much more common in the elderly. Mortality was much higher among elderly when compared to younger patients with co-morbidities. In a prospective study,[9] the occurrence of anaemia, hypoalbuminaemia, hypernatremia, hypokalaemia and deranged liver function tests (LFTs) were found in the geriatric age group, when compared to younger patients, signifying that there may be clinically silent extra pulmonary involvement. According to a study, diabetes triples the risk for active tuberculosis, so with the rising trend of diabetes, tuberculosis epidemic will sustain among older people who are affected by diabetes.[3] Older adults are more likely to develop atypical forms of tuberculosis such as intestinal

tuberculosis, bone and joint tuberculosis, genitourinary tuberculosis, TB meningitis or sputum smear-negative pulmonary involvement. They are harder to diagnose and treat than conventional pulmonary tuberculosis.[3] Another study stated[14] that the proportions of pulmonary TB (PTB), and the extra pulmonary TB were similar in younger and older age groups but the EPTB forms differed; *as genitourinary TB was found to be more common among the elderly males, while extra thoracic lymph node TB was seen less frequently.*

Miliary tuberculosis*:* It has been seen that obvious symptoms like intermittent high grade fever, early onset of meningitis, serositis are absent in the elderly. Instead, the chronic form of progressive, protracted illness with absent or low grade fever without any symptoms may be present and are difficult to recognize.[20,21] Examination often reveals anaemia and hepatosplenomegaly thus confusing the picture. *A normal chest x-ray may be compatible with miliary tuberculosis.*

Tuberculous meningitis*:* Due to dormant foci of infection in the nervous system; miliary disease it is commonly seen among the elderly. Expected signs like headache, vomiting and fever and the meningeal signs are often absent.[14] Clinical features include a change in personality, altered behaviour, memory loss, urinary incontinence, social withdrawal or mental confusion. Some of these symptoms are associated with old age which makes the diagnosis more difficult or delayed. History of dementia or obtundation often without fever or nuchal rigidity and a CSF examination may help in establishing diagnosis. A high index of suspicion for tuberculous meningitis must be maintained until the suspicion is disproven. *Tuberculous meningitis is associated with exceedingly high mortality among elderly persons; neurological sequelae or deficits are common among survivors.*

Genitourinary tuberculosis: *Symptoms commonly seen* are dysuria and abnormal frequency. 20% patients are asymptomatic and their disease is recognized due to an abnormal urinary sediment. Sterile pyuria may help to establish the diagnosis.[9] The kidney is the major site of involvement, and as many as 20–30% of patients are asymptomatic. Genitourinary tuberculosis may involve the ureters, bladder, prostate, epididymis, and seminal vesicles. Presenting symptoms may include dysuria, urinary frequency, flank pain, and hematuria. Diagnosis may be considered in the presence of abnormal urinary sediment, pyuria without bacteruria, or hematuria. *Significant disease may result in pelvic or scrotal masses and draining sinuses; systemic manifestations (fever, anorexia, weight loss) may be absent.*

Bone and Joint Tuberculosis: Osteo-articular tuberculosis is frequently diagnosed among the elderly. The lesion may be a combination of osteomyelitis and arthritis, and may occur as a result of reactivation of dormant foci. Diagnosis is often delayed because symptoms may be attributed to old age. Fever may be absent in the elderly patients which further complicates the diagnosis.[9,14] Diagnosis may be suspected with unexplained unifocal inflammation or destruction of bone or joint. To prevent delay in diagnosis tuberculosis should be included in the differential diagnosis of all elderly patients presenting with nonspecific pleuro-pulmonary symptoms or unexplained fever, anorexia, weight loss, change in behaviour or mentation or organ dysfunction. The thoracic and lumbar spines are commonly involved; cervical disease is unusual. Paravertebral abscesses, or cold abscesses, are often associated with spinal infection. Primary symptoms of spinal tuberculosis include pain over the involved vertebrae; neurological deficits and sinus tracts may occur with more advanced disease. Tuberculous arthritis commonly involves the large, weight-bearing joints; however, in elderly persons, peripheral joints (i.e. the knees, wrists, ankles and metatarsophalangeal joints) may be involved. Pain and swelling of the involved joints and loss of range of motion can sometimes occur. *In the presence of degenerative joint disease / arthritis, diagnosis of coexisting tuberculous arthritis can be easily overlooked.*

Gastrointestinal tuberculosis*:* Abdominal tuberculosis remains under diagnosed in the elderly. Due to the absence of prominent symptoms and the presence of motility disorders commonly seen among the elderly, it becomes a challenge to come to a conclusive diagnosis.

DIAGNOSIS

Factors like diminishing mental cognition and co-morbidities makes it difficult to come to a conclusive diagnosis among the elderly. One of the challenge is their inability to give an exact account of their signs and symptoms. Hence the most likely reason for failure of recognition of pulmonary TB is the paucity of respiratory symptoms.[9] Most cases of pulmonary tuberculosis in elderly patients are reactivation disease; 10%–20% of cases result from primary infection or reinfection. Although reactivation tuberculosis classically involves the upper lobes of the lung (apical and posterior segments), several studies have shown that pulmonary tuberculous infection in many elderly patients manifests in either the middle or the lower lung lobes.[16] Other findings include atypical radiological findings like solitary nodules

mass like densities which make the diagnosis more complex in view of malignancy as a possible differential diagnosis in this group. Thus, clinicians must exercise caution when interpreting radiographic evidence of tuberculosis in older patients because of the possibility that infection may take hold in an atypical location in the lung fields.[2] Another factor is their inability to produce sputum. Atypical clinical manifestations of TB in older persons can result in delayed diagnosis and initiation of treatment.[16] *HRCT scan was found to be superior than chest radiography.* On CT, primary tuberculosis presents in association with lobar pneumonia combined with enlargement of lymph nodes in the hilum / mediastinum. Commonly affected sites are the middle lobe, the lower lobes or the anterior segment of an upper lobe. The appearance is air space consolidation and is homogeneous, dense, and well defined. Anatomically it is confined to a segment or a lobe. Primary tuberculosis may appear as a solitary cavitary lesion in about 10% of patients. On CT scans, the wall of cavity may be thick / thin and smooth / irregular. An air-fluid level in the cavity is common.

Sputum Examination: Sputum examination for *M. tuberculosis,* using both smear and culture, is indicated for all patients[13,14] who have pulmonary symptoms and/or radiographic changes compatible with tuberculosis. For suspected pulmonary tuberculosis, it is recommended that 2 sputum specimens; one obtained in the morning and one spot be used for routine mycobacteriological studies as per RNTCP guidelines. *These specimens should be subjected to smear examination and then cultured for M. tuberculosis.*

Other diagnostic interventions should be considered for elderly patients who are unable to expectorate sputum. Use of flexible fiber optic bronchoscopy to obtain bronchial washings/bronchial biopsy specimens have immense diagnostic value for both TB as well as malignancy[2]. *In frail elderly patients, however, the risk of such a procedure should be carefully weighed against the benefit of potentially making a diagnosis of tuberculosis.*

Molecular diagnostic test or NAAT: Nucleic acid amplification tests, facilitate rapid detection of *M. tuberculosis* in respiratory tract specimens; recommendations for interpretation and use of the nucleic acid amplification (NAA) test have been recently updated by the Center for Disease Control and Prevention.[22] As per a CDC report NAA testing should be performed on all TB suspects having signs/ symptoms of TB. NAAT testing does not replace the need for AFB smear and culture. All current guidelines and recommendations for culture-based testing should remain in effect. Hence a comprehensive diagnostic algorithm must include other diagnostic tools apart from smear microscopy (eg. XpertMTB/RIF and MGIT culture) while evaluating the elderly for TB diagnosis. The rapid diagnostic techniques are especially useful for elderly population who are at risk of acquiring MDR TB.

Older adults have a reduced ability to produce sputum[3] hence induced sputa or fasting gastric aspirates can be tested.

Histologic examination of tissue biopsy from various sites, such as the liver, lymph nodes, bone marrow, pleura and synovium that reveals the characteristic tissue reaction (caseous necrosis with granuloma formation) is also useful for diagnosis of tuberculosis disease. *The biopsy material can also be subjected to smear, culture and molecular diagnostic tests of TB to increase the chances of diagnosis.*

Mantoux test tends to give false negative results[20,21] in older patients due to immunological deficits or anergy. Moreover, the "booster effect" of skin-test reactivity to antigen increases in prevalence in the elderly population to negate the associated potential for false-negative results. Tuberculin sensitivity is known to wane with old age. Factors like advancing age, malnutrition, may be associated with non-reactive tuberculin, despite active disease. Available data suggests that negative tuberculin reaction found in the elderly is due to failing immune response to tuberculin antigen and can be restored progressively by repeated administrations.[22] *A two stage TB skin testing is recommended in the elderly initially classified as negative reactors.*[16]

THERAPEUTIC CHALLENGES

Elderly with tuberculosis present problems not only for diagnosis but also for treatment. Main issues are poor compliance with treatment, poor tolerance of drugs and the presence of underlying or associated diseases. The main cause of failure of treatment in tuberculosis, whatever the age, is poor patient compliance, and in the elderly this problem is accentuated.[14,23] Old people especially the very old are unreliable about taking tablets regularly, at the right time or in the right dose, particularly if several drugs are to be taken concurrently. Poor memory, poor eyesight and mental confusion may be contributory factors. The geriatric age group often neglect their treatment and also lack the will to complete the full course of treatment. Hence countries world over have adopted the supervised intermittent chemotherapy targeting these patients. Presence of side effects of drugs further leads to poor compliance. Doses of drugs must be carefully monitored and regulated in the presence of hepatic and/or renal failure. A retrospective review quoted that elderly

people were three times more likely to have reactions to antituberculous drugs as compared to younger patients.[24]

A watch must be kept for the *side effects of drug treatment* because the old persons, particularly the very old, cannot be relied upon to recognize the symptoms. Studies including those from India have definitely shown advancing age as an important predictor of hepatotoxicity due to INH and rifampicin.[5,17] Rifampicin combined with INH has an additive hepatotoxic effect. It is recommended that clinical assessments along with liver function tests should be performed before administering isoniazid (H), rifampin (R) and pyrazinamide (Z) in view of hepatic derangement with TB medication. Advancing age as an important predictor of hepatotoxicity due to H, R and Z has been well documented.[25,26] Time to time (monthly) laboratory monitoring of LFT is also recommended.[22]

Streptomycin should be used cautiously in the elderly. Ethambutol may cause diminution of visual acuity, central scotomas and disturbance of red-green vision attributable to optic neuritis. Visual impairment is common in elderly and testing of visual acuity along with colour discrimination should be performed before initiating ethambutol. Elderly patients have increased risks of suffering from renal toxicity, ototoxicity, visual acquity, and vestibular disturbances. Hence, drug interactions must be considered in old people who are likely to be on treatment for other diseases at the same time: e.g., INH can reduce the anticonvulsant action of phenytoin; rifampicin can interfere with the action of digoxin, tolbutamide and corticosteroids.

In most cases, all that is needed to overcome the unwanted effects of drug interactions is an adjustment of dosage.

A study from Korea documented higher drug induced hepatitis, cutaneous toxicity, neurotoxicity, gastrointestinal disturbances, arthralgia, and flu-like syndrome in the elderly[24]. Many studies suggested that the most common adverse event was gastrointestinal discomfort which was higher in the geriatric age group compared to the younger adult group.[3,12,16]

Staff working with the elderly needs to be aware of potential drug adverse effects for prompt intervention and appropriate management.

Another challenge in the treatment of geriatric TB is the presentation of TB in insidious manner or so called ***cryptogenic TB***. As per the 2 case reports, tuberculosis may manifest in a completely different way. As per a clinical description from Cairo, seven patients were admitted with unexplained fever ranging from 1-4 months with non specific constitutional symptoms with hypochromic/normochromic anaemia, elevated ESR and a positive tuberculin test. Investigations revealed no signs of TB. As per the report 5 patients responded within 1 week of initiating treatment. The study suggested that a high degree of suspicion and a rapid evaluation is important to avoid complications. Another case report suggested that tuberculosis should always be considered as a possible cause of unexplained renal failure even if the classical pyelographic features of tuberculosis, i.e. calyceal distortion and calcification, are absent.[27,28]

Since the evolution of specialized scans in the last 2 decades the challenges posed by ***cryptogenic TB*** *in geriatric population has been solved to a great extent. CT has revolutionized the diagnosis as typical CT findings in bronchogenic spread of pulmonary tuberculosis like centrilobular branching linear structure, poorly defined peribronchiolar nodules 2-3 mm in size, acinar shadows 4-10 mm in size,[29] and even in extra-pulmonary sites come before any changes can be appreciated on conventional radiology.*

Newer ATT and geriatric population

Bedaquiline belongs to a new class of drugs called *diarylquinolines*, and is indicated as part of combination therapy in adult patients (≥18 years) with pulmonary multidrug-resistant tuberculosis (MDR-TB). Bedaquiline is the first new drug developed specifically to treat TB in over 40 years. **Bedaquiline** may be added to a WHO-recommended regimen in MDR-TB adult patients under the following conditions

- When an effective treatment regimen containing four second-line drugs in addition to pyrazinamide, according to WHO recommendations, cannot be designed;
- Resistance to any fluoroquinolone in addition to multidrug resistance.

Bedaquiline should be given for a maximum of six months on top of the WHO recommended combination treatment regimen. The manufacturer recommends 400 mg daily (4 tablets) for 2 weeks followed by 200 mg 3 times per week for the remaining 22 weeks. Bedaquiline is available as 100 mg tablet for oral administration. Its bioavailability is enhanced in presence of food. It is highly plasma protein bound (>99%) and shows tri-exponential decline in plasma concentration with effective half-life of approximately 24-30 hours and terminal half-life (t1/2, term) of approximately 4-5 months. It is metabolized by CYP3A4 to N-monodesmethyl metabolite,

which is 4-6 times less potent than the parent drug. ***Enzyme inducers can reduce the efficacy of bedaquiline, whereas enzyme inhibitors can predispose to its adverse reactions.*** *The geriatric patients with co-morbidities and especially the ones on additional prescription medicines may have fluctuating serum levels of the drug which can result in treatment failure or higher side effects.*

The most common side-effects reported with bedaquiline therapy are nausea (30%), arthralgia (26%), headache (22%), hemoptysis (14%), chest pain (9%), anorexia (7%), and rash (6%). ***Important cardiovascular adverse effect is QT prolongation. Concurrent use of other QT-prolonging drugs causes additive QT prolongation. This is the reason that it should be used with caution in geriatric population.*** Other important adverse effect is elevation of hepatic transaminases, which is moderate and reversible on discontinuation of therapy. *As of now, the geriatric age group has not been included in the clinical studies of bedaquiline to determine whether they respond differently from younger patients [30,31]. WHO strongly recommends the acceleration of phase 3 trials to generate more evidence.*

Delaminid: It is a recent drug developed for TB treatment and is also the first approved drug in the class of nitro-dihydro-imidazo-oxazoles for MDR treatment. Delaminid is used as part of a combination regimen for pulmonary MDR-TB when an effective treatment regimen cannot be made due to resistance/tolerability. Delaminid may be added to a WHO-recommended regimen in adult patients with pulmonary MDR-TB under the following conditions:

- Four second-line drugs along with pyrazinamide (Z) as per WHO recommendations cannot be designed.
- When there is evidence of Fluoroquinolone resistance / second-line injectable drug in addition to MDR.
- When there is higher risk for poor outcomes eg. drug intolerance or contraindication, extensive or advanced disease.[32,33]

Physician should exercise caution, when delamanid is used in persons 65 years and older, or in those with diabetes, hepatic or renal impairment, or alcoholics etc, given that data on efficacy and safety under such conditions are extremely limited / unavailable.

CONCLUSION

It is evident that there is an increasing pool of vulnerable older adults who may develop active tuberculosis by reactivation of previous ''latent'' or new tuberculosis infection. *Clinical presentation is usually atypical as sometimes clinical features are masked by other co-existing disease.* Diagnosis is difficult as tuberculin test is negative because of age related anergy; radiological features are also atypical as COPD usually co-exists. *As far as treatment is concerned, dosage of drugs need to be adjusted as there are higher chances of side effects due to concomitant therapy, poor compliance and other challenges peculiar in this age group.* Various factors like social marginalization, reduced mobility and financial dependency to discourage health care seeking among the elderly which often delays the diagnosis, leading to poor outcomes. Death rate of 8% among new smear positive elderly TB patients has been documented in previous studies.[24] *A high index of suspicion for TB in this vulnerable population at the time of diagnosis is, thus, undoubtedly justifiable[16].* Positive factors like family support, financial assistance, medication collection from time to time and emotional support hold special significance for successful treatment completion. *Further, there is a possibility of MDR-TB as a result of reinfection with a drug-resistant strain of TB which has to be kept in mind of the treating physician. The drug sensitivity tests should be done at the RNTCP accredited laboratory.* TB in geriatric population is a bigger problem with regards to its presentation and treatment. *Programme managers should develop appropriate interventions in consultation with geriatric specialists, for effective management of TB in this vulnerable population.[5]*

REFERENCES

1. Situational analysis of elderly in India. Central Statistics Office Ministry ofStatistics & Programme Implementation Government of India, 2011. http://mospi.nic.in/mospi_new/upload/elderly_in_india.pdf.
2. Shobita Rajagopalan. Tuberculosis and Aging:A Global Health Problem. *Aging and Infectious Diseases* 2001 October; 33:1034-1039.
3. Joel Negina,SeyeAbimbolaa,c, Ben J. Marais; Tuberculosis among older adults – time to take notice; *International Journal of Infectious Diseases,* 2015;32:135–137.
4. Rath SP, Das B, Mishra SK (2011) Demographic dynamics of India's population- A reference study of census-2011 with backdrops and future trends. Int J ofBusiness and Management tomorrow 1:1–22(http://www.ijbmt.com/issue/90.pdf).
5. BanuRekhaVaithilingamVelayutham, Dina Nair, VedachalamChandrasekaran, et al ;Profile and Response to Anti-Tuberculosis Treatmentamong Elderly Tuberculosis Patients Treated under the TB Control Programme in South India;PLOS one; 2014 March; 9: 3.e88045
6. WHO.Global tuberculosis report 2013. http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf Accessed 2013 Dec 7.
7. Ananthakrishnan R, Kumar K, Ganesh M, Kumar AMV, Krishnan N, et al.(2013) The Profile and Treatment Outcomes of the Older (Aged 60 Years andAbove) Tuberculosis Patients in Tamilnadu, South India. PLoS ONE 8(7):e67288. doi:10.1371/journal.pone.0067288
8. Arora VK, Singla N, Sarin R (2003) Profile of geriatric patients under DOTS inRevised National Tuberculosis Control Programme. *Indian J Chest Dis AlliedSci* 2003;45(4):231–235.
9. Rita sood. The problemof geriatric TB;Review article. *Journal of Indian Academy of Clinical Medicine.* 2000 Apr-Jun;5(2):156-62.
10. Arora VK, Bedi RS. Immunoglobulin status of geriatric pulmonary tuberculosis patients of Himachal Pradesh. *Ind J Chest Dis Allied Sci* 1989;31:233-6.
11. Storla DG, Yimer S, Bjune GA. A systematic review of delay in the diagnosis and treatment of tuberculosis. BMC 2008; Public Health 8:15.
12. Morris CD: The radiography, haematology and biochemistry of pulmonary tuberculosis in the aged. Q J Med 1989, 71(266):529–536.
13. Pardeshi G, Deshmukh D. Disease characteristics and treatment outcomesin elderly tuberculosis patients on DOTS. *Ind J Comm Med* 2007;32:292–294.

14. Hauer B, Brodhun B, Altmann D, Fiebig L, Loddenkemper R, et al.Tuberculosis in the elderly in Germany. *EurRespir J* 2011;38(2):467–470.
15. Yong Soo Kwon, Su Young Chi, In Jae Oh, KyuSik Kim, Yu Il Kim, Sung Chul Lim and Young Chul Kim; Clinical characteristics and treatment outcomes of tuberculosis in the elderly: a case control study; Kwon et al. BMC Infectious Diseases 2013;13:121.
16. Sandhyarani Moharana, M Lipika, DhirendraNathMoharana, SubhransuSekharPattnaik, SantanuPadhy, Tapan Kumar Sahoo.Pulmonary Tuberculosis in Elderly - Peculiarities and Dissimilarities: A Geriatic Clinic Experience.*International Journal of Scientific Study* 2017 July; 5(4):50-53.
17. Leung CC, Li T, Lam TH, Yew WW, Law WS, Tam CM, *et al.* Smoking and tuberculosis among the elderly in Hong Kong. *Am J RespirCrit Care Med* 2004;170:1027-33.
18. El-Khushman H, Momani JA, Sharara AM, Haddad FH, Hijazi MA, Hamdan KA, *et al.* The pattern of active pulmonary tuberculosis in adults at King Hussein medical center, Jordan. *Saudi Med J* 2006;27:633-6.
19. Arora VK, Bedi RS. Geriatric tuberculosis in Himachal Pradesh – A clinico-radiological profile. *JAPI* 1989;37:205-06.
20. Perez-Guzman C, Vargas MH, Torres-Cruz A, Villarreal-Velarde H. Does aging modify pulmonary tuberculosis?: A meta-analytical review. *Chest* 1999 Oct;116 (4):961–7. 24.
21. Pottumarthy S, Morris AJ, Harrison AC, Wells VC. Evaluation of the tuberculin gamma interferon assay: potential to replace the Mantoux skin test. *Journal of Clinical Microbiology* 1999 Oct; 37(10): 3229–32.
22. Centers for Disease Control and Prevention. Nucleic acid amplification tests for tuberculosis. MMWR Morb Mortal Wkly Rep 2000; 49:593–4.
23. Central TB Division (CTD), Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India. Managing Revised National TB Control Programme in your area – A training course. Dated April 2005.Module 4 – Administering treatment. Pg: 77–114; New Delhi: CTD.
24. Lee J H, Han DH, Song JW, Chung HS. Diagnostic and therapeutic problems of pulmonary tuberculosis in elderly patients. *J Korean Med Sci* 2005;20:784–789.
25. Teale C, Goldman JM, Pearson SB. The association of age with the presentation and outcome of tuberculosis: a five-year survey. *Age Ageing* 1993;22(4):289–293.
26. Pande JN, Singh SP, Khilnani GC, Khilnani S, Tandon RK. Risk factors for hepatotoxicity from antituberculosis drugs: a case-control study. *Thorax* 1996;51(2):132–136.
27. J.J. · Scoble J.E. Thomas A.C. · Eastwood J.B. Cryptogenic Tuberculosis as a Preventable Cause of End-Stage Renal Failure. *Benn Am J Nephrol* 1988;8:306–308.
28. Farid Z, Kilpatrick N1 E and Kamal "I. Cryptogenic Tuberculosis-1990 cairo – egypt. Journal of Tropical Medicine JTM Jan. (1993) Vol. 2 No. 3 Fand et al.,31-32.
29. Soo Lee and Jung-Gi Im.CT in Adults with Tuberculosis of the Chest: Characteristic Findings and Role in Management Kyung. *AJR* 1995;164:1361-1367-1367.
30. Companion Handbook to the WHO Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis,Geneva: World Health Organization; 2014.
31. The Use of Bedaquiline in the Treatment of Multidrug-Resistant Tuberculosis, Interim Policy Guidance Geneva: World Health Organization; 2013.
32. The Use of Delamanid in the Treatment of Multidrug-Resistant Tuberculosis: Interim Policy Guidance. Geneva: World Health Organization; 2014.
33. Guidelines for use of delaminid in the treatment of DRTB in India, Revised ntional Tuberculosis control programme. Central Tuberculosis Division, Director General Health Services, Ministry of health and family welfare, Nirman Bhawan New Delhi, 2018.

Insurance Policies In Elderly

SANDEEP P. TAMANE*

INTRODUCTION

Senior Citizen Medical Insurance Policy offers medical coverage to individuals between the age group of 60- 75 years.

Some of the unique benefits of Senior Citizen Medical Insurance include Cashless Hospitalization, Pre existing diseases, no medical test and day care expense.

According to the new guidelines by IRDA, every health insurance provider has to offer coverage to individuals upto 65 years of age. These guidelines help individuals to get coverage at later stages of their life. They also allow them to switch insurers if they are not satisfied with their current insurance provider.

Main challenge is to choose the right insurance provider by comparing different plans available in the market.

FEATURES OF SENIOR CITIZEN HEALTH INSURANCE PLAN

These are-

- People above the age of 60 years get health cover under Senior Citizen Health Insurance Plans.
- Most of the plans do not require pre Medical screening.
- Offers free- lock in period on the plans.
- Senior Citizens can avail Annual health check ups.
- They can also avail Cashless have service under this plan if patient is admitted for more than 24 hours.

This facility includes Medical bills, doctor fees, room charges etc.

- Pre hospitalization and post hospitalization is covered based on number of days.
- Most plans Cover pre existing conditions.
- Certain medical amenities such as ambulatory services are also generally covered.

*Consultant Physician and Geriatrician, Deenanath Mangeshkar Hospital and Research Center, Pune, Maharashtra

FACTORS TO CONSIDER WHILE COMPARING MEDICLAIM POLICIES FOR SENIOR CITIZENS

1. Coverage
2. Co payments
3. Lifetime renewal
4. Waiting periods
5. Pre existing conditions
6. Free- look period

SENIOR CITIZEN HEALTH INSURANCE EXCLUSIONS

Common exclusions include-

- Pre existing conditions or injuries
- Expenses arising out of self- inflicted acts
- Expenses arising from Drug Abuse
- One or more Medical conditions diagnosed within 30 days of purchasing the policy
- Expenses related to Non- allopathic treatment
- Treatment cost of injuries caused due to an act of foreign army or a civil war
- A cosmetic surgery
- The cost of Dental treatment or lenses / spectacles, unless arising from an accident
- Treatment cost of AIDS

HOW TO CLAIM MEDICLAIM FOR SENIOR CITIZENS?

Mediclaim for Senior Citizens allows the policyholders to file health insurance claim when they are hospitalized or have to avail emergency medical treatment. These policies facilitate raising a mediclaim to avail Cashless treatment at a network Hospital or for expense reimbursement post discharge.

In any case, the policyholder must inform the insurer about the same within 24 hours of the hospitalization.

In order to file mediclaim, online claim forms must be filled in and submitted along with the medical bills and reports as supporting documents.

TAX BENEFITS

Senior Citizen are also entitled to avail tax exemption under section 80D of the Income Tax Act 1961,as a part of the health insurance policy.

INSURANCE COVER RELATED TO CORONA VIRUS

We know that the worst affected by COVID 19 are the Senior Citizens and therefore Insurance Cover related to this is the need of the hour.

Attention should be paid to this.

CONCLUSIONS

Adequate Health Insurance Cover is mandatory for Senior Citizens.

It is also important to choose a correct Insurance provider to avail maximum health benefits.

Senior Citizens can also get Income tax exemptions related to their health insurance policies.

Drugs to be Avoided in Liver Diseases

A.K. Manchanda*

DRUGS TO BE AVOIDED IN OLDER PEOPLE WITH LIVER DISEASES

Class of the drug	Examples of the drug	Comments
Anti Hypertensive	Methyldopa Hydralazine Diuretics (except Potassium sparing)	Causes acute or chronic severe hepatitis Autoimmune hepatitis Electrolyte imbalance: Can precipitate Hepatic encephalopathy
Oral Hypoglycemic drugs & Insulin	Metformin Sulfonylureas and Meglitinides Thiazolidinediones Dipeptidyl-peptidase-4 inhibitors Sodium-glucose co-transporter 2 inhibitors Glucagon-like peptide-1 receptor agonists Insulin and insulin analogues	Avoid in severe Liver disease Avoid in Severe hepatic diseases Avoid when liver enzyme more than 3 times normal, Avoid in edema Vildagliptin to be avoided in advanced liver diseases All DPP Inhibitors to be avoided in Severe hepatic diseases Safe in mild Liver disease. Avoid in severe Liver disease Safe in mild Liver disease. Avoid in severe Liver disease Newer Insulins preferred in all stages of Liver disease. Dose modification required
Anti Convulsants	Topiramate, Levetiracetam Phenytoin Carbamazepine, Lamotrigine Valproate	Dose modification required Acute liver injury. can be severe and lead to acute liver failure and death. Anticonvulsant Hypersensitivity Syndrome Asymptomatic serum aminotransferase elevations to fulminant acute hepatitis
Analgesics/ NSAID	NSAID Opioid analgesics	Severe complications like gastrointestinal bleeding, hepatic encephalopathy, hepatorenal syndrome. May precipitate encephalopathy.
Antibiotics	Ketoconazole, miconazole, fluconazole, itraconazole Beta-lactam antibiotics Amino glycosides Vancomycin, Tetracycline Amoxiclav, Erythromycin Chloramphenicol Nalidixic acid, Nitrofurantoin, Macrolide antibiotics (Erythromycin, Azithromycin) Griseofulvin, INH+ Rifampicin, Pyrazinamide	Use with caution Leucopenia Renal failure Hepatic Toxicity Cholestasis Higher risk of bone marrow suppression Not indicated for prolonged use. Contraindicated
Cardiovascular Drugs	Labetolol Captopril, Amiodarone, and Ticlopidine	Severe hepatotoxicity Hepatotoxicity

*Medical Director and Senior Consultant, Curewell Diabetic and Cardiac Centre, D47, Bali Nagar, New Delhi-110 016

News from Kolhapur

A report by Dr. Mahaveer Mithari

Geriatric Society of India®, Kolhapur Chapter happens to be fortunate enough to conduct one of the unique first ever of its kind public awareness program namely, 'Sukhant Jivanacha' (*सुखांत जीवनाचा*) in this region of Western Maharashtra. The said event was organised on the auspicious day of Christmas morning i.e. 25th December 2019 at Shahu Smarak Auditorium, Kolhapur. It would be worth mentioning that auditorium with capacity of 600 person was jam-packed with people gathering /occupying places in passages and corridors. We had record registration of 800 plus senior citizens.

'*सुखांत जीवनाचा*' as the name implies, clearly explains the theme, tips and chats for happy terminal end of life. Whole of the GSI executive team had geared up for the organisation, almost since November 2019. Our own parent body Kolhapur medical association (KMA) had extended their helping hands for the successful accomplishment of the Grand event.

Dr Shiv Kumar Iyer and Dr. Pradeep Kulkarni from Pune played the anchor role for the panel discussion. There were total 11 panellist, rest being local, comprising of intensivist, palliative physician, neurologist, psychiatrist, oncologist, lawyer, journalist and social worker. Various topics such as living will, palliative care, pain relief in Cancer patients intensive Care and its cut off line, legal aspects of termination of end stage treatment so on and so forth where discussed in details. There were lot many interactive curies from the audience which were lucidly answered and clarified. Decision lasted for almost two hours leaving behind the audience spellbound and wiser to some extent. Dr. Iyer's captaincy was the key to the success of the panel discussion.

The program was aptly associated with another innovative activity; publication of short book, ' *ज्येष्ठाधार* '. The book comprised of various articles pertaining to elders physical, mental and social health aspects, post retirement activities, immunization schedule, drug schedule, various government schemes at etc etc. The short book will definitely aid the senior citizens. and from their reference data in their routine second innings life. Almost 500 copies of of ' *ज्येष्ठाधार* ' where distributed free of cost to the attendees. The book publication was followed by distribution of certificates to the successful candidate of 'health workers 'course namely 'certificate course in in disabled senior citizen care' conducted by GSI earlier.

The whole event was intermingled with melodious music and songs dedicated to the senior citizens, so as to render is charming and relaxing mood while experiencing such a serious topic.

News from Odisha

A report from Dr. Kaushik Ranjan Das

A meeting of GSI Odisha branch was held on 16th February 2020 under the Chairmanship of Dr. Dhirendranath Moharana at the Old auditorium of SCB Medical College & with formal launching of "Geriatric Society of India Odisha branch".

The following are office bearers: -

Chairman
Dr. D. N. Moharana

Vice Chairman
Dr. B. N. Mohapatra
Dr. Purna Chandra Dash
Dr. Jayanta Kumar Panda
Dr. Ashoke Kumar Parida

General Secretary
Dr. Prasanna Kumar Rathor

Assistant secretary
Dr. Amulya Kumar Das
Dr. Birja Prasad Biswal

Treasurer
Dr. Santosh Kumar Swain

Executive Committee Members
Dr. Niranjan Tripaty
Dr. Annapurna Devi
Dr. Sudhir Ranjan Samal
Dr. Ashok Kumar Behera

On this occasion, Geriatric Society of India Eastern Zonal branch organized its 2nd CME at Old Auditorium of SCB Medical College,Cuttack ,Odisha on 16th February 2020 in association with department of PG Medicine, SCB medical College.

The CME being attended by 110 delegates.

President GSI, Dr. Agam Vora, President Elect Dr. Prabha Adhikari, Zonal Coordinator (Central) Dr. Sandeep P. Tamane graced the occasion. The other dignitaries were Dr. B.N.Mohapatra, Dr. Arunansu Talukdar, Dr. Kaushik Ranjan Das.

Some senior doctors were felicitated on this occasion.

Dr. Prasanna Kumar Rathor, Organizing Secretary and Dr. Santosh Kumar Swain, Joint Organizing Secretary were presented Appreciation Awards on behalf of Geriatric Society of India® HQ & GSI Eastern Zonal branch for their remarkable contribution in organizing the event.

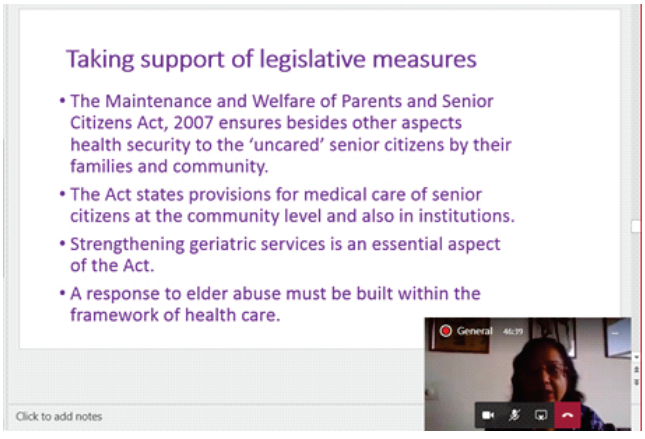
Scientific Sessions were on

- Geriatrics - How Different by Dr. Krishnanjan Chakraborty
- Comprehensive Geriatric Assessment by Dr. Kaushik Ranjan Das
- Imaging in Geriatric Patients by Dr. Ashoke Kumar Das
- Acute Infective Exacerbation of COPD & Choice of Antibiotics at Outpatient Services by Dr. Agam Vora
- Prepare for Old Age by Dr. Sandeep Tamane
- Tuberculosis in Geriatric Population by Dr. Monoranajn Das
- Diabetes in Elderly by Dr. D. N. Moharana
- Management of Osteoporosis in Elderly by Dr. Jayanta Kumar Panda
- Management of Geriatric Depression by Dr. Arunansu Talukdar & Dr. Gargi Dasgupta
- Diabetes & Aging, Unique Considerations & Goal of Care by Dr. Ipsita Mishra
- Antibiotic Stewardship in Geriatric Patients by Dr. Prabha Adhikari
- Role of Prucalopride in Geriatric IBS-C by Dr. Soumik Ghosh
- Nano Medicine & its Application in Geriatrics by Dr. Prabhakar Rao.

Vote of thanks by Dr. Santosh Kumar Swain.

News from Vijayapura

A Report by Dr. Anand P. Ambali



Department of Medicine & Geriatric Clinic, Shri B. M. Patil Medical College Hospital & Research Centre, Vijayapura, & Geriatric Society of India® organized a guest lecture to commemorate World Elder Abuse Awareness Day 2020 on 16th June 2020.

The program was both online as well as offline. The venue for off line was Dr. B. C. Roy Seminar Hall, Room no 309.

The lecture was delivered by Dr. Mala Kapur Shankardass, Associate Professor Maitreyi College, University of Delhi. She discussed in detail regarding "Elder Abuse: Addressing challenges".

A total of 117 delegates participated in the program.

Dr. A. P. Ambali welcomed the gathering and introduced the speaker.

Dr. Mala Kapur discussed in detail about elder abuse, types & examples of abuse, prevalence in India, medical and social effects of the abuse on the older people, how the medical fraternity should deal with such cases strongly. Her messages mentioned about the "Maintenance & Welfare Of Parents & Senior Citizen Act, 2007" ensures besides other aspects health security to the 'uncared' senior citizens by their families & community.

The act states provisions for medical care of senior citizens at the community level and also in institutions.

Strengthening geriatric services is an essential aspect of the act.

A response to older abuse must be built within the framework of healthcare.

This program was organised in collaboration with National Program of Health care of Elderly (NPHCE), International Network of prevention of Elder Abuse (INPEA) and Geriatric Society of India®. Dr. M. B. Biradar, DSO represented NPHCE, Vijayapura District.

Dr. Sharanabaswappa Badiger, HOD conveyed vote of thanks.

News from Kalaburagi

A report by Dr. P. S. Shankar

Prof. Dr. P. S. Shankar was felicitated on the occasion of Graduation Day ceremony at ESIC Medical College, Kalaburagi on 26th February 2020.

Dr. Vivek Handa was felicitated on the occasion of Graduation Day ceremony at ESIC Medical College, Kalaburagi on 26th February 2020.

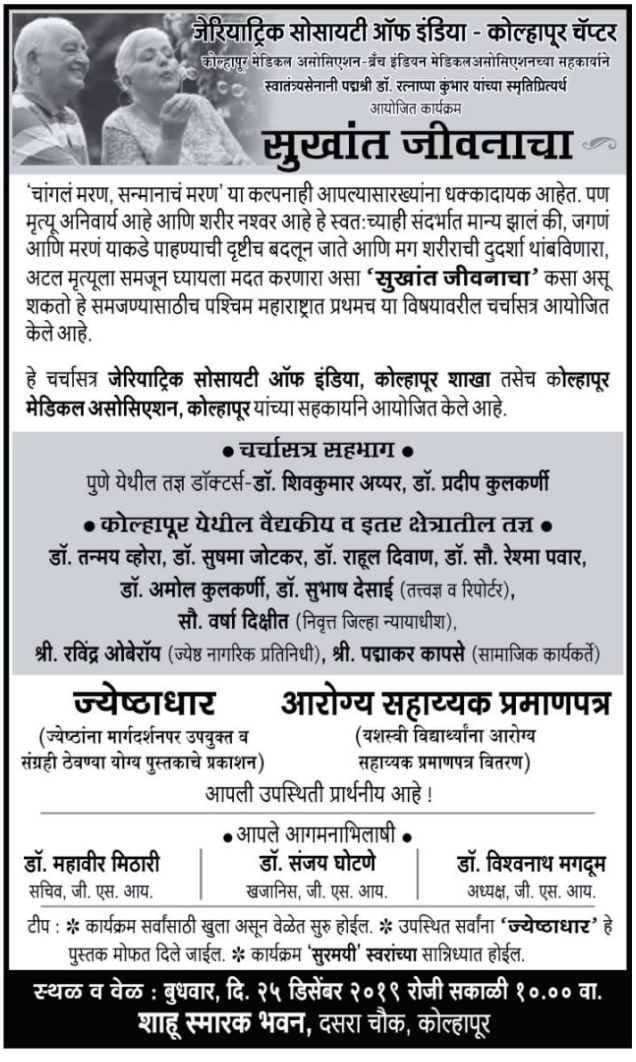
New from Derlakatte, Karnataka

A report by Dr. Prabha Adhikari MR

Yenepoya Medical College, Derlakatte, Karnataka organized Yen -Senior Care programme for active ageing which is a free programme filled with Education, Entertainment, Engagement, Empowerment and enjoyment held through google meet. 250 participants registered for the programme. We share the details with all the members so that it can be replicated anywhere during this COVID time where elders are locked up and not allowed to socialize. The programme was launched with a lecture by Dr Anitha Sebastina D Souza, Professor of Occupational Therapy on the topic Occupational Therapy for Prevention of Brain Ageing.

News from Mysore

Dr. Shilpa Avarebeel, Assistant Professor in department of Geriatric medicine from JSS Medical College was granted academic leave from JSSAHER and was working at the Royal Bournemouth and Christchurch hospital, NHS trust for a year from April 2019 to June 2020 as a Registrar in Geriatric Medicine. She was sponsored by Medical training Initiative programme through Royal college of physicians, London. She has successfully completed Fellowship in Geriatric Medicine through Royal college of Physicians, London.Dr. Avarebeel Works under the guidance of Dr Prathiba Pereira, Professor & HOD –Geriatric Medicine, JSS medical College, Mysore.



Courtesy: artists of Indian Arts firm, Hubballi

DELENG/2012/42798 Dt. 12 June 2012
Price Rs. 20 per copy

All Members are Requested to
Kindly update their
Email ID / Telephone No:
by sending mail to
secretariat office of GSI.