

# Suggestions for endless research on 2016

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## Abstract

In a moment of reflection of the past year of 2015, as to what we have achieved in medical research and what we need to do in the future we realize that although we have performed an enormous progress in medical research in the past we still have to do much more. In nuclear medicine there are many problems to solve like, how can we differentiate between infection, inflammation and cancer or between lymphomas and adenocarcinomas. In bone scans we need to differentiate traumatic lesions acute or chronic and lesions from another origin. Dosimetry and radiation burden is another problem. In HJNM we have previously published related papers. Not to mention radiation sickness due to modern atomic or hydrogen bombs. Labeling antibodies and genetic material is another issue. Additionally, in general medical knowledge is still unable to solve many unknown, difficult or tragic problems of our lives, like cancer, some viral infections, research in immunology, collagen diseases, genetics, radiation treatment, psychological disorders, anesthetics, the Hayflick phenomenon, hypertension, asthma, the function of the gastrointestinal tract, infectious diseases, physical exercise, all of which are briefly mentioned. We hope that even under the present financial problems and considering that almost 90% of medical truth is still unknown, our research in 2016 will be very important. In this paper we also discuss means for a more genuine and effective research.

## Introduction

In nuclear medicine there are many problems to solve like, how can we differentiate between infection, inflammation and cancer or between lymphomas and adenocarcinomas. In bone scans we need to differentiate traumatic lesions acute or chronic and lesions from another origin. Dosimetry and radiation burden is another problem. In HJNM we have previously published related papers. Not to mention radiation sickness due to modern atomic or hydrogen bombs [1-6]. Labeling antibodies and genetic material is another issue. Additionally, in general medical knowledge we know very little about factors that cause the different kinds of cancer or about cancer treatment. Recently immunotherapy is suggested to support cancer treatment [7-9]. We do recall some details that make lymphatic system unique i.e. lymph vessels at some points have valves and function like small hearts or that spleen is the largest lymph cells producing organ of our body.

Recently medical research yielded important results. We now know that a basic function of our body, cellular information is transmitted not by proteins, but by RNA to DNA resulting in protein synthesis [10]. In several haematopoietic cancers, chromosomal translocations and epigenetic research are important for the identification of transcriptional alterations [11]. Not to forget that "the food we eat may control our genes" [12]. Chromosomes, DNA and other genetic materials survive in a normal body environment.

Although radiotherapy now uses protons and more sophisticated equipment, only a small number of cancer patients are completely cured. Are patients exposed to high levels of radiation during medical diagnostic examination, like heart tests? [13].

Hippocrates said, about 2400 years ago: "what we can not treat by drugs, we can treat by knife", meaning surgery. It would be welcome in our times to better use therapeutically more drugs and less surgery.

We would like to know more about the cause and treatment of other diseases like, collagen diseases, rheumatic diseases, psychological disorders like depression, neurological disorders like Parkinson's disease, Alzheimer's dementia, cerebral palsy and many others.

Another problem is to estimate the effect on the brain of multiple exposures of anesthetics in pediatrics [14]. The length of time for infants to be exposed to various anesthetics like sevoflurane is critical to whether they may develop adverse neurological side effects [15].

There are some unique physiological phenomena that we are unable to understand. One is the Hayflick phenomenon. This phenomenon refers to the ability of the embryonic cells of our body to grow and reproduce as our age increases and to finally transform a baby into an old man. Dr Leonard Hayflick arbitrarily considered that all our embryonic cells can reproduce about 150 times [16]. Does this mean that we can live longer than 100 years? [17]. What tactic is best to follow in order to support the uneventful growth and reproduction of our body?

Other important issues that need further research are hypertension and asthma [18, 19]. We do not know all causes of hypertension like causes of "morning hypertension" and its relation to morning "brain sleep". Is morning hypertension related

to the level of some hormones excreted at that time? At about 07:00 hours in the morning we have the maximum concentration of testosterone in our blood. Is this related to hypertension? Is abstaining from "brain sleep" related to hypertension? What is the effect of muscular exercise on the tone on our vessels in normal and in atherosclerotic subjects, as related to hypertension? Why hypertensive young people, may become hypotensive when old? Is a systolic blood pressure of about 150mmHg in the internal carotids enough for sufficient brain blood circulation in the atherosclerotic old man? Hypertension is considered the main risk factor for cardiovascular diseases and cardiovascular diseases are considered the leading cause of death [18-20].

As for asthma we do not know the exact mechanism causing allergic effects and bronchospasm. Genetic factors play a decisive role but they are not the only factors. Deterioration of the physical condition of our body, the so called "meilleur intérieur" and also environmental factors may contribute.

In gastroenterology, we know very little of the relative and successive function of our gastrointestinal tract when eating a vegetarian or a Mediterranean meal. How long it will take to fully digest and also metabolize these meals? Is it better for half gastric emptying time to drink 200mL of tap water before, or after a meal? What if we have no breakfast as Hippocrates strongly suggested or if on the contrary we have 5 meals a day?

Do we know if the physical development of a newborn will be delayed if we feed the newborn only with cold or with hot milk? Experiments we have performed in newborn mice showed clearly that cold milk not only caused oesophagitis but also delayed growth of these animals [21].

In August 2016 in Rio, the Summer Olympics will be a mass gathering that may contribute to a further spread of mosquito-borne diseases like Chikungunya, Zika and dengue [19]. Do these infectious diseases develop only in a hot or in a cold environment like influenza?

Another point of interest is what the Greek physician Galenus (130-200A.C.) from ancient Pergamus in Asia Minor said: "For our body, physical exercise and diet should be symmetrical and on measure for all parts and organs of our body". Galenus considered that athletes should not exercise only a certain part of their bodies [22]. What is the optimum level for physical exercise for every age, athletes, men and women? What is the lifespan for athletes? Do athletes exercise mainly some parts of their body which become hypertrophic, in order to win metals in athletic games?

In alcoholism there is still much to discuss about how one can explain the greater sensitivity of women as to men in consuming and metabolizing alcohol [23, 24].

Individual research is more costly and usually less effective than multi group and multi national research. International or multinational Institutes should supervise medical research in order to be more effective and less costly [25]. A detailed review of the efficiency and social interest of research should be scrutinized by the sponsoring Institutes [26]. Errors can be avoided or minimized. Some times

medical errors are unavoidable especially in hospitals. Research procedures should be aware of that. It has been estimated by the US Institute of Medicine's landmark (1999) report that avoidable medical errors contributed annually to 44,000-98,000 deaths in US hospitals. Hospital-based errors were the 8th leading cause of death nationwide. More errors apply to patients aged 65 years and older [27]. It is obvious that in the future older ages shall increase...[28].

Research papers often miss to study important issues related to their subject of study like financial level, race, different social customs, climate, religious habits, different diets, addiction to drugs etc. [29]. In countries, where funding for research and also for medical care dramatically decreased, no real research can be expected [30, 31]. Nevertheless one can still think successfully. Our mind is the key organ that understands "sees and listens". The ancient Greek philosopher Epimachus (540-450B.C.) from the island of Kos said: "The mind sees and the mind listens...better than all other organs" [32, 33]. Sir Newton just by thinking and observing described gravity. Another common error in research studies is to present percentages of results when the total number of studied cases is less than a hundred, or to conclude that two groups are different even when the standard deviations of these groups extend to mutual range of values thus showing that both groups are alike. The Public Health England (PHE) in August last year published a strategy "to join researchers in PHE and elsewhere, on research questions relevant to the evidence needed for public health"[34].

It is important in publishing research papers in medical journals to realize which papers are fake. In HJNM papers are checked at least 4-5 times before publication. During the last two years we found two fake papers submitted for publication. Some authors have presented a great number of cases out of which very few were studied while the rest were controls. Papers may be rejected even the last minute before publication if authors are unable to reply to our questions. In 2015 important international publishers retracted many articles from subscription journals because of peer-review fraud [35].

One could very reluctantly suggest the following: Research data from different institutes that are interested in similar research subjects can be shared, repeated or continued among researchers from different countries [36, 37]. This cooperation will minimize bias and produce better statistics [38, 16]. We could also have International or Continental Medical Research Authorities who shall announce simple rules securing credibility and importance of research studies. Authors and medical journals would indicate that these rules have been followed. Cooperating Journals will be widely known. These Medical Institutes could be financially supported by the participating countries and could even support financially certain research projects of common interest.

### Bibliography

1. Kampoura-Nifli E, Nifli AF, Vontas A et al. The point of view of the

- people of Thessaly for a potential nuclear accident. *Hell J Nucl Med* 2002; 3: 160-163.
2. Grammaticos P, Fountos G. The physician should not harm but benefit the patient. *Hell J Nucl Med* 2006; 9: 82-4.
  3. Iakovou I, Karavida N, Kotzassarlidou M. The computerized tomography scans and their dosimetry safety. *Hell J Nucl Med* 2008; 11: 82-5.
  4. Okkalides D. Recent international regulations: Low dose-low rate radiation protection and the demise of reason. *Hell J Nucl Med* 2008; 11(2):86-89.
  5. Grammaticos P, Lyra M. Medical radiation exposure and accidents. Dosimetry and radiation protection. Do we only benefit the patient? *Hell J Nucl Med* 2010; 13(2): 106-110.
  6. Palumbo B, Sinzinger H. The Fukushima nuclear accident temporarily increased patients reluctance for nuclear medicine investigations. *Hell J Nucl Med* 2012; 15(1): 28-32.
  7. Wilson S. The Promise of Immunotherapy. In The Fight Against Cancer, <http://www.medicaldaily.com/promise-immunotherapy-fight-against-cancer-366906>, 2015; December 27.
  8. Kaufman HL. Precision Immunology. The promise of Immunotherapy for the Treatment of Cancer. *J Clinical Oncology* 2015; 33: 1-3.
  9. Weintraub A Jimmy Carter. Melanoma and the promise of immunotherapy in the elderly. Forbes, <http://www.forbes.com/sites/arlene-weintraub/2015/08/21/jimmy-carter-melanoma-and-the-promise-of-immunotherapy-in-the-elderly/#3f4115d21d79>, 2015, August 21.
  10. DeVita VT, Rosenberg SA. Two Hundred Years of Cancer Research. *N Engl J Med* 2012; 366 (23): 2207-14.
  11. Dawson MA, Kouzarides T, Huntly BJP. Targeting Epigenetic Readers in Cancer. *N Engl J Med* 2016; 367 (7): 647-57.
  12. Hodge A-M C Vitamins, Minerals and MicroRNA. *Scient Amer* December 2011
  13. Feller S. Radiation during heart tests higher for patients in U.S., United Press International Inc., [http://www.upi.com/Health\\_News/2015/12/28/Radiation-during-heart-tests-higher-for-patients-in-US/7771451330191/](http://www.upi.com/Health_News/2015/12/28/Radiation-during-heart-tests-higher-for-patients-in-US/7771451330191/), 2015; December 28.
  14. Warner DO, Flick RP. Anaesthetics, infants, and neurodevelopment: case closed? *The Lancet* 2016; 387: 202-4.
  15. Davidson AJ, Disma N, de Graaff JC et al. Neurodevelopmental outcome at 2 years of age after general anaesthesia and awake-regional anaesthesia in infancy (GAS): an international multicentre, randomised controlled trial. *The Lancet* 2015; 387: 239-50.
  16. Hayflick L. Biological aging is no longer an unsolved problem. *Ann. of the NY Acad of Sci* 2007; 1100: 1-3.
  17. Marcus MB, More Americans are living past their 100th birthdays, <http://www.cbsnews.com/news/more-americans-are-living-past-their-100th-birthdays/>, 2016; January 21.
  18. GBD 2013 Risk Factors Collaborators, Global, regional and national comparative risk assessment of 79 behavioral, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systemic analysis for the Global Burden of Disease Study 2013. *The Lancet* 2015; 386: 2287-323.
  19. Health security: the defining challenge of 2016. *The Lancet* 2015; 386: 2445.
  20. GBD 2013 DALYs and HALE Collaborators, Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition. *The Lancet* 2015; 386: 2145-90.
  21. Grammaticos P, Emmanouil-Nikoloussi E, Trontzos Ch et al. Changes in esophageal mucosal morphology in rats fed with milk of low or high temperature. Department of Histology, Aristotle University of Thessaloniki and Nuclear Medicine Laboratory, AHEPA University Hospital, Archives of the XIIth International Symposium on Morphological Science, University of Thessaloniki, August 30, 1995.
  22. Galenus VI, 133. In: Mitropoulos K. Galenus. Published in Greek in Thessaloniki. Galenus 1962; p165.
  23. Smyth A, Teo KK, Rangarajan S. Alcohol consumption and cardiovascular disease, cancer, injury, admission to hospital, and mortality: a prospective cohort study. *The Lancet* 2015; 386: 1945-54.
  24. Wilson MH, Habig K, Wright C et al. Pre-hospital emergency medicine. *The Lancet* 2015; 386: 2526-34.
  25. Schwartz R. The Emperor of All Maladies-The Beginning of the Beginning. *N Engl J Med* 2011; 365 (25): 2353-55.
  26. Shaw D. The right to participate in high-risk research. *The Lancet* 2014; 383: 1009-10.
  27. Medical errors in the USA: human or systemic?. *The Lancet* 2011; 377: 1289.
  28. Xu J. Mortality Among Centenarians in the United States 2000-2014, U.S. Department of Health and Human Services, NCHS Data Brief, No. 233, 2016; January.
  29. Ware JH, Harrington D, Hunter DJ, D'Agostino R.B. Missing Data. *N Engl J Med* 2012; 367; 14: 1353-4.
  30. Karamanoli E. 5 years of austerity takes its toll on Greek health care. *The Lancet* 2015; 386: 2239-40.
  31. Dovey D, Beans, Beans. The Magical Fruit... And 8 Other Food And Drinks That Give You Gas, <http://www.medicaldaily.com/beans-beans-magical-fruit-and-8-other-food-and-drinks-give-you-gas-366486>, 2015; December 23, 2015.
  32. Venosa A. Have Insomnia? Researchers Identify Brain Circuit Responsible For Wakefulness, Sleep, <http://www.medicaldaily.com/have-insomnia-researchers-identify-brain-circuit-responsible-wakefulness-sleep-366880>, 2015, December 25.
  33. Eumenides, the poet, comedian and philosopher from Kos. In: Natsoulis Tasos Words and phrases, traditional. 11th edn. Smyrniotakis Ed. G, Genadiou 6, Athens, Greece. Year after 1996 not specified, page 365.
  34. McCarthy M. Will Public Health England lead research? *The Lancet* 2015; 386: 2232-3.
  35. Haug CJ. Peer-Review Fraud-Hacking the Scientific Publication Process. *N Engl J Med* 2015; 373 (25): 2393-9.
  36. Longo DL, Drazen JM, Data Sharing. *N Engl J Med* 2015; 374 (3): 276.
  37. Taichman DB, Backus J, Baethge C et al Sharing Clinical Trial Data -A Proposal from the International Committee of Medical Journal Editors. *N Engl J Med* 2016; 374 (4): 384-6.
  38. Little R.J, Ralph D' Agostino R, Cohen ML et al. The Prevention and Treatment of Missing Data in Clinical Trials. *N Engl J Med* 2012; 367 (14): 1355-67.

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Editors of the Hellenic Journal of Nuclear Medicine are privileged to cooperate with authors and with distinguished reviewers who try to better evaluate the papers submitted for publication.

Authors benefit of the guidance of the reviewers and the Journal is proud to publish important papers. It was unfortunate that some of the papers submitted presented facts without statistical support. In case of doubt, we ask the opinion of a third reviewer. We thank the following colleagues for reviewing papers for the Hellenic Journal of Nuclear Medicine during the last year (2015): B. Ajdinovic, D. Antoniou, D. Apostolopoulos, V. Artiko, S. Baloyiannis, A. Bantis, T. Basoglu, S. Basu, G. Cheng, F. De Geeter, G. Fountos, S. Gaberscek, G. Gerasimou, A. Georgakopoulos, P. Georgoulas, R. Kumar, M. Lyra, M. Matovic, E. Mazokopakis, E. Moralidis, E. Papanastasiou, N. Pianou, G. Rubini, H. Sinzinger, E. Skoura, T. Spyridonidis, H. Van Isselt, P. Valsamaki, T. Yamamoto, A. Zafirakis, A. Zissimopoulos.