OPINION

Bridging ancient wisdom and contemporary medical science: Contemplating on Hippocrates' *Theory of Humours*

IOANNIS G. LEMPESIS 1 , VASILIKI EPAMEINONDAS GEORGAKOPOULOU 1 , GEORGIOS P. CHROUSOS 2,3 and DEMETRIOS A. SPANDIDOS 4

¹Department of Pathophysiology, Laiko General Hospital, National and Kapodistrian University of Athens;
²Clinical, Translational and Experimental Surgery Research Centre, Biomedical Research Foundation Academy of Athens;
³University Research Institute of Maternal and Child Health and Precision Medicine and UNESCO Chair on
Adolescent Health Care, National and Kapodistrian University of Athens, Aghia Sophia Children's Hospital, 11527 Athens;
⁴Laboratory of Clinical Virology, School of Medicine, University of Crete, 71003 Heraklion, Greece

Received December 31, 2023; Accepted February 28, 2024

DOI: 10.3892/wasj.2024.233

Abstract. Ancient Greek medicine, influenced by religion, attributed disease to divine forces and developed treatments based on faith and the placebo phenomenon. Ancient Greek Medicine, beginning with Hippocrates, was influenced by the pre-Socratic natural philosophers and was based solely on evidence and the use of reason. Hippocrates employed the doctrine of the four humours, which corresponded to the elements 'fire', 'air', 'earth' and 'water', to understand and explain disease and traditional drug action. This system foreshadowed the endocrine and biochemical aspects of human physiology and pathophysiology, and used the homeostatic concepts to explain health as 'eucrasia' (good mixing) and disease as 'dyscrasia' (bad mixing) of the humours. Modern hyper-specialized, precision medicine and hyper-compartmentalized science can still benefit from revisiting ancient wisdom towards a holistic approach, to achieve the 'golden mean' in the consideration of health and disease.

Bridging ancient wisdom (Hippocrates and the four humours) and contemporary medical science

Ancient Greek medicine, influenced by other, receding civilizations, attributed healing powers to gods, such as Apollo and

Correspondence to: Dr Vasiliki Epameinondas Georgakopoulou, Department of Pathophysiology, Laiko General Hospital, National and Kapodistrian University of Athens, 17 Agiou Thoma street, 11527 Athens, Greece

E-mail: vaso_georgakopoulou@hotmail.com

Key words: Hippocrates, history of medicine, medical philosophy, endocrinology, homeostasis

his son, Asclepius (1,2). In ancient medical centres founded around temples to Asclepius, known as 'Asclepeiia', priests applied 'treatments' based on divine faith and the placebo phenomenon. Subsequently, Ancient Greek medicine, 'liberated' from religious influences, was based on evidence and logical thinking (3). It advanced knowledge of physiology, pathophysiology, nosology and rational therapy and was largely attributed to the works and influence of Hippocrates and his school (1,2).

Hippocratic thinking and work were greatly influenced by pre-Socratic philosophers, predominantly including Pythagoras, Alcmaeon, Empedocles and Democritus (1,2). As a result, the Hippocratic doctrine established the clinical images and fixed time periods for the resolution of various diseases (2). Plato and Aristotle combined the significance of number 'four' with the doctrine of the 'four elements, which corresponded to the qualities 'dry', 'cold', 'hot' and 'moist', according to the schematic diagram presented in Fig. 1 (2). The four elements 'fire', 'air', 'earth' and 'water' were rearranged into their qualitative components. These elements corresponded to the four humours of the body: 'Blood', 'phlegm', 'yellow bile' and 'black bile'. These elements were combined to create a complex human personality system (1,2,4). The doctrine of the four humours, further developed by Galen, and Arabian and Persian physicians, influenced the understanding of diseases and the actions of drugs. Remedies and compounds were classified numerically based on their degrees of quality. For example, sugar was classified as cold, warm, dry and moist, while cardamoms were warm, cold and dry (2).

The system of the four humours somehow foreshadowed the endocrine and biochemical aspects of human physiology and pathophysiology (2). It could also be further claimed that this system encompasses an understanding of the homeostatic mechanisms of life. Ancient Greek natural philosophers, beginning with Pythagoras, initially described the concept of a 'steady state' of the body and soul with the words 'harmonious

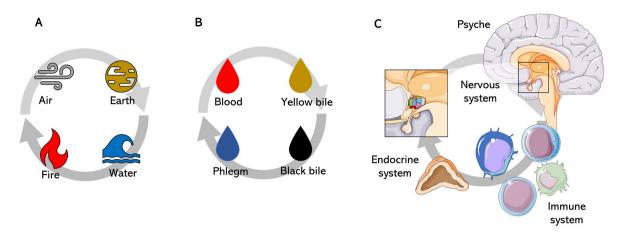


Figure 1. (A) Summary of the ancient theories of the four elements, (B) which in turn inspired the Hippocratic theory of the four humours. (C) sImbalances in the proprotions of these caused disease and a proposal of a current date analogy of the regulatory hyper-system, the psycho-neuro-endo-immune axis. Parts of this image was derived from the free medical site http://smart.servier.com/ (accessed on November 30, 2023) by Servier, licenced under a Creative Commons Attribution 3.0 Unported Licence.

balance' and 'isonomia'. Later, Epicurus referred to 'eustatheia' (eustasis) to express this fundamental concept. Homeostasis, which is derived from the Greek language, meaning 'steady state', was coined in 1930 by Walter Cannon to redefine this key concept at the beginning of the 20th century (5,6).

Galen, an ancient Greek physician, observed that women with 'melancholic natures' had a higher incidence of tumours of the reproductive organs. This observation led to the establishment of a connection between psychological stressors and the development of cancer dating back to the second century CE (7). 'Melancholia', as a term, describes an imbalance caused by excess of black bile (melaina chole) based on the Hippocratic theory of the humours (1,4,8,9). Hippocrates' humoural theory of the pathology of diseases further affected medicine in various ways throughout the medieval period, including Byzantine and Arabic, until the Renaissance and beyond (10).

There are three possible outcomes that may occur as a consequence of the interplay between stressors that distrupt homeostasis and adaptive responses that are triggered by stressors and re-establish it: An ideal match, which causes the organism to return to its basal homeostasis, also known as 'eustasis', an insufficient match, which leads to 'dyshomeostasis' or 'cacostasis', or a perfect match, which leads to a new improved equilibrium, also known as 'hyperstasis', are the three types of matches that may occur when encountering a stressor (5,11,12).

Currently, in the era of modern medicine, when the understanding of biology has grown immensely and technology has provided monumental study tools, an analogy could be performed between the ancient Hippocratic theory of the four humours and the regulatory psycho-neuro-endo-immune supersystem that deals with stress and comprises a huge nexus reflecting the above imbalances (Fig. 1) (11,13-17). Ancient wisdom teaches that to treat the disease of a patient, one should take a holistic approach, considering medicine as both an art and a science. Medicine requires an ethical, humanistic approach, strong compassion, robust factual knowledge, highly interpretive capacities to translate scientific biomedical knowledge,

focus into specific health problems and exquisite judgement (18).

Other key messages from revisiting the thoughts of Ancient Greek Physicians and Philosophers indicate that they were able to successfully and respectfully integrate medical knowledge from other civilizations, for instance Egyptian traditions that potentially preceded the theory of humours of Hippocrates (19), the abandoning of theocratic medicine and other philosophical speculations influenced modern Evidence-Based Medicine, emphasizing thorough history-taking, holistic concepts and understanding human nature rather than speculating (4).

In conclusion, in the era of the hyper-specialized precision medicine and the hyper-compartmentalized science, an integrated re-thinking of biomedical science and a renewed approach to treating the patient rather than the disease, can draw examples from the Hippocratic tradition.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

Not applicable.

Authors' contributions

IGL and GPC conceptualized the study. VEG, IGL, GPC and DAS substantially contributed to data interpretation, and wrote and prepared the draft of the manuscript. All authors have read and approved the final manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

DAS is the Managing Editor of the journal, but had no personal involvement in the reviewing process, or any influence in terms of adjudicating on the final decision, for this article. GPC is an Honorary Editor of the journal, but had no personal involvement in the reviewing process, or any influence in terms of adjudicating on the final decision, for this article. The other authors declare that they have no competing interests.

References

- 1. Bujalkova M, Straka S and Jureckova A: Hippocrates' humoral pathology in nowaday's reflections. Bratisl Lek Listy 102: 489-492, 2001.
- Garrison FH: An introduction to the history of medicine: with medical chronology, suggestions for study and bibliographic data. 3rd Edition. W.B. Saunders company, Philadelphia, PA, 1922.
- 3. Hashmi JA: Placebo Effect: Theory, Mechanisms and Teleological Roots. Int Rev Neurobiol 139: 233-253, 2018.
- Marcum JA: Hippocrates and the Hippocratic Tradition: Impact and Development of Medical Knowledge and Practice? In: Handbook of Philosophy of Medicine. Schramme T and Edwards S (eds). Springer Netherlands, Dordrecht, pp821-837, 2017.
- 5. Chrousos GP: Stress and disorders of the stress system. Nature reviews. Endocrinology 5: 374-381, 2009.
- 6. Lempesis IG, Georgakopoulou VE, Papalexis P, Chrousos GP and Spandidos DA: Role of stress in the pathogenesis of cancer (Review). Int J Oncol 63: 124, 2023.
- 7. Mravec B, Tibensky M and Horvathova L: Stress and cancer. Part I: Mechanisms mediating the effect of stressors on cancer. J Neuroimmunol 346: 577311, 2020.

- 8. Jackson SW: Melancholia in Ancient Greece and Rome. In: Melancholia and Depression. Yale University Press, New Haven, CT, pp29-45, 1986.
- 9. Burton R: The anatomy of melancholy. JW Moore, Philadelphia, PA, 1857.
- van den Tweel JG and Taylor CR: A brief history of pathology: Preface to a forthcoming series that highlights milestones in the evolution of pathology as a discipline. Virchows Arch 457: 3-10, 2010.
- 11. Chrousos GP and Gold PW: The concepts of stress and stress system disorders: overview of physical and behavioral homeostasis. Jama 267: 1244-1252, 1992.
- 12. Charmandari E, Tsigos C and Chrousos G: Neuroendocrinology of stress. Ann Rev Physiol 67: 259-284, 2005.
- 13. Agorastos A and Chrousos GP: The neuroendocrinology of stress: the stress-related continuum of chronic disease development. Mol Psychiatry 27: 502-513, 2022.
- Stefanaki C, Pervanidou P, Boschiero D and Chrousos GP: Chronic stress and body composition disorders: implications for health and disease. Hormones (Athens) 17: 33-43, 2018.
- Franchimont D, Kino T, Galon J, Meduri GU and Chrousos G: Glucocorticoids and inflammation revisited: the state of the art. NIH clinical staff conference. Neuroimmunomodulation 10: 247-260, 2003.
- Chrousos GP, McCarty R, Pacak K, Cizza G, Sternberg E, Gold PW and Kvetnansky R: Stress: Basic mechanisms and clinical implications. Ann NY Acad Sci 771: 192-203, 1995.
- 17. Chrousos GP: The hypothalamic-pituitary-adrenal axis and immune-mediated inflammation. N Engl J Med 332: 1351-1363, 1995
- 18. Bærøe K: Medicine as Art and Science. In: Handbook of the Philosophy of Medicine. Schramme T and Edwards S (eds). Springer Netherlands, Dordrecht, pp1-14, 2015.
- 19. Loukas M, Tubbs RS, Louis RG, Jr., Pinyard J, Vaid S and Curry B: The cardiovascular system in the pre-Hippocratic era. Int J Cardiol 120: 145-149, 2007.



Copyright © 2024 Lempesis et al. This work is licensed under a Creative Commons Attribution 4.0 International (CC BY 4.0) License.