Leukemia (2007) 21, 591–592

www.nature.com/leu

EDITORIAL

The Hippocratic treatise 'On glands': the first document on lymphoid tissue and lymph nodes

Leukemia (2007) **21,** 591–592. doi:10.1038/sj.leu.2404618

The first document on the anatomy and physiopathology of lymphoid tissue is to be found in the Hippocratic treatise 'On glands' ('*Peri adenôn*').[1] This short book is a milestone in the history of haematology and clinical immunology. It belongs to the Hippocratic Corpus, a collection of medical writings composed during a period of about three centuries, mostly from the fifth to the third century BC. This collection of inestimable value represents the central nucleus of ancient Greek medical literature. The date of our text is disputed.[2] According to some, the treatise is not before the Hellenistic era (third century BC). According to others, it belongs to an older period, the end of the fifth or the beginning of the fourth century BC The modern scientist stands amazed before the innovative concepts expounded in this ancient medical document. Indeed, the functional anatomy of the lymphatic system and lymph nodes emerges with impressive precision without any antecedent in the Greek medical literature. The Author identifies lymph nodes with the general term of 'glands' ('*adenes*') (Chapter 1). The tradition still in use to name lymph nodes with the word lymph 'glands' goes certainly back to this text. The Author proceeds with rigorous method from a nearly histological definition of lymph glands, via a short account on their functional significance during health and disease, to a well-ordered topographic classification. Lymph glands are described as whitish and phlegmy structures, which present a wholly consistence to the touch and can be easily squeezed by the fingers (Chapter 1). Indeed, their constitutive substance is depicted as 'spongy, rarefied and friable'. Lymph glands possess much fat and are richly vascularized. This is the reason because they undergo significant bleeding once they are cut. Then, the Author provides an absolutely modern interpretation of their physiopathological significance. Lymph glands are said to 'attract and receive' fluids (Chapter 3). Indeed they receive the moisture that flows to them from different regions of the body via plentiful afferent vessels (Chapter 2). If the amount of moisture is moderate, there is no fluid accumulation in any part of the body because lymph glands drain off such liquid. By contrast, when glands are overfilled by humours, they become swollen and inflamed, and can transmit their disease to the rest of the body. They cause, for instance, the formation of tubercles accompanied by fever. In addition, lymph glands may become ill 'in sympathy with the body'. Three fundamental concepts concerning the physiopathology of lymph nodes and lymphatic vessels come out for the first time in the medical literature. First, the lymphatic system is made up of lymphatic vessels and the glands through which they pass. Second, the drainage function of lymph glands is firmly established. Third, their involvement in inflammatory processes and systemic diseases is also foreshadowed, because it is asserted that lymph glands are subject to flogistic responses and enlargement as a consequence of either local or general affections. Then, the Author proceeds by enumerating the principal gland stations. For the most part, lymph glands are situated near the great flexures of the body (Chapter 3). It is claimed that these organs are particularly numerous where there is much internal fluid to be drained and in regions rich of blood vessels, whereas they lack where the body is dry. This is indeed a skilful observation insofar as lymphatics can be recognized in nearly all tissues and organs, which contain blood vessels. Such non-vascular structures as cartilage, nails, hair and cornea have none. In the head – maintains the Hippocratic Author – glands are scattered around the ears and near the jugular vessels of the neck. These are indeed the posterior and pre-auricular lymph nodes, and the superficial and deep cervical lymph nodes, respectively. Glands are said to be numerous in the axillary and inguinal flexures, the axillary and inguinal lymph nodes of modern nomenclature. Remarkably, the intestinal glands are also mentioned (Chapter 5). They are described as quite large, very numerous and placed to the omentum. Here, the Author provides a fascinating explanation as to the drainage mechanism of intestinal glands. The fluid produced by the bowel is firstly absorbed by the omentum and then passes into mesenteric glands. Of course, this implies the existence of small, hollow channels running through the mesenteric folds – the lacteal or chyliferous vessels – and bearing the intestinal lymph to the lymph nodes scattered in the mesentery. There are also glands near the kidneys (Chapter 6). These glands are larger than the other glands. Here, the Author is likely mentioning the aortic lymph nodes, which are very large indeed. At last, the Author describes the glands of the throat, which are called 'paraisthmia' (Chapter 7). These are located to the isthmus of the fauces on both sides and are to be interpreted as the palatine tonsils. As a matter of fact, this book does not mention the spleen and the thymus among lymphoid organs. Other Hippocratic treatises, however, provide information about the spleen, in particular about spleen enlargements in acute or chronic pathological conditions. Remarkably, the words used to describe its structure are almost identical to those utilized to depict lymph glands. In 'Ancient medicine', for instance, a Hippocratic text dating from the end of the fifth century BC, the spleen is referred to as 'soft and spongy' (Chapter 22).[3] Its texture is rich of 'porous hollows'. Thus, the spleen easily 'draws and attracts' fluids, and is subject to become swollen and to harden as a consequence of general feverish conditions. Enlargement of the spleen as a result of fever is also reported in the fourth century Hippocratic treatise 'Places in man'.[4] Here, the Author maintains that it is 'one and the same pathological process that makes both the spleen swell and the body waste' (Chapter 24). Some details of the spleen's gross anatomy are also provided. The organ is described as an abdominal structure that is connected to the abdominal wall by the omentum (Chapter 3). As to the thymus, it will be first described by Galen of Pergamon (129-about 216) various centuries later as a 'loose, rarefied flesh' composed by two horns, localized deeply to the sternum, close to the heart and the bifurcation of the great vein (superior vena cava). Remarkably, Galen made the truthful observation that the thymus reaches its greatest size during the first years of life and then progressively disappears.[5]

'On glands' is a great book. Its Author should be recognized as a far-seeing pioneer in haematology and medical sciences. He shaped some basic concepts, which represent still common wisdom in today's medical reasoning.

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