

MEGAS ALEXANDROS (Alexander The Great):

His Death Remains a Medical Mystery

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More than 2000 years ago, Alexander the Third of Macedonia conquered the then known world and ruled an empire that extended from the Balkan Peninsula to the Indus River. Alexander changed the course of human history when he sparked the spread of Greek culture throughout the ancient world. Also as the world's first statesman, he foresaw the advantages of multicultural societies and was clever enough to transmit these ideas to the generations that followed. Alexander was educated by one of the most prominent of Greek philosophers: Aristotle, who shaped Alexander's superior intellect inculcating in him a desire to know new countries and cultures. From this interest came the energy that years later drove him to explore the limits of the known world. Alexander called this impulse his *pothos* (thirst for knowledge). Even more, Aristotle implanted in Alexander his interest in philosophy and in the art of healing. Alexander was attracted not only to the theory of medicine but, also tended his friends when they were sick, prescribing for them diets and various courses of treatment. Even though Alexander was taught that his was the best culture that he helped to spread throughout the known world, he was able to appreciate the achievements of other cultures.

To promote a common culture throughout his domains, Alexander developed many strategies:

- a) Despite being devoted to the Greek gods especially Zeus and Dionysus, he respected the religions of the people he conquered. Indeed, he even participated in their main religious ceremonies such as those dedicated to Melkart in Phoenicia and to Amon in Egypt.
- b) He promoted intercultural marriages between his soldiers and foreign women, and he himself married Roxanne a Persian noble woman.
- c) He introduced foreign clothes, customs and symbols coming to his own court.
- d) He accepted and even promoted the incorporation of non-Macedonian people into important positions in his army and government, if they deserved these appointments because of their knowledge and responsibility.
- e) He founded approximately 70 cities (the Alexandrias), all of them strategically placed throughout his entire kingdom; they functioned as a sort of vertebral spine of his empire, but also acted as foci for spreading Hellenic culture. They continued to function in that way for many centuries after Alexander's death.

Alexander's Death

The cause of Alexander's death has been scrutinized closely as his life and achievements. If he were seen as a patient his medical report would say: A 32 year-old Macedonian noble, a war veteran with the history of: -Heavy alcoholism -Extensive traveling throughout Asia Minor, the Middle East as far as the Indian frontier, which meant respected exposure to a variety of transmissible endemic diseases. -Several penetrating wounds the most important of which was to his right chest; this was complicated by a hemopneumothorax that he had suffered about one year before.

Previous febrile episodes: The recent death of a male sexual partner from a febrile illness that was not characterized further.

In this context (according to historical records) Alexander abruptly became ill after a royal banquet, and he died two weeks later of a febrile illness, associated with an intense right-sided abdominal pain. Three days before his death, he was unable to speak but he could recognize companions and move his eyes in response - a clinical condition that resembles Guillain-Barré syndrome or a locked-in state. Several days elapsed before the body could be prepared for burial and, during this time, signs of post-mortem

putrefaction were notably absent, probably because he spent his last days in a comatose state. At the time, people interpreted the preservation of his body as a sign of his divine condition.

Even though he was a heavy drinker, alcoholism does not seem to be the cause of death - this would imply the development of acute hepatitis but icterus was not mentioned in any records of the day.

Since Alexander had many enemies and he was the only person who became ill after the banquet there is a strong possibility, that he was poisoned using wine as vehicle; the poor description of Alexander's illness in the royal diaries is also suspicious of foul play because, Hippocratic medicine, as it was then practiced, would have required an extensive description. Methanol or lead intoxication, through contaminated wine, are other causes proposed to explain Alexander's death. However, none of these causes explains entirely the characteristics of his disease.

Fever seems to have been the main symptom of his fatal disease, unless conspirators had adulterated the documents and invented Alexander's febrile syndrome. Other entities proposed to explain Alexander's fatal illness included: acute viral hepatitis, acute cholecystitis, cholangiolitis, acute pancreatitis, hepatic amebiasis, enteritis due to *Campylobacter jejuni*, gastric or duodenal ulcer perforation, pleural empyema and lower-lobe pneumonia. However, none of these explains completely Alexander's condition and moreover some of them would have generated signs such as icterus or diarrhea which Alexander did not present.

Four other diseases have been proposed in previous articles that could have explained Alexander's clinical case as a whole: malaria secondary to *Plasmodium falciparum*, schistosomiasis induced by *Schistosoma haematobium*, typhoid fever and porphyria. Epidemiologically, three of these diseases were common in ancient Babylon, especially malaria and typhoid fever. Alexander was described as having a sudden pain, which some authors concluded may have represented a rupture of an hepatic abscess or an intestinal perforation and a subsequent peritonitis induced by *Salmonella typhi* infection. Moreover, this bacterium can induce Guillain-Barré syndrome. On the other hand, *Plasmodium falciparum* can induce intestinal and cerebral ischemia due to arterial thrombosis, while *Schistosoma haematobium* parasite can lay its eggs in the urinary bladder and central nervous system explaining abdominal and neurological symptoms.

Acute intermittent or variegate porphyria may be triggered by the ingestion of alcohol and typically these patients present with acute abdominal pain, mental symptoms, autonomic instability (including fever) and polyneuropathy.

Acute endocarditis is another possible diagnosis and some points support this hypothesis:

a) He had been wounded many times on the battlefield and probably those lesions became infected and were the portal of entry for *Staphylococcus Aureus* (a species that accounts for 50-70 % of acute endocarditis).

b) Before his last illness, Alexander had had previous febrile episodes, and therefore might have already been ill before the banquet was arranged.

c) Neurologic complications occur in one third of patients with bacterial endocarditis and triple the general mortality rate of the disease. Any artery may be affected by emboli or mycotic aneurysm. Alexander's neurological picture could be explained by a basilar artery compromise which leads to a locked-in state: a condition in which there is a paralysis of the limbs and most of the bulbar muscles so that the patient can communicate only by moving the eyes or the eyelids. In this entity the patient's intelligence is preserved. The abdominal pain in the upper quadrant could be explained by the rupture of an hepatic abscess.

The cause of Alexander the Great's death probably will remain as a mystery forever but his highly productive life makes his death and its cause insignificant.

Many historians believe that Alexander's efforts to achieve an ecumenical civilization set the stage for subsequent appearance of the Roman Empire whose emperors sought to imitate him: *imitatio Alexandri* was their motto. The Roman Empire inherited the Alexandrian concept of an empire based on a multicultural society since it considered any person inside its borders as a Roman citizen regardless of his race, religion, or language. This important concept that was forged in people's mind was considered unthinkable before Rome.

Alexander and his idea of a universal culture had no boundaries. This concept of mankind went beyond the political arena to the religious one. Thus the Roman Empire and Christianity developed closely

together; while the former reinforced the concept of universality of mankind, the spread of the latter was assisted by unity and continuity of the Empire.

Alexander's greatness was based not only on his military achievements, but also on his interest in forging an ecumenical civilization, he was the visionary progenitor of our modern multicultural societies.

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