A MEDICAL-HISTORICAL EXAMINATION OF THE DEATH OF ALEXANDER THE GREAT

Abstract: Alexander the Great's cause of death has been contentious since antiquity. Historians and physicians alike have proposed a multitude of hypotheses. However, neither party is without their analytical flaws. The historians often neglect obvious medical refutations. Meanwhile, the physicians often err by forsaking disciplined historical methodology. Therefore, the authors of this paper subject these prior hypotheses to both medical and historical criticism, in order to provide a multidisciplinary approach to a longstanding mystery. Some hypotheses have more weight than others, as is discussed. The most probable of the poisoning hypotheses, which aligns with the Vulgate tradition of Alexander's death, cites the use of Veratrum album, a plant derived bane. When the Court tradition is considered, i.e. that no foul play occurred, acute pancreatitis induced by alcohol abuse holds greatest credence as a hypothesis. It is hoped that the approach used will not only increase clarity regarding Alexander's death and challenge weak ideas but also provide an approach by which speculation about other medical diagnoses in history may be tempered and critiqued.

Keywords: Alexander the Great, Retrospective Diagnosis, Regicide, Murder, Death

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INTRODUCTION

lexander the Great's cause of death has long been contentious. The secondary sources describing his death are divergent. Diodorus tlaims that Alexander collapsed after consuming a bowl of wine and died eleven days later. Plutarch contends that he was struck by fever during a feast, succumbing almost two weeks later. Justin – a dubious historian – avers that poison claimed Alexander. Plutarch and Arrian reject poison.¹

Modern medical experts uphold pathologies relating to both of these storylines with equal fervour. A search of the medical literature database PubMed was conducted using the term "Alexander the Great" and found fifty-five articles. The twenty articles that explored his death posited causes ranging from arsenic, to typhoid fever, to malaria, to even grief. Alexander must either have been history's most extreme example of multi-morbidity or many of the proposed *causae mortis* are wrong.²

The uncontested fact is that Alexander died on June 10, 323 BC in

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BOSWORTH 2008; WELLS 1963; PERRIN 1919; BRUNT 1983

² OLDACH/RICHARD/BORZA/BENITEZ 1998

Babylon, when he was only thirty-two. However, unlike Richard III - another historical character whose cause of death and physical health have attracted attention - Alexander's pathologists lack a body. The primary evidence pertinent to Alexander is generally sparse. This lack of physical evidence makes a conclusive cause of death virtually impossible to determine. This paper will thus not seek to conclusively identify a single cause. It will instead examine the merits of already proposed causes of death using a framework that could be useful when critiquing retrospective diagnoses of historical figures. This is examination is needed for three reasons. Firstly, conclusions based on weak premises should not go unchallenged, especially when they are published in reputable academic journals. Secondly, there is historical value in narrowing the options for Alexander's death and refining knowledge, as much of the proceeding literature of the topic has increased uncertainty with an expansive list of hypotheses with uneven merit. Finally, the approach of this paper may provide a systematic way of approaching historical medical cases, which seem to continually invite curiosity and speculation.

This paper will first consider the textual accounts associated with the 'Vulgate' (the Romance) and 'Court' narratives of Alexander's death - regicide by poison and a febrile illness, respectively. A discussion and critique of the medical diagnoses proffered for each account will follow, using patient history, current medical literature, and epidemiology.3

Before such an analysis can be undertaken, crucial assumptions need to be identified to provide a framework for approaching long-dead patients as if they arrived in a contemporary hospital. First, it will be assumed that all diseases acted in Alexander's day as they do today. Second, only a disease's typical symptoms, not its rare ones, will be considered admissible as evidence for the disease. Third, details will not be proposed beyond what the secondary histories provide. Fourth, this paper will assume that climatic conditions have not substantively changed since Alexander's day. Fifth, the world during the reign of Alexander will be considered to be geographically identical to that of today. Any of these assumptions can be overruled only if the most chronologically proximal (to Alexander) documentation that is reliable provides evidence to the contrary. These assumptions are almost inevitably inaccurate to some degree. Rivers move, lakes disappear, regions warm and cool, and pathogens constantly evolve in response to their environment. However, the assumptions are necessary. If variables are arbitrarily changed, a multitude of diseases can become possible without any evidentiary basis. Additionally, change is far from guaranteed; many infectious disease, for instance, demonstrate relatively little evolution (even on a genetic level) from the ancient world until the present day, as will be demonstrated in the infectious diseases examined herein.4

PATIENT HISTORY

"Alexander was born early in the month Hecatombaeon, the Macedonian name for which is Loüs, on the sixth day of the month" in the year 356 BC, according to Plutarch. He was an apparently healthy child with a ruddy complexion. Plutarch notes that the "temperature of his body...was a very warm and fiery one", possibly suggesting fever. However, the accuracy of this observation might be questioned as it formed the basis of a physiological explanation - using the four humours - for the pleasant aroma that exuded from the child. Maple Syrup Urine Disease - a genetically inherited enzyme deficiency - can cause infants to smell sweet. Alexander almost certainly did not have this disease. The condition almost uniformly results in severe neurological problems and death. If the reported smell is more than a literary device, there is a more plausible explanation. The body odour emitted by babies triggers a neural reward mechanism in mothers that emulates the reward mechanism produced by food, possibly causing the observer to liken an infant's odour to sweet-smelling bread.⁵

Plutarch provides a possible indication of a congenital spinal deformity - "the poise of the neck, which was bent slightly to the left." If accurate, it did not seriously limit the young Alexander. For instance, he tamed an intractable horse, was invited to compete in the Olympian games, and helped lead an army into battle at age sixteen. Alexander demonstrated an above average intelligence. Plutarch alleges that Aristotle educated Alexander in philosophy, metaphysics, ethics, politics, and medicine.6

Aside from the invitation to the Olympian games, Alexander displayed superior physical fitness throughout early adulthood, scaling a supposedly insurmountable cliff face with three hundred elite soldiers, ten percent of whom failed in the endeavour. He also personally led his troops up ladders into a besieged city, fighting off the enemy soldiers single-handedly for a time.7

Alexander received notable wounds on several occasions. At the battle of the Granicus in 334 BC, an enemy soldier struck a powerful blow with a scimitar or battle-axe to Alexander's helmeted head. He received another violent blow to his head and neck from a stone during the assault on Cyropolis in 329 BC. Another enemy hit Alexander's neck with a stone, resulting in a temporary blurring of vision. Arrows twice struck Alexander. The first, during the Parthian campaign of 331 BC, broke a bone in his lower leg and required surgery to have the bone fragments removed. The second instance occurred six years later in the battle at Malli. The arrow pierced Alexander's armour above the nipple and resulted in profuse blood loss and potential lung damage.8

Alexander once suffered a febrile illness that resulted in coma and temporary speech loss. He also experienced prolonged dehydration during his pursuit of Dareius and, far more severely, during the crossing of the Gedrosian desert. The geographical locations where Alexander received his wounds testify to his extensive travels throughout the Middle East and the western portion of India (using modern geographical terms).9

There is debate over the extent to which Alexander consumed alcohol. However, even accepting Plutarch's more

- PERRIN 1919; ZINNANTI/LAZOVIC 2012; LUNDSTRÖM et alii 2013
- PERRIN 1919
- BRUNT 1983; WELLS 1963
- BRUNT 1983; PERRIN 1919
- BRUNT 1983; PERRIN 1919

³ BOSWORTH 2008; APPLEBY et alii 2014

⁴ ROSEN 1995

moderate assessment of Alexander's drinking patterns, which on one occasion resulted in the death of a close friend, Alexander's alcohol consumption still would have fallen outside the limits of what current experts consider safe.¹⁰

The few surviving primary sources (e.g. inscriptions and coins) pertinent to Alexander the Great provide scant information. Reconstructions of Alexander's life derive primarily from the secondary literary sources that were written almost exclusively after his death. The credibility of these sources is briefly summarized in the following table, which gives the authors in approximate chronological order. $^{\! 11}$

HISTORIAN	DATE OF ACCOUNT	CREDIBILITY
	C	ONTEMPORARY WITH ALEXANDER
Deeds of Alexander by Callisthenes of Olynthus	329 BC	Callisthenes' unctuous account exists only in fragments and received criticism from Polybius – a Greek historian of the Second Century BC – for its amateurish military descriptions. In 327 BC, Alexander imprisoned Callisthenes for objecting to his leadership style. Shortly thereafter, Callisthenes either died in prison or was executed.
Onesicritus	c. 315 BC	Onesicritus accompanied Alexander for at least large portions of his exploits. His primary account is lost and is known exclusively through other ancient sources, which portray him as a liar who embellished his own importance.
Nearchus	c. 315 BC	The account of Nearchus, Alexander's fleet-commander, appears to begin in the latter half of Alexander's campaign, including India (a section that Arrian cites), the crossing of the Gedrosian, and his ocean voyage, which he glowingly relates. His account displays obvious disdain for Onesicritus and may have been written in response to him.
Cleitarchus	c. 310 BC	Cleitarchus' account forms the beginning of the romantic and rhetorical Alexander Vulgate and derives from Callisthenes as well as the memoirs of Onesicritus and Nearchus. Although lost itself, Cleitarchus's <i>History</i> is featured, potentially verbatim, in certain portions of Diodorus and Curtius Rufus's accounts.
Histories of Ptolemy I Soter	c. 305 BC	Ptolemy gives a highly accurate account based on his experience as one of Alexander's generals and on the <i>Ephemerides (Royal Ephemerides)</i> . Arrian relies heavily on Ptolemy for his <i>Anabasis</i> . Ptolemy's <i>Histories</i> survive by reconstruction, largely though Arrian. Some more modern scholars approach Ptolemy sceptically.
Aristobulus	c. 300 BC	Aristobulus accompanied Alexander on his conquests and gives versions of events that present Alexander in highly favourable terms, sometimes sycophantically so. Aristobulus' history is known primarily through quotes and citations from Arrian and Plutarch.
Ephippus	c. 320-300 BC	Ephippus, a contemporary and possible official of Alexander, is thought to be somewhat unreliable and speaks disdainfully of Alexander, attributing his death to over-drinking, among other critiques. Only some of his account exists in extant. Diodorus (among others) cites him.
	NON	I-CONTEMPORARY WITH ALEXANDER
Library of the History of the World History by Diodorus of Sicily	c. 50 BC	Diodorus bases his account of Alexander on that of Cleitarchus, to whom his reliability is thus married. He is not particularly critical of his sources. The account forms part of a larger history of how Mediterranean civilization came to be united under Rome – his audience.
The History of Alexander the Great by Quintus Curtius Rufus	Disputed – c. 50 or 75 AD	Curtius' account exists only in part. The account is written in a highly theatrical manner and, while highly readable, should be treated cautiously.
<i>Life of Alexander</i> by Plutarch of Chaeronea	First Century AD	Plutarch provides not a historical account but a biography of Alexander, designed to compare and contrast with that of Julius Caesar, and the information Plutarch presents needs to be treated accordingly. Plutarch often provides anecdotes that are unsubstantiated by other sources.
Anabasis of Alexander by Flavius Arrianus (Arrian)	c. 120-150 AD	Arrian himself proved an adept governor of Cappadocia and held a firm grasp of history, natural science, and ethnography, giving him a distinct competence. Arrian's <i>Anabasis</i> provides an excellent history of Alexander, critically cleaving the apocryphal and the authentic histories of his predecessors.
Epitome of the Philippic History of Pompeius Trogus by Marcus Justinus (Justin)	3rd C AD	Justin's history was written approximately six hundred tumultuous years after Alexander and is likely an abridged version of another account, featuring its most interesting aspects. It should be treated accordingly.

RETIEF/CILLIERS 2006; PERRIN 1919; DAWSON/GRANT/LI 2005

BOSWORTH 2008; PEARSON 1952; BENGSTON 1997; HAMMOND 1993

THE ACCOUNT OF ARRIAN

While in Ectbatana (a city in contemporary western Iran), Alexander received word that Hephaestion, whom he "valued equally with [his] own head," was dying after seven days of fever. Alexander hurried to Hephaestion but arrived too late. Alexander grieved deeply, refusing food and lying on the ground mourning for three days. He also dedicated a cavalry brigade in Hephaestion's honour and ordered a lavish funeral, complete with athletic games. Grief dominated Alexander for many more days before he was diverted to do battle in the winter (of 323 BC). Alexander then marched towards Babylon, receiving embassies from around the known world as he went.12

While on the way, Alexander was met by Chaldean philosophers who indicated that entering Babylon "at that time would not be for his good," citing an oracle of the god Belus. Alexander, suspecting that the Chaldeans' "courtesy" was inspired by self-interest, quoted the poet Euripides in response, "The best prophet is he that guesses well." Nevertheless, the Chaldeans did persuade Alexander to try leading his army through the east entrance and not the west. Owing to marshes and shoals that blocked his eastern approach, Alexander ultimately reassumed a western approach.13

In mid-spring, Alexander took a cruise through the swamps outside of Babylon, where his headdress was blown from his head into the water near the tombs of the Assyrian kings, supposedly an omen of what was to come. Upon re-entering the city, Alexander began planning two extravagant temples in honour of Hephaestion. Some days later, Alexander was at a drinking party and about to retire, when Medius, described by Arrian as "the most influential of the Companions [at that time]," invited him to continue the revelry at his house.14

It seems clinically useful to cite at length what Arrian presents as the most accurate account, in his view, which comes from the Royal Ephemerides. He says that this record is generally consistent with the accounts of Ptolemy and Aristobulus:15

[Day 1] He revelled and drank at the dwelling of Medius; then rose up, took a bath, and slept; then again supped at the house of Medius and again drank till far into the night. After retiring from the drinking party he took a bath; after which he took a little food and slept there, because he already felt feverish. [Day 2] He was carried out upon a couch to the sacrifices... After performing the sacred rites he lay down in the banqueting hall until dusk. In the meantime he gave instructions to the officers about the expedition and voyage, ordering those who were going on foot to be ready on the fourth day, and those who were going to sail with him to be ready to sail on the fifth day. From this place he was carried upon the couch to the river, where he embarked in a boat and sailed across the river to the park. There he again took a bath and went to rest. [Day 3]... he took another bath and offered the customary sacrifices. He then entered a tester bed, lay down, and chatted with Medius. He also ordered his

officers to meet him at daybreak. Having done this he ate a little supper and was again conveyed into the tester bed. The fever now raged the whole night without intermission. [Day 4]... He took a bath; after which he offered sacrifice, and gave orders to Nearchus and the other officers that the voyage should begin on the third day. [Day 5]... He bathed again and offered the prescribed sacrifices. After performing the sacred rites, he did not yet cease to suffer from the fever. Notwithstanding this, he summoned the officers and gave them instructions to have all things ready for the starting of the fleet. In the evening he took a bath, after which he was very ill. [Day 6]...He was transferred to the house near the swimming-bath... Though he was now very dangerously ill, he summoned the most responsible of his officers and gave them fresh instructions about the voyage. [Day 7]... he was with difficulty carried out to the sacrifices, which he offered; and nonetheless gave other orders to the officers about the voyage. [Day 8]... Though he was now very ill, he offered the prescribed sacrifices. He now gave orders that the generals should remain in attendance in the hall, and that the colonels and captains should remain before the gates. But being now altogether in a dangerous state, he was conveyed from the park into the palace. When his officers entered the room, he knew them indeed, but could no longer utter a word... During the ensuing night and day [Day 9] and the next night and day [Day 10] he was in a very high fever... It is said that when his soldiers passed by him he was unable to speak; yet he greeted each of them with his right hand, raising his head with difficulty and making a sign with his eyes...soon after Alexander died.

Arrian then acknowledges, but dismisses for lack of credence, what he considered a theory of regicide. In this plot, Antipater - the regent of Greece and whose position was in question – acquired a poison from Aristotle. Antipater gave the poison to his son Cassander, who conveyed it to his younger brother Iolaus, Alexander's cup-bearer. Medius, being the one who invited Alexander to drink, was also alleged to be involved. Arrian also repudiates a story in which Alexander attempted to drown himself in the Euphrates after realizing that death was upon him but was restrained by his wife.16

THE ACCOUNT OF PLUTARCH

In Ecbatana, Hephaestion contracted a fever, to which he succumbed after failing to listen to the advice of his physician. Alexander's grief upon hearing of his friend's death "knew no bounds." Alexander proceeded to crucify the physician, ordered the cessation of music, sheared the tail of all horses and mules, and removed the battlements of neighbouring cities. Then, to alleviate his suffering, he went to war against a nation, slaughtered every male from youth upwards, and spent 10,000 talents on Hephaestion's tomb and funeral.17

As Alexander neared Babylon, his admiral Nearchus informed him that Chaldean sorcerers counselled against entering the city, to which Alexander paid no heed. Arriving at the walls, Alexander noticed a flock of ravens clawing at each other above him. Several of the birds fell dead at his feet.

¹² BRUNT 1983

¹³ BRUNT 1983

¹⁴ BRUNT 1983

¹⁵ BRUNT 1983

¹⁶ BRUNT 1983

¹⁷ PERRIN 1919

Shaken by what he interpreted to be a bad omen, Alexander refused to enter the city and camped outside, spending his time in his tent, engaging in athletics, and sailing on the Euphrates.¹⁸

The numerous omens [the clinically irrelevant ones have been omitted from this summary] made Alexander exceedingly sensitive to the divine, paranoid, and suspicious of his friends, particularly Antipater and his sons. Alexander even violently assaulted Cassander.¹⁹

Alexander, persuaded by an earlier oracle that advised celebrations and sacrifices in Hephaestion's name, began feasting and drinking. After one evening of entertainment, he acquiesced to the supplications of Medius to continue the revelry at his house. After a day of drinking at Medius', he began to have a fever. Plutarch, citing Aristobulus, says that as the fever intensified Alexander consumed more wine to assuage his thirst, became delirious, and died. Plutarch goes on to provide a nearly identical version of the Royal Ephemerides entries quoted by Arrian.²⁰

Some accounts, according to Plutarch, alleged that Alexander fell ill while drinking a "bowl of Heracles" and that Alexander felt pain as though he were stuck in the back by a spear. Plutarch contends that these were invented theatrically to adorn the story. Plutarch reports that accusations of poison did not emerge for five years, when Alexander's mother, Olympias, "put many men to death, and scattered abroad the ashes of Iolaus, alleging that Iolaus had administered the poison." Plutarch relates the conspiracy as follows: Aristotle counselled Antipater to regicide; the ice cold droplets of poison water were collected from a waterfall in Nonacris and stored in an ass' hoof - the only container capable of holding water of such "coldness and pungency". Plutarch notes that most writers dismiss the poison theory. He himself strongly repudiates it on the basis that "[Alexander's] body, although it lay without special care in places that were moist and stifling [for many days], showed no sign of such a destructive influence, but remained pure and fresh."21

THE ACCOUNT OF DIODORUS

Chaldean astrologers communicated to Alexander through Nearchus that only by avoiding Babylon and rebuilding the temple of Belus (destroyed by the Persians) will he avoid imminent death. Although initially concerned, philosophers assuaged Alexander's fears. He entered the city and where he conducted numerous diplomatic meetings with various foreign emissaries. Alexander also held a funeral for Hephaestion - his dearest friend and adviser (and perhaps sexual partner) - who had recently suffered a sudden death from fever. He began preparation to deify Hephaestion and erect a colossal and costly monument in his honour. Shortly thereafter, while on a boat tour of the great swamp of Babylon, Alexander's diadem was caught from his head by a reed, causing the king great concern as to the event's meaning. Before he could alleviate his concern with sacrifice, he was summoned to engage in a comus, a festival involving

18 PERRIN 1919

alcohol consumption to the point of collapse. As Alexander drank a huge beaker of unmixed wine, he suddenly "shrieked aloud as if smitten by a violent blow" and was hastily led by the hand to his chamber. The abdominal pain grew more acute; the physicians were unable to bring relief. Alexander, realizing that death was upon him, took off his ring, declared that "the strongest" should have his empire, and died. Diodorus adds that some historians hold that it was poison, insinuating that Alexander's death resulted from the alcohol consumption itself.22

THE ACCOUNT OF JUSTIN

The course of events leading up to Alexander's arrival at Babylon closely resembles that presented by Diodorus. From the perspective of medical evidence, the only critical difference seems to be the omission of the boat cruise.

Upon entering the city, Alexander gave himself to entertainment and incessant drinking. While returning from one banquet, Medius - a friend - invited Alexander and his attendants to continue their revelry at his home. Alexander acquiesced. In mid-drink Alexander uttered groans "as if he had been stabbed with a dagger" and was carried away "halfdead" from the table. Alexander was "excruciated with such torture that he called for a sword to put an end to it, and felt pain at the touch of his attendants as if he were all over wounds." Four days later, Alexander perceived his pending death, allowed his soldiers to bid farewell, gave burial instructions to his generals, and bequeathed his kingdom to "the most worthy." On day six, Alexander lost the ability to speak and gave his ring to Perdiccas, one of his generals. Justin then proceeds to eulogize about Alexander but does not provide the day of his demise, which Justin claims was caused by poison, though alleged by the conspirators to be from drink.23

THE ACCOUNT OF QUINTUS CURTIUS RUFUS

A significant portion of Curtius' Chapter Ten has been lost. The preserved section begins as Alexander's soldiers visit him as he lay dying.

Alexander assumed an alert posture in his bed as the entire mourning army filed past and saluted him. Alexander asked, "After my death will you find a king who deserves such men?" After the soldiers had left, Alexander collapsed. His voice growing weak, he gave his ring to Perdiccas, conveyed his kingdom "to the most worthy," and with his dying words asked that he only be paid divine honours "when they themselves [his friends] were happy." Alexander died moments later.24

Curtius asserts that many believed that Alexander died of poison, slipped into his drink by Iolaus, the son of Antipater, a general. The poison was supposed to have been concocted in Macedonia from the "Styx". The poison was said to be capable of consuming iron and only "an ass' hoof" could carry it. Curtius explains that the weight and credence of this account was lost amidst gossip as Antipater assumed the throne of Macedon and Greece and murdered all of

¹⁹ PERRIN 1919

²⁰ PERRIN 1919

²¹ PERRIN 1919

²² WELLS 1963

²³ YARDLEY 1997

²⁴ ROLFE 1946

Alexander's even distant relatives.²⁵

HISTORICAL ANALYSIS OF THE ACCOUNTS

Until the mid 1950s, historical scholarship viewed the 'Court' tradition of Alexander's natural death to be unimpeachable. Since then, a number of scholars have contended for the verisimilitude of the 'Vulgate' poisoning account, perhaps none better than Bosworth.²⁶

Many empires have employed propaganda to camouflage events that give an unfavourable veneer (e.g. Soviet Russia). The rulers who succeeded Alexander were likely no different. Propaganda becomes difficult to discern from truth in secondary accounts. Modern scholars know Alexander almost exclusively through sources that date 300 or more years after his death.

Within a year of his death, rumours of conspiracy had already emerged. All five of the secondary sources agree upon their existence and there is no argument about the general nature of alleged conspiracy, as already presented. Alexander's symptoms almost assuredly saw their onset at Medius' house, as sources on both sides of the poison theory claim that Alexander fell ill there. The differences centre on what happened at Medius' house.²⁷

Antipater had a motive for instigating the killing. He had begun to fall out of favour with Alexander and potentially stood to lose his position, if not his life. Though not sufficient to convict, a motive is certainly necessary. The other members of Alexander's inner circle may also have begun to harbour ill-will against their regent and his growing megalomania, demonstrated by his superfluous funeral arrangements for Hephaestion and almost addictive inclination towards conquest, manifesting in plans for a virgin western campaign. Epheppus states that Alexander assumed the guise of the god Ammon at banquets, dressing with purple robes and a horned headdress - a detail corroborated by coinage and the Alexander Sarcophagus. Alexander also seemed to associate himself with the persona of other gods and had incense burned to his deity. The accounts provide information to suggest that Antipater capitalized on the growing dissent and went on the offensive to protect his position. Antipater, Bosworth argues, recognized patterns in Alexander's behaviour that foreshadowed earlier purges of officials. Hence, he sent his son Cassander to broker an arrangement of power among the generals, who would be executed after Alexander's death. Cassander then supplied his brother, Iolaus the cupbearer, with the necessary means to enact the scheme. Conspiracy would explain why peace reigned for an unexpectedly long period after the death of a ruler with no ready heir. It would have been relatively easy to manipulate documents to hide the conspiracy; and once the tenuous truce broke among the all-too-human generals, it would have been equally easy to spread incriminating evidence against a rival faction. Notwithstanding, it is important to recognize that the Vulgate accounts of Alexander's death were propagated extensively by the mother of Alexander, Olympias, who viewed Antipater and his sons as the murderers. One might question the objectivity of

Olympias, who was not a witness and whose maternal desire for justice may have clouded her reason. If Alexander's death was natural, fortune shone brightly upon the arguably overextended army and Antipater's family.28

MEDICAL ANALYSIS OF THE VULGATE NARRATIVE

Several basic assumptions can be made based upon the contents of the Vulgate accounts. First, if there was something abnormal about Alexander's wine, he is not recorded as having tasted it. He made no comments to this effect at Medius' house or in the following (at minimum four) days when he was still lucid and capable of speech. Accordingly, the poison was likely completely or almost completely tasteless. Second, the conspirators would have required knowledge of the poison - the poisonous nerveagent sarin, for instance, synthesized in 1938 AD, is not a possibility. Third, the poison needed to have been relatively available to the conspirators. Fourth, the method of administration needed to have been discrete, regardless of whether it was in the wine. No one saw it administered.25

Diodorus' intimation is unlikely to be true, based on his account. The classic symptoms of alcohol intoxication are slurred speech, nystagmus (involuntary eye movement), impaired judgement, incoordination, unsteady gait, memory impairment, stupor, or coma - not sudden pain. Moreover, because intoxicated patients will likely be oblivious to the pain accompanying abdominal injuries, the medical literature recommends that physicians conduct assessment for such injuries. Alcoholic ketoacidosis may cause abdominal pain. However, this condition requires the patient to be malnourished, which seems highly unlikely for a young, fit, and apparently healthy ruler of the known world. According to Diodorus' account, non-alcoholic poison is more likely.30

Forensically, there are three obvious objections to Curtius' "Styx" poison theory. First, if the chemical (likely an acid or strong base) was powerful enough to erode steel readily, Alexander should have noticed, particularly as he is said to have been lucid until at least the fourth day after the incident. Second, Alexander is unlikely to have been able to speak four days after consuming the poison if he was exposed to a powerful corrosive. Third, while conspirators might have taken steps to cover up and suppress the evidence, a corrosive poison would likely damage the cup from which Alexander was drinking. He probably dropped, or at least spilled, the cup when he was seized by pain. The fabrics and flooring upon which the wine fell would assuredly have been stained (burned?) in ways uncharacteristic of wine. The historians record no such observations.

Notwithstanding, Mayor, a Stanford folklorist and science historian, and Hayes, a toxicologist, sought to identify the poison residing in the Styx – a waterfall in north central Peloponnese, Greece. According to their research, individuals - ranging from ancient scholars to locals in 1920s - held that the water from the Styx destroys clay and metal vessels and refused to drink from it. However, sporadic

ROLFE 1946

²⁶ BOSWORTH 2008; BOSWORTH 1971

²⁷ BOSWORTH 1971

BOSWORTH 1971; HAMILTON 1953; BOSWORTH 2008

²⁹ VISWANATH/GHOSH 2009; SCHEP/SLAUGHTER/VALE/ WHEATLEY 2014

³⁰ YOST 2002; ALLISON/MCCURDY 2014

chemical analyses starting in 1815 AD failed to identify any irregularities. Mayor and Hayes note that while ancient mining techniques might have released lethal minerals such as arsenic, zinc, cadmium, and selenium, they found no evidence of local mining in antiquity. Mayor and Hayes thus propose that a natural source was responsible.31

Mayor and Hayes dismiss the highly corrosive but rare hydrofluoric acid. It has been known to naturally rise to lethal levels only as the result of volcanic activity, which is incongruous with the area's geology. Perhaps a superior refutation lies in the fact that hydrofluoric acid results in serious, deep local burns and critical circulatory and vascular problems - even when exposure is relatively limited and topical. Alexander exhibited no burns.³²

Mayor and Hayes, inspired by accounts of "black water" at the Styx, propose that the stream might have had a significant amount of dissolved organic matter that could culture "soil-derived bacterium of exceptional lethality." They settled upon the relatively recently discovered Micromonospora echinospora, which resides in limestonederived caliche and produces the secondary metabolite calicheamicin – a substance more toxic than ricin. According to Sheridan et al., the massive organ damage caused by the poison would cause symptoms resembling those of Alexander - weakness and fatigue, swelling of mouth and throat, severe pain, and fever.

However, calicheamicin, which is used as a chemotherapeutic, acts by causing irreparable double-strand breaks in DNA. Poisons that damage DNA, as opposed to those like botulinum toxin that target neuromuscular communication, are relatively slow acting. They work by impairing protein production and cell division. The cell will die after it no longer possesses the proteins required to maintain life. If too few cells can replicate to repair the damage in an organized manner, organs fail. If Alexander died of calicheamicin, it would have required administration well before Alexander emptied Heracles' cup at the house of Medius. Moreover, Mayor and Hayes only find matches for the symptoms of calicheamicin by an ostensibly arbitrary synthesis of the accounts of Alexander's demise (e.g. fever does not appear in the Vulgate accounts of Diodorus, Curtius, or Justin). Such a synthesis might have merit, but it needs justification.33

The corrosive properties of the Styx might merely be a hyperbolic adornment in keeping with the rest of Curtius's history of Alexander. It should be noted, however, that calicheamicin requires no special storage and should merely be handled in accordance with standard industrial hygiene protocols. It is not even structurally stable in highly acidic or basic environments. Finally, the apparently recent discovery of calicheamicin suggests that it is an implausible contrivance for a nearly 2500-year-old regicide.34

Milns proposes strychnine poisoning. Theophrastus - a philosopher, botanist, and contemporary of Alexander - described the substance in his *Enquiry into Plants*. One publication notes, however, that unlike the reported timeframe of Alexander's death, a typical lethal dose of strychnine will kill its victim within three to five hours. An acute non-lethal dose administered repeatedly, as Milns suggests, is also impossible, as this would induce muscle fasciculation, difficulty walking, mild to moderate muscle spasms along the spine, and tremors. The accounts of Alexander's death only suggest that he had difficulty walking without help.35

Aconite and hemlock, plant-derived poisons available in the Fourth Century BC, were ruled out because death results rapidly. The symptoms also do not match Alexander's: aconite induces gastrointestinal, cardiac, and neurological problems (e.g. nausea, heart arrhythmias, and numbness); hemlock triggers a dramatic parasympathetic response (e.g. salivation and respiratory paralysis). Schlep et al. also dismiss oil of wormwood, another ancient plant derivative, because Alexander did not suffer delirium, mania, and visual disturbances. Schlep et al. eliminate colchicine, contained Colchicum autumnale. Its typical gastroenteritis-like symptoms only begin to appear after ten hours. Severe symptoms emerge after seven days. Once significant symptoms appear, death results from sepsis and organ failure within thirty-six hours. Arsenic is dismissed because its central features - diarrhoea, vomiting, and intestinal perforation - do not correspond to Alexander's symptoms.³⁶

Veratrum album (false hellebore) poisoning appears plausible given this paper's assumptions, Alexander's symptoms, and the progression of the illness. Alexander's contemporaries knew of Veratrum album. Theophrastus documents the plant and its effects in his Enquiry into Plants. It was readily available, growing in alpine pastures in Europe and Western Asia. The plant contains alkaloids that can be easily extracted with alcohol during fermentation. Administration would have been virtually undetectable – the poison existing in an alcohol solution. Moreover, its taste would likely have escaped Alexander's notice, especially if he was slightly intoxicated. Accidental consumption in food and alcoholic beverages has been repeatedly documented.³⁷

The poison binds to the type-2 sodium voltagegated channels of nerves, increasing permeability to sodium and calcium and delaying depolarization along the neuronal axon. Neuromuscular communication becomes uncoordinated. Victims will likely experience sudden epigastric and substernal pain and vomiting fifteen minutes after ingestion. Excepting the vomiting (which may fail to present), this corresponds to what Alexander suffered before he finished his wine. Slow heart rate, low blood pressure, and pronounced muscular weakness soon follow. This could explain why Alexander's required assistance to reach his chamber. With modern medical treatment, patients rarely deteriorate further. However, if untreated, further symptoms generally emerge over the next week or two, including an inability to move or communicate, coma, and death. This would be especially true if additional doses were administered. Alexander's case bore many of these features:

MAYOR/HAYES 2011

³² MAYOR/HAYES 2011; SHERIDAN et alii 1995

³³ LODE et alii 1998

³⁴ PFIZER 2011; LODE et alii 1998

MAYOR/HAYES 2011; HORT 1916; SCHEP/SLAUGHTER/VALE/ WHEATLEY 2014; MILNS 1968

SCHEP/SLAUGHTER/VALE/WHEATLEY 2014

³⁷ SCHEP/SLAUGHTER/VALE/WHEATLEY 2014; HORT 1916; SCHEP/ SCHMIERER/FOUNTAIN 2006; ZAGLER et alii 2005; GILOTTA/BRVAR

silently saluting his troops from bed, gradual weakening and loss of speech, coma, and death within days (assuming Bosworth's synthesis of the accounts).38

The absence of nausea and vomiting, which are generally noted symptoms, does diminish the possibility of Veratrum album poisoning. The inability of Veratrum album to guarantee death also creates a practical objection. If Antipater wanted to kill Alexander, he may have opted for a poison that assured Alexander's demise and alleviated his tenuous situation. Conversely, by sharing the attributes of an illness, Veratrum album would have provided deniability for Antipater should Alexander survive. Furthermore, extra doses could be easily administered. Finally, Theophrastus describes in his Enquiry into Plants how an individual could build up tolerance to Veratrum album. Researchers also noted increasing drug tolerance when Veratrum alkaloids were investigated as a treatment for high blood pressure circa 1950. If Iolaus followed Theophrastus' instructions, he may have been able to sample the wine and prove its 'safety'.39

The long time course of Veratrum album poisoning presents a textual problem. It requires that Alexander's conspirators edited the Court Ephemerides to avert accusations of poison but left the length of Alexander's illness as it actually happened. A slow death might have been the best scrap of truth to leave intact. Most poisons kill quickly.

MEDICAL ANALYSIS OF THE COURT TRADITION

The court tradition holds that Alexander's final illness resulted from natural causes. Ashrafian notes that statues and coins of Alexander – some of the only surviving primary witnesses of Alexander - portray him with horns and a slight leftward tilt of the head. He believes that these features testify to congenital scoliosis or epidermal nevus syndrome and that Alexander died of associated organ pathologies.⁴⁰

This hypothesis is highly problematic. The articles that Ashrafian cites as evidence for pathologies arising from congenital scoliosis describe patients dramatically more incapacitated than Alexander could possibly have been. Alexander died after having just completed a harrowing westward march from India to Babylon on foot and horseback without displaying extraordinary discomfort or difficulty (excluding thirst and hunger). If Alexander's spine was seriously compromised by neurofibrosis, the Gedrosian desert or the recent hand-to-hand combat at the battle of Malli would surely have eliminated Alexander. 41

Epidermal nevus syndrome and its related cardiopulmonary and neurological problems seem equally unlikely. In patients with chronic renal failure, proper hydration is critical. If Alexander's kidneys and/or circulatory system were so compromised as to immobilize him for ten days until his death, they would likely have been problematic in the Gedrosian, where Alexander was regularly dehydrated and over-exerted.42

Finally, the theory's premise relies on a questionable

interpretation of the primary artefacts. As Russell notes, figures in classical art regularly feature a head-tilt. If they were not stylistic but instead meant to depict actual physical features, there was an epidemic of spinal problems that preferentially targeted athletes, poets, and even Apollo. The horns on Alexander's head on coins were almost certainly used to deify him. By Ashrafian's logic, Christian saints, frequently depicted in works of art with halos and floating crowns of stars, suffered from head trauma and concussions. With the exception of St. Stephen, this seems rather dubious.43

If an environmental contaminant (such as lead, which the ancient Romans and Greeks used to coat wine vessels) had poisoned Alexander, the dose would have needed to be acute given the sudden onset. Other individuals should have exhibited symptoms. This was not reported. Additionally, Alexander's fever makes lead poisoning in particular unlikely.44

Marr and Calisher propose West Nile virus (WNV). Alexander's symptoms resemble those of WNV: abrupt onset of fever, headache, malaise, back pain, muscle pain, and a lack of appetite. Severe muscle weakness and change in consciousness typically precede death in WNV. The accounts describe a similar deterioration in Alexander. In an outbreak in Ontario, Canada, 40% of deaths occurred within 30 days of onset. If Alexander had contracted WNV, his recorded death ten days after clinical onset is reasonable, especially since he did not receive modern supportive care. It should be noted, though, that Alexander was almost thirty-three, whereas the median age of death from WNV is seventy-two.⁴⁵

WNV was first detected in humans in 1937 in Uganda and samples of human sera from modern Iraq (which includes ancient Babylon) have tested positive for WNV antibodies. As Marr and Calisher suggest, discovering the disease in 1937 does not preclude its prior existence in humans. However, since birds are the natural reservoir for WNV, the virus could have spread broadly without the aid of globalization. The relatively rapid expansion of WNV out of Africa after 1937 seems to indicate a non-ancient genesis. 46

In subtropical climates, such as modern Iraq, human infections generally occur in summer or early fall. Seasonal cases in Israel, which has a similar climate and the same latitude as Iraq, typically start appearing in humans in August. Marr and Calisher note that this militates against the WNV hypothesis since Alexander became sick in late May. The Marr and Calisher suggest that summer may have come sooner in Babylon in Alexander's era. This contests our assumption that climatic variables cannot arbitrarily be changed. Moreover, a study of harvest records in the Neo-Babylonian Period indicates the opposite: the Babylonian climate was cooler than in the present day and summer came 10-20 days later. The authors cite Plutarch for possible avian cases of WNV in the Fourth Century BC: "When [Alexander]

³⁸ SCHEP/SCHMIERER/FOUNTAIN 2006; SCHEP/SLAUGHTER/VALE/ WHEATLEY 2014

³⁹ HORT 1916; FREIS/STANTON 1948

⁴⁰ ASHRAFIAN 2004

⁴¹ CRAIG/GOVENDER 1992; BRUNT 1983; PERRIN 1919

⁴² LIGTENBERG 1999; BRUNT 1983

RUSSELL 2004; BOSWORTH 2008; St. Stephen

WALDRON 1973; OLDACH/RICHARD/BORZA/BENITEZ 1998; **NEEDLEMAN 2004**

⁴⁵ ORTON/STRAMER/DODD 2006; MARR/CALISHER 2003; PETERSEN/MARFIN 2002; PEPPERELL et alii 2003; MARR/CALISHER

⁴⁶ HUBÁLEK/HALOUZKA 1999; CAMPBELL/MARFIN/LANCIOTTI/ GUBLER 2002; MARR/CALISHER 2003

arrived at the walls [of Babylon], he saw many ravens flying about and clawing one another, and some of them fell dead at his feet." If this is not an added literary device, "clawing" seems to be a more likely explanation for the ravens' deaths. Given the epidemiological evidence, Alexander almost certainly did not die of WNV.47

Williams and Arnott propose that a carotid dissection killed Alexander. A carotid dissection occurs when blood separates the inner and outer layers of a blood vessel, occluding the vessel. More seriously, a blood clot may form in a relatively unimportant vessel, break off, and travel to the brain, where it can block key vessels. Carotid dissections are often caused by trauma to a blood vessel. The authors argue that the blow to the neck that Alexander suffered at Cyropolis in 329 BC may have resulted in a carotid dissection. They hold that Alexander's loss of speech and coma before death support this possibility.⁴⁸

However, this fails to explain any of the remaining symptoms in both the Court and Vulgate narratives. Loss of speech and coma can be ascribed to multiple fatal conditions. Furthermore, Alexander did not present with the most common symptom of the pathology, head and neck pain on one side of the body. The probability of sequelae of a carotid dissection appearing six years after Alexander's neck trauma is also exceptionally unlikely.⁴⁹

Some have focused on Alexander's drinking habits. Plutarch defensively maintains that the young Alexander, "[I]n spite of his vehement and impulsive nature, showed little interest in the pleasures of the senses and indulged in them only with great moderation," and publicly despised his father's drinking habits. However, it has recently been pointed out that exposure to parental substance use disorder (SUD) during adolescence increases the odds of developing SUD by 3.61 times. In his mid-twenties Alexander appears to have adopted his father's habits. Curtius reports that Alexander's attributes "were marred by his inexcusable fondness for drink." This cannot simply be attributed to Curtius' theatrical style. The fastidious Arrian - while defending Alexander's alcohol-induced murder of Clitus remarks, "On that occasion he showed himself the slave of two vices, anger and drunkenness." Liappas et al. has lately advanced a thorough clinical case for Alexander's alcohol abuse. But Alexander was unlikely at thirty-two to suffer from alcoholic liver disease, although alcohol abuse may have suppressed his immune system and made him vulnerable to infections.50

Alexander almost certainly did not die of alcohol poisoning. Acute alcohol poisoning happens over a period of hours, with a gradual loss of psychomotor and cognitive capacities and mood variations until consciousness is lost. Vomiting and nausea often emerge as an individual's bloodalcohol concentration increases. Diodorus and Justin - who allege that Alexander's problem manifested during Medius' party - claim that the problem presented as a sudden, sharp

pain. Plutarch and Arrian say that Alexander became ill with fever the day after the party. Neither fever nor late onset accords with alcohol poisoning.51

The Vulgate tradition has been the focus of three hypotheses that do not require the hand of an assassin acute pancreatitis, perforated peptic ulcer, and spontaneous perforation of the oesophagus. Chronic alcohol abuse accounts for 30% of acute pancreatitis cases; 5% of alcohol abusers will suffer from acute pancreatitis. In severe acute alcoholic pancreatitis, alcohol - working through an undefined mechanism with another initiating factor – causes a build-up of digestive enzymes in the pancreas. This often results in the pancreas digesting itself, necrosis, multi-organ failure, sepsis, and death.52

Acute pancreatitis typically presents with epigastric abdominal pain and fever. Sepsis often follows and accounts for 80% of deaths in severe acute pancreatitis. Severe sepsis is characterized by organ dysfunction, bacterial infection, and the presence of two of four criteria, of which only a fast heart rate, fever, and rapid breathing would have been detectable in Alexander's day. The remaining surgical events perforated peptic ulcer and oesophageal perforation feature similar symptoms and may result in sepsis, but are only weakly associated with the apparent causative agent alcohol - and thus contest our second assumption that rare aetiologies and symptoms will not be admitted.53

According to Diodorus and Justin, Alexander presented with pancreatitis' characteristic epigastric pains. The gradually worsening fever, weakness, ultimately diminished mental capacity, coma, and death are consistent with sepsis. Finally, as the author of the pancreatitis theory notes, the ten-day course of Alexander's illness is consistent with acute pancreatitis.54

The theory's plausibility, however, loses some of its force by the fact that abdominal pain in alcohol-induced pancreatitis has a more gradual onset than in other pancreatitis aetiologies - unlike the "dagger stab" or "sudden blow" reported by Diodorus and Justin respectively. The theory also requires a plausible synthesis of the narratives of Diodorus and Justin (who describe the abdominal pain) with those of Plutarch and Arrian (who describe the fever and detail Alexander's deterioration).55

Several studies point to Anopheles mosquitoes as Alexander's 'murderers.' Malaria, the feared payload of the Anopheles, possesses an instinctive appeal. It plagued much of the ancient world. Babylon bordered a swamp, a favourite breeding ground of mosquitoes, which Alexander toured. A recent analysis of teeth from Imperial Period cemeteries in Italy demonstrate that the deadly Plasmodium falciparum strain of malaria likely claimed thousands of lives. With complications, untreated malaria may kill in less than two weeks. Furthermore, malaria is the clinical assumption if someone presents with fever in a malarial area. However, fever and fatigue are almost the only clinical features that

CAMPBELL/MARFIN/LANCIOTTI/GUBLER 2002; MARR/CALISHER 2003; NEUMANN/SIGRIST 1978; PERRIN 1919

⁴⁸ WILLIAMS/ARNOTT 2004

⁴⁹ BOUSSER 2004

⁵⁰ PERRIN 1919; YULE et alii 2013; ROLFE 1946; BRUNT 1983; LIAPPAS/ LASCARATOS/FAFOUTI/CHRISTODOULOU 2003; NAVEAU et alii 2005; PAULA et alii 2010; ROMEO et alii 2007

KRESHAK 2012

⁵² BATTERSBY 2007; YANG/VADHAVKAR/SINGH/OMARY 2008; LANKISCH/APTE/BANKS 2015

⁵³ BATTERSBY 2007; VONLAUFEN/SPAHR/APTE/FROSSARD 2014; FELNER/SMITH 2012

⁵⁴ BATTERSBY 2007

⁵⁵ LANKISCH/BANKS 1998

align with malaria in the accounts of Alexander's death. The headaches, violent bursts of emotion caused by fever, and sweats typical of malaria were not present. Thus, while possible, malaria is not the most likely cause of death.⁵⁶

Typhoid fever provides an ostensibly superior reckoning of the febrile pattern. It features a gradually worsening fever without sweats. Propagated by poor hygienic practices, typhoid has been the scourge of many armies throughout history and DNA evidence from dental pulp suggests that it was responsible for the Fifth Century BC Plague of Athens. Abdominal pain may also appear, though not until the second week of infection. However, typhoid rarely claims its victims in less than three weeks. Alexander died within ten days of the illness' onset. Additionally, the Court accounts do not allude to gastrointestinal symptoms or headaches, which often present as typhoid progresses. If Alexander did experience abdominal pain, Diodorus and Justin state that it occurred from the onset.⁵⁷

CONCLUSION

We shall probably never know with absolute confidence how Alexander the Great died. Yet based on the accounts of his last days, we can eliminate most of the proposed hypotheses with reasonable confidence.

Lethal poisons are particularly conducive for evaluation. Options for poisoning in antiquity were relatively limited compared to today. Even fewer of the available poisons could produce the course of Alexander's symptoms. Veratrum album, the near tasteless plant poison extracted by an alcohol solution, seems the most plausible. It aligns with Alexander's symptoms, was known in antiquity, was likely available to the conspirators, could be gradually re-administered in wine to give the appearance of illness, and might even be consumed by Alexander's cupbearer and alleged poisoner Iolaus if he had built up tolerance to the drug.

If Alexander died of natural causes, determining the precise pathology proves a more difficult challenge. Unlike intentionally administered poison, Alexander's contemporaries did not need to know of the disease for it to kill. We, as his modern coroners, do not stand in a vastly more enlightened position. He may have died of an infection that has since mutated into passivity, as did the devastating Spanish Flu of 1918. One cannot even begin to speculate about such infections.58

None of the proposed infectious diseases - as they exist today - align well with the course of Alexander's illness. Acute pancreatitis, a non-infectious pathology, which is unlikely to have changed dramatically since the days of Alexander's conquest, fits remarkably well with the accounts of Alexander's death. The chief argument against this hypothesis is that it requires an onset described in the Vulgate tradition but a disease course described in the Court tradition. There is a plausible way of reconciling the two. Alexander's sudden pain while consuming wine, as described in the Vulgate tradition, would have given any witness ⁵⁶ CUNHA 2004; SVENSON/MACLEAN/GYORKOS/KEYSTONE 1995;

MARCINIAK et alii 2016

CUNHA 2004; HOFFMAN et alii 1984; PAPAGRIGORAKIS/ YAPIJAKIS/SYNODINOS/BAZIOTOPOULOU-VALAVANI 2006

CHANDRA/KASSENS-NOOR 2014

the immediate impression of poisoning. Consequently, if someone had modified the Court Ephemerides, as Bosworth proposes, they may have done so to avert questions, realizing that an innocent conscience is a poor counter-argument to any vigilantes who recognized their motive and opportunity. Bosworth himself alludes to the possibility that Eumenes, one of Alexander's generals who attended the ill-fated banquet, may have done just this. Diodorus may correctly conclude that Alexander died of drink, albeit through a different pathological mechanism. However, time has likely claimed any confident diagnosis as it claimed what remained of Alexander.59

If anything in the ultimate sense is worth remembering about the tracing of Alexander's death, it is the words of Prince Hamlet: "Why may not imagination trace the noble dust of / Alexander, till he find it stopping a bung-hole?" (5.1.210-211) ... "O, that that earth, which kept the world in awe / Should patch a wall t' expel the [winter's] flaw!" (5.1.222-223)60

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