



Review

Familial epilepsy in the pharaohs of ancient Egypt's eighteenth dynasty

Hutan Ashrafian*

The Department of Surgery and Cancer, Imperial College London at St. Mary's Hospital Campus, London, UK

ARTICLE INFO

Article history:

Received 1 May 2012

Revised 6 June 2012

Accepted 9 June 2012

Available online 16 August 2012

Keywords:

Familial

Temporal

Lobe

Epilepsy

Pharaohs

Religiosity

Akhenaten

Tutankhamun

ABSTRACT

The pharaohs of Egypt's famous eighteenth dynasty all died early of unknown causes. This paper comprehensively reviews and analyses the medical literature and current evidence available for the New Kingdom rulers – Tuthmosis IV, Amenhotep III, Akhenaten, Smenkhkare and Tutankhamun. The integration of these sources reveals that the eighteenth dynasty rulers may have suffered from an inherited condition that may explain their untimely deaths. The description of recurring strong religious visions, likely neurological disease and gynecomastia, supports the theory that these pharaohs may have suffered from a familial temporal epilepsy syndrome that ultimately led to their early downfall.

© 2012 Elsevier Inc. All rights reserved.

1. Introduction

The pharaohs of the mid-to-late eighteenth (XVIIIth) dynasty have become among the most famous rulers of the ancient world [1]. These kings ruled their empire at a time of massive socio-political and cultural upheaval, yet died prematurely. It follows therefore that physicians, archeologists and historians have pursued explanations for why these rulers died so young. This has led to thousands of publications and hundreds of theories of death amassed over 150 years. In order to collate and assess the medical evidence regarding these pharaohs, I performed a systematic search of the medical and historical literature from the 19th century onwards on the death and disease of the late XVIIIth dynasty kings. The pharaohs included Tuthmosis IV, Amenhotep III, Akhenaten, Smenkhkare and Tutankhamun (Fig. 1). These individuals were chosen as they are all related to one another, albeit in a complex fashion. They all have a varying degree of unusual artistic representation, with the latter three being subject to an untimely mortality.

2. Tuthmosis IV

One of the least well documented of the pharaohs, Tuthmosis IV is known for small campaigns in Nubia and Syria. He came to power following the death of his father Amenhotep II after a brief power struggle with his surviving brothers (some had died before their father). A summary of the medical studies of him is revealed in Table 1.

He is most famed for a profound religious experience that he documented in the well-known "Dream Stele" that is found between the paws of the Great Sphinx at Giza. Initially hunting in the Valley of Gazelles southeast of the Sphinx, the young prince Tuthmosis moved closer to the great statue. At midday with the sun at its zenith the king required sleep and was "seized" by a vision of a god speaking to him to inform him of his rightful inheritance to the throne. Although the pharaohs claimed their power largely through their gods, such an account of a vision is very rare and may be explained by a pathological religiosity (see Akhenaten).

Howard Carter was the first to discover his tomb in modern times, entering it in 1903 (KV 43) in the Valley of the Kings. The pharaoh's body however had been moved by XXI dynasty High priests to another site and had been found by Victor Loret in 1898 in KV35.

Examination of some of the few sculptures attributed to him reveals mild adult gynecomastia (abnormal or excessive enlargement of the breasts). His mummy revealed a close resemblance to the mummy of Amenhotep II. Although the historical record reveals an age of death at approximately mid-forties to a possible sixth decade, current X-ray evidence only allows a maximum age of late thirties or early forties [2,3].

3. Amenhotep III

Amenhotep was probably the son of Tuthmosis IV and is regarded as a great builder, who was both economically successful and a patron of the arts. Towards the end of his reign, there is increasing prominence of the depiction of the god Aten. He fathered at least six children by his main wife Tiye although it was believed that he had a

* Fax: +44 20 3312 6309.

E-mail address: h.ashrafian@imperial.ac.uk.

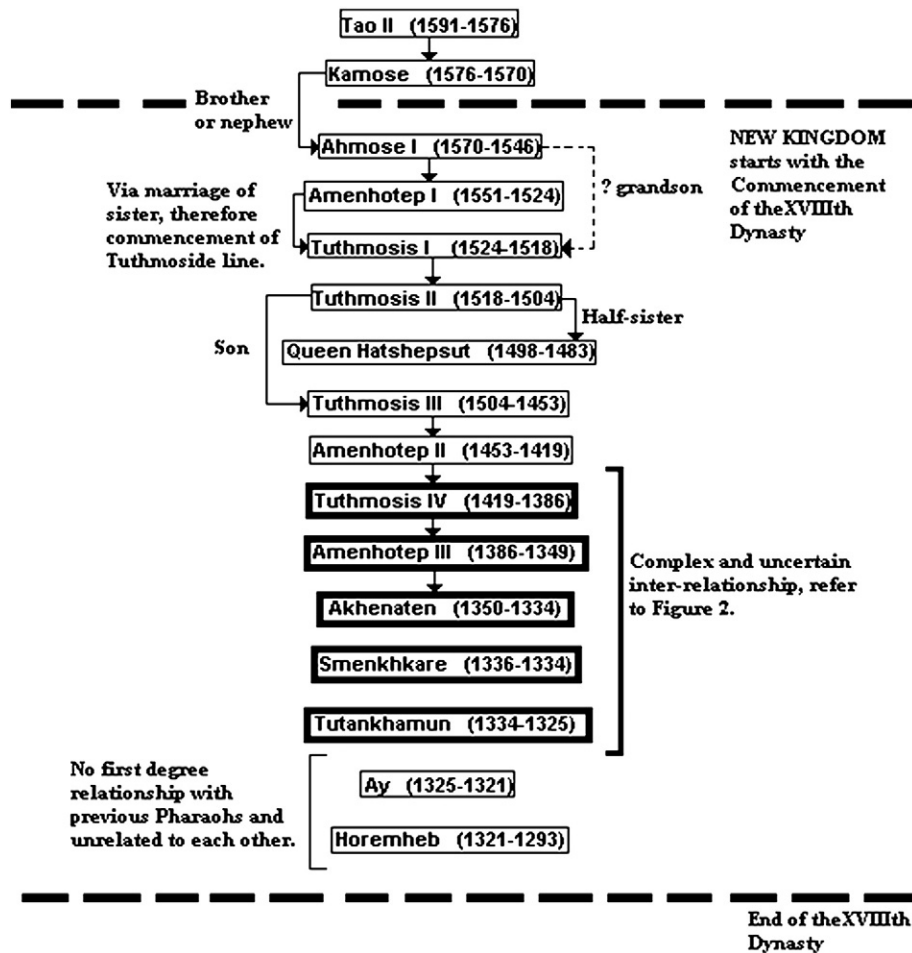


Fig. 1. Pharaohs and regnal dates of the XVIIIth dynasty. All dates are in BC and the (↓) implies a father to son inheritance. Of medical note, Tao II died from a traumatic death [114,115]; Amenhotep II is likely to have suffered from ankylosing spondylitis [2,116]. The 4 pharaohs in highlighted boxes are all noted to have had adult feminization and gynecomastia. The latter three all died early and unexpectedly and will form the basis for the remainder of this paper.

total of 317 wives. He died at approximately 50 years of an unknown disease, having ruled for 38 years and 7 months. His tomb KV22 was discovered in August 1799, although his mummy was revealed in 1881.

His last years were spent in ill health, and both his mummy and other depictions of him from Amarna show that he developed poor dentition (with abscesses) and gynecomastia [7] (based on his statue at the Metropolitan Museum of Art), and was shown to be obese by his 38th regnal year. X-ray analysis of his mummy reveals a biological age of death somewhat earlier than middle age at approximately early to mid forties. He measured 1.561 m in height [2,8].

4. Akhenaten

Few pharaohs have been the subject of as much speculation and argument as Akhenaten. He has been regarded as a great many things, some of which include him as a heretic, a futurist, a prophet, a despot, the world's first monotheist, a revolutionary, a poet, an inspiration for the authors of the Bible, the father of modern civilization and to some as the Biblical Moses. A summary of the medical studies on him is revealed in Table 2.

Akhenaten proclaimed the Aten or the sun disk, previously a relatively minor deity as a new supreme god. As a result of this alteration

Table 1
Medical studies on Tuthmosis IV and their reports.

Ref.	Diagnosis
[4]	In 1903 examination of the mummy and X-rays reveal a death at young age. The pharaoh was 1.64 m tall and became the first ancient Egyptian to be x-rayed, being transported by taxi to one of Cairo's first X-ray centers.
[4]	Further examination in 1903 revealed that he was young, clean-shaved, effeminate, and an extremely emaciated man, of 5 ft 6 in. in height. He had dark reddish-brown hair. The epiphyses of the tibia were fully joined, indicating an age of at least 20 and probably more than 24. Because the epiphyses of the crest of the ilium were not joined, however, he felt the king could not have been more than 25 years old.
[4]	It is not uncommon for Egyptians to exhibit a delayed union of epiphysis crista and bone texture, therefore an estimate of a low age of death, although perhaps as high as 28 or more.
[5]	Age of death probably older than 28.
[2]	Death between 30 and 40 years of age.
[6]	There is a close cephalographic relationship between the skulls of the "so-called" mummies of Thutmose IV, Amenhotep III and Tutankhamun. This reveals close, probably father-to-son relationships.

Table 2
Medical studies and hypotheses of Akhenaten's pathology.

Ref.	Diagnosis
[13]	Early 1800's – initially considered to be a female and confused with the ancient female Akencheres mentioned by the ancient author Manetho
[14,15]	Akhenaten had been castrated by Nubians from the South
[16]	Akhenaten was actually a woman.
[4]	He suffered from hydrocephalus with chin dysmorphism.
[17]	Associating Akhenaten as oedipus and reaffirming homosexuality
[4]	X-rays revealed delayed epiphyseal closure
[18]	His head was artificially deformed.
[19]	He suffered from progressive lipodystrophy or pulmonary tuberculosis
[20]	He had familial pathological obesity.
[21]	It was on balance unlikely that he had artificial head deformation.
[22]	His actions represent those of a religious fanatic.
[23]	Representations consistent with Babinski–Frölich's syndrome – adiposogenital dystrophy
[24]	Reaffirmation of artificial head deformation
[25]	On further review, there was no evidence of head molding
[26]	No evidence of head molding
[27]	With some collaboration with Carter, he proposed Akhenaten to be a homosexual based on the paze stela
[28]	Difficulty of associating Babinski–Frölich's syndrome with Akhenaten's likely fatherhood
[29]	Discovery of 'sexless' colossus at Karnak associated with Akhenaten
[30]	Akhenaten was devoid of genitalia on examination of the colossus
[31]	No underlying pathology, Pharaoh's dimensions are comparative to modern Egyptians.
[32]	No evidence of hydrocephalus but platycephalia
[33]	Proposal of morphology to be consistent with rickets
[34]	Akhenaten suffering from rickets unlikely
[35]	Akhenaten actually the Biblical/Torahic Moses
[36]	Akhenaten had acromegaly, with no evidence of head molding
[37]	Proposal that Akhenaten suffered from hypogonadism with pituitary hyperfunction
[37]	Further proposal that Akhenaten may have suffered from liver tuberculosis or liver cirrhosis with portal hypertension secondary to bilharziasis – psychologically feminine
[38]	No disease, just artistic privilege, or artistic imagery, for example Akhenaten being bisexual embodiment of the sun god, the mother and father of all mankind who impregnated himself to create the universe. Other authors simply attributing the abnormal morphology due to inbreeding.
[39]	The concept of rickets is readdressed.
[40]	Suggestion that Akhenaten may have had pituitary cranial dysplasia or pituitary tumor with pituitary hypofunction and secondary hypogonadism – being psychologically feminine
[41]	Further reaffirmation of pituitary tumor and not rickets and no evidence of head molding – psychologically feminine
[42]	Re-proposition of head molding theory
[43]	Proposal that Akhenaten suffered from parasitic tapeworm infection with intracranial cyst formation explaining the diencephalo-pituitary pathology
[44]	Akhenaten unlikely to have been homosexual based on the Paze stela
[45]	'Sexless' colossus from Karnak probably not Akhenaten but Nefertiti
[46]	Proposal that Akhenaten had Marfan's syndrome
[47]	Marfan's syndrome further suggested
[10]	History and morphology consistent with myotonic dystrophy
[48]	Familial aromatase excess syndrome may explain abnormal morphology
[49]	Familial gigantiform cementoma with brittle bone disease may explain morphology and early demise
[50]	Aromatase excess syndrome, Sagittal craniosynostosis syndrome, Antley–Bixler syndrome
[51]	Antley–Bixler syndrome is unlikely.
[12]	Unlikely to have female characteristics, gynecomastia, Marfan syndrome or Antley–Bixler syndrome
[52]	Homocystinuria
[53]	'Fertile eunuch syndrome', partly Kallmann's syndrome

of deities, he changed his name from Amenhotep IV to Akhen-aten or "servant of the Aten" as a sign of reverence. He then proceeded to move his capital to a city he built from scratch in the desert called Akhet-aten, "horizon of the Aten/Sun", known today as the ancient city close to Tell el Amarna. By doing so, all of the political, religious and economic centers also had to be moved to this site in an extremely short period. The Aten was then proclaimed as the Supreme God,

changing the national religion of ancient Egypt from a polytheistic base to monotheism. This was a totally new change and had never before existed in antiquity.

Artistic depictions of the king also changed throughout his life. Although initially depicted with the standard pharaonic model of his predecessors, as Akhenaten became older and progressed through his reign, there is a clear change in his representations. He is depicted with increasingly distinct characteristics of feminization. These include wide hips and thighs, gynecoid morphology, progressive gynecomastia [7] (based on several statues at the Egyptian Museum in Cairo) with a slender neck and emphasized lips. Other statues near Karnak reveal a nude Akhenaten with no genitalia and profound gynecomastia, although some scholars interpret this as an unfinished statue or even maybe that of the king's wife Nefertiti (despite the presence of a beard).

The source of these changes is explained by a profound vision that Akhenaten experienced which the sun god Aten appeared to him in the form of a solar disk between two mountains, guiding him to make changes in his kingdom. There was very powerful conviction to do this as he was essentially overriding two thousand years of tradition and practice. This extremely strong vision that was used to execute such a massive upheaval in ancient Egypt is another example of religiosity, the extent of which is rare among pharaohs, and as with Tuthmosis IV, may be explained by an underlying pathological condition.

In his fifteenth year, Akhenaten appointed a co-regent Smenkhkare. He died in his seventeenth regnal year aged approximately thirty-three of an unknown cause. To date, his mummy has not been found [9–11], although many suggest that the unidentified mummy of tomb KV55 is likely Akhenaten (which has also been historically suggested as the mummy of his co-regent Smenkhkare) [12].

5. Smenkhkare and his misidentification with Akhenaten

Smenkhkare is considered to be one of Egyptology's most controversial figures; he ruled as pharaoh for 2 to 5 years and also died of an unknown death, early in his twenties. He may have been a son or brother to Akhenaten (Fig. 2), and may have even fathered Tutankhamun. His sudden prominence coincides with the disappearance of Nefertiti – the wife of Akhenaten, initially confusing Egyptologists that the two may have been one in the same. Although this is largely now dispelled, his reign had minimal long-term significance.

Fifteen years before the discovery of tomb KV64 and Howard Carter's discovery of Tutankhamun, Theodore M. Davis and Edward Ayrton discovered the semi-tampered tomb of KV55. Davis initially believed that he had found Queen Tiye's tomb whereas Arthur Weigall, representative of the then antiquities service, believed it to be that of Akhenaten. To discern the sex of the mummy, Dr. Pollock of Luxor and an unidentified American obstetrician were asked to examine the mummy while in the tomb, who on the evidence of the pelvis believed it to be a female. However the then Professor of Anatomy in Cairo, Grafton Elliot Smith, was asked for his opinion and he promptly concluded that although the mummy's pelvis had a mildly gynecoid dimension, it was likely that of a young man in his mid-twenties. As he believed this to be Akhenaten, he further went on to propose his theory of Frölich's syndrome with feminization and delayed epiphyseal closure. He also noted on the large size and thinness of the cranium that he considered pathological and proposed hydrocephalus, which was accepted by A. R. Ferguson of the Cairo School of Medicine (see above).

Professor Douglas Derry who followed Smith as Professor of Anatomy in Cairo reviewed the skull and rejected the hydrocephalus theory, proposing non-pathological platycephalia while also noting a strong resemblance to Tutankhamun's skull. It was at one time considered that the mummy in KV55 was too young to be that of Akhenaten and led to the proposal (first suggested by Norman de

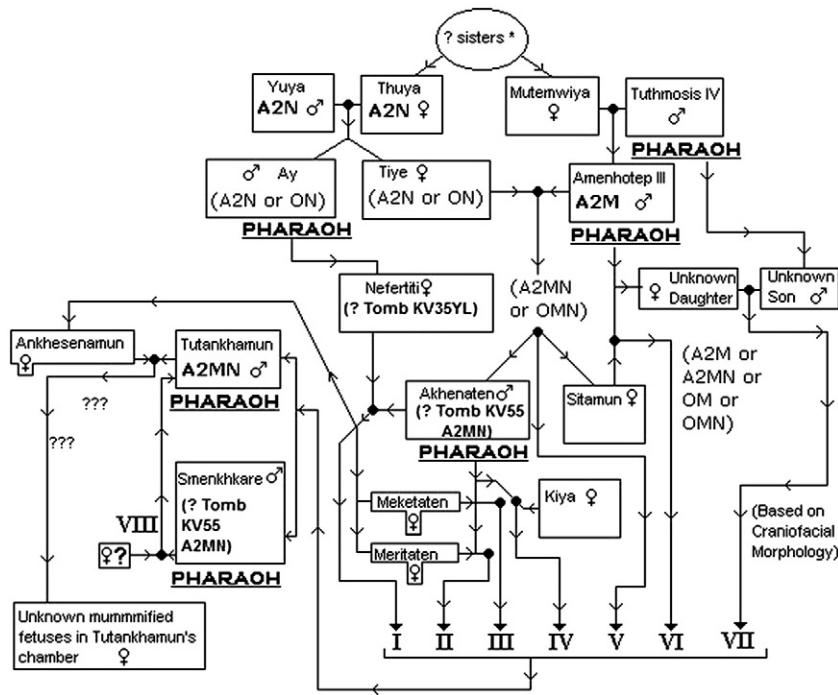


Fig. 2. Familial interrelationships of the late XVIIIth dynasty pharaohs with known ABH-MN serology in bold and calculated serologies in plain brackets. I–VII represent the seven possible genetic routes to the birth of the likely siblings Smenkhkare and Tutankhamun whereas VIII considers the possibility that Smenkhkare is actually Tutankhamun's father. * = Thuya and Yuya are maternal great grandparents to Tutankhamun; they are both likely to be non-royal, and if Thuya was a sister of Queen Mutemwiya, it would make them both decedents of Queen Aahmose-Nefertari, the ancestor of all Tuthmoside Queens. An alternative is that Queen Mutemwiya was a Mitannian princess (Indo-Iranian empire based in Syria) with no direct Egyptian background. It is also interesting to note that some scholars believe Nefertiti to be Tadukhipa, the daughter of Tushratta, King of the Mitanni. Alternatively, Kiya may have been the Mitannian Tadukhipa, or even the daughter of an unrelated noble. This being the case, if possibility III were to be assumed, it would imply that both Tutankhamun's mother and great grandmother would be Mitannian. In summary, theories I–IV acknowledge Akhenaten to be Tutankhamun's father; theories V and VI list Amenhotep III as his father, whereas VII considers this to be Tuthmosis IV and theory VIII Smenkhkare.

Garis Davies) that the identity of the body was Smenkhkare, a theory that is no longer generally accepted.

Preliminary work on the mummy's dentition by J. E. Harris and Fawzia Hussein indicates an age of death in the mid thirties [2,40,54]. A factor that confuses the issue is the theory that Smenkhkare was actually Queen Nefertiti [55]. Recent examinations by Joyce Filer and Nasry Iskander however reveal that the body is likely to be that of a young man although there is potential discrepancy between skull and lower skeleton dates of death. Both sections nevertheless, point to the mummy in KV55 being a young man at death, with the skull portraying excellent dentition [56]. An age of death has been proposed to be at the lower end of 20–25.

In summary, therefore, based on the historical record, Smenkhkare died young. Possible depictions of Smenkhkare also reveal adult onset gynecomastia. Although the identity of the mummified body KV55 is still not known (and may never be so), if it represents either Smenkhkare or Akhenaten, then it suggests that this individual was a first degree relative to Tutankhamun based on recent genetic analysis [12] and serology (Fig. 2). The skeleton has close similarities to that of Tutankhamun, particularly the skull, and also reveals the likelihood of late onset feminine changes, although the sella turcica is structurally normal.

6. Tutankhamun

Following his discovery in 1922 by the English archeologist Howard Carter (1874–1939), Tutankhamun's death has been the source of immense speculation. From the historical record it was clear that he followed the pharaohship form Akhenaten and Smenkhkare and only briefly reigned for nine years, dying in his late teenage years and earning the modern description as the “boy king”. On his

death, his vizier and regent, Ay became pharaoh. Several statues of Tutankhamun [7] reveal the presence of prominent gynecomastia.

What is unique about Tutankhamun is that his mummy and tomb were found largely intact which serves to allow us to readily identify his body, something that is not so simple for the bodies of many other pharaohs over the years have been hoarded together. He therefore remains as a reliable point of comparison. A summary of the medical studies on him is present in Table 3.

Soon after the tomb's discovery, Howard Carter enlisted the help of Douglas Derry, the professor of anatomy at the medical school of the Egyptian University in Cairo to conduct an autopsy of Tutankhamun in 1925. From that, they concluded that he was 18 or 19 years old at death with a height of 5 ft 6.5 in. (1.63 m), requiring an extra 2.5 cm to allow for shrinkage. He had high cheekbones with mildly protruding teeth with well-proportioned eyes and lips. He did not exhibit any obvious morphological deformity, which is also reflected in his artistic representations.

Unfortunately due to extensive amounts of unguents, the mummy was found to be stuck to its 3 coffins and the team had to cut and chisel the mummy to expose it. The autopsy was carried out in the desert sun, and heated instruments were utilized so as to combat the resin coating of the mummy. This resulted in the dislodgement of the head from the body at C7 and the separation at the lumbar vertebra leading to a displacement of trunk and legs from the pelvis. Furthermore the arms were removed from the chest, whereas the forearms, hands and feet were amputated, permitting removal of jewelry. He was noted to have a shaved head, which was unusual for contemporary mummies.

This early analysis did not yield much information as to the cause of death, and therefore a less intrusive autopsy was permitted to R. G. Harrison of the University of Liverpool in the 1960s. This study was largely X-ray-based, and in addition to confirming much of Derry's

Table 3
Medical studies on Tutankhamun and their reports.

Ref.	Diagnosis
[63]	1922 – tomb discovered, noted rushed mummification and burial, resulting in poor condition of mummy. Noted shaved head of mummy was unusual.
[64]	Cause of death likely to be murder.
[65]	Tutankhamun suffered from leprosy (derived in part from work on the Talmud). Other biblical scholars were proposing the possibility of the biblical plague as the cause of death.
[66]	First autopsy – age of death and height determined, death may be attributable to tuberculosis.
[67–70]	Tutankhamun and Smenkhk are likely brothers. Intracranial fragment of likely ethmoid origin on the left side in addition to the left posterior fossa egg shell thinning leading to a possibility of traumatic head injury; unlikely tuberculosis. No evidence of flat feet, but accentuated arches (see Fig. 2).
[71]	Possibility of assassination
[72]	Death by trauma on the back of the skull, possible weapon may have been an arrow.
[73]	Feminizing adrenal tumor proposed
[74]	Klinefelter's or Wilson's disease or "Tutankhamun syndrome"
[75]	Epidemic feminization or more likely artistic style in the depiction of the Pharaoh.
[76]	He suffered from adolescent gynecomastia.
[77]	Tutankhamun suffered from an inherited condition; he suffered from inbreeding and may have had celiac disease.
[78]	He was assassinated.
[79]	Potential family history of deformity in Tutankhamun's likely offspring (fetal mummies found in his coffin) – scoliosis, spina bifida, and Sprengel deformity.
[2]	Intracranial fragment on X-ray, with possibility of head trauma as part of embalming process.
[7]	There seems to be a familial gynecomastia in the late XVIIIth dynasty (see Fig. 2).
[80]	Tutankhamun suffered from an inherited condition; he suffered from inbreeding and may have had celiac disease.
[81]	Difficult to ascertain genetic inheritance which is likely very complicated (see Fig. 2).
[82]	Intracranial fracture of unknown cause.
[83]	Accident with chariot fall (as missing sternum and ribs) leading to death.
[47]	Blow to the head explaining results of posterior fossa calcification, and possible evidence of movement of the fragment of bone in the skull as a sign of post-mortem embalming.
[84]	Removal of ribs and sternum unusual in mummification therefore reveals a possible significant injury received before death, which required a removal of these body parts, therefore querying a violent death.
[85]	These authors quote the need for further DNA analysis in order to help delineate the illnesses of Tutankhamun.
[86]	Shaved head of mummy reveals probable intracranial pathology, but unlikely traumatic head injury or homicidal death
[48]	He suffered from familial aromatase excess syndrome
[87]	Death was due to traumatic head injury.
[87]	He had Klippel–Feil disease, with increased risk of traumatic head injury.
[87]	Death secondary to snake/insect bite or crippling disease allowing susceptibility to a blow on the head.
[87]	Assassination via head injury and underlying cervical spine abnormalities (secondary to Klippel–Feil).
[58]	Diagnosis of Marfan's disease and postulation of intracranial malignancy as cause of death, also diagnosing pectus carinatum and inherited disease.
[59]	Unlikely Klippel–Feil disease, as no radiologic evidence of intracranial pathologic changes of underlying brain disease, traumatic head injury or homicidal death – further stating that original X-ray images show that the bone fragment lies on the right (not on the left) and the posterior fossa thinning is within normal limits.
[88,89]	Tutankhamun's curse – although this is largely seen as a factor that resulted in the death of those that came into contact with the dead mummy after the tomb was re-opened. This is hypothesized to be a very long-lived pathogen residing in the tomb, not necessarily having been the cause of death of the young Pharaoh.
[49]	Proposal that Tutankhamun suffered from Familial gigantiform cementoma with brittle bone disease.
[60]	CT scan of Tutankhamun: Tutankhamun died approximately at age 19, stating that murder was unlikely. They reveal the possibility of Tutankhamun suffering from a fractured left lower femur.
[90]	Tutankhamun died of an infection set in by a wound in the left knee
[91]	Tutankhamun's likely offspring (fetal mummies found in his coffin) suffered from skeletal dysplasia

Table 3 (continued)

Ref.	Diagnosis
[12]	No signs of gynecomastia and craniosynostoses (such as Antley–Bixler syndrome) or Marfan syndrome were identified. Evidence for avascular bone necrosis – Köhler disease II, plasmodium falciparum malaria (based on Genetic testing for STEVOR, AMA1 and MSP1)
[92]	Unlikely malaria or Köhler's disease suggests sickle cell disease and Gauche's disease
[93]	Sickle-cell anemia
[94]	The gestational ages of Tutankhamun's likely offspring are approximately 24.7 and 36.78 weeks. Skeletal congenital anomalies of the 36.78-week mummy were ruled out.

original findings, revealed the removal of the sternum and much of the rib-cage, presumably by embalmers. Of note however, Harrison's work concentrated on the discovery of a bone fragment inside the mummy's skull revealing the possibility of traumatic head injury. James E. Harris performed further X-rays in 1978 with particular focus on the mummy's teeth.

Since then most of the studies on the death of Tutankhamun have relied on these pieces of evidence. To a large extent, this may be due to the state of the mummy which has largely deteriorated since initially found, and has therefore been kept away for long-term preservation purposes. Between 1925, 1978 and 2005, when the mummy had been exposed for examination, the mummy's color and state of skin had deteriorated, particularly noted in the eyelids. Furthermore, the right ear and his penis are now missing [7,47,57–60].

More recently, computed tomography (CT) scanning [61] and magnetic resonance imaging [62] have been introduced to discern increased accuracy for the study of mummies. The application of CT to Tutankhamun's mummy has achieved unique 3-D images of the boy king, accurately revealing his underlying bone structure with associated pathological clues [60]. From this study, an age of death of approximately 18–20 years has been confirmed, overall with a healthy habitus. He was slender with a height of approximately 170 cm. His skull was elongated (dolichocephalic) but not pathologically so and is in keeping with previous family members. He also had large front incisors, characteristic of the Tuthmosid line with mild overbite and cleft palate. There is a subtle spinal scoliosis, and the missing ribs and sternum are likely to be artificially removed secondary to embalming or by Carter's archeological team.

The area on the back of the skull indicates a longstanding partially healed blow, although this would not be consistent with an acute cause of death or as a cause of the intracranial fragments noted by Harrison, which are likely to be due to embalming and removal of brain tissue for mummification.

Of note, a fracture of the left lower femur was revealed at the level of the epiphyseal plate. This fracture is of different morphology than those on other mummies and may have occurred in life. This being the case, an acute fracture of this type, which commonly occurs in young males, may have been the cause of death. Furthermore, the left patella was noted as loose by Carter's team, and the new CT also reveals further fractures of the right patella and right lower leg which may be consistent with a pre-death accident.

We are still unsure of the identity of Tutankhamun's father (the mummy in the tomb KV55), and whether this was Akhenaten, Smenkhkare or another individual. The possible combinations of his parenthood are depicted in Fig. 2.

In summary, objective medical analysis gives us the following facts regarding Tutankhamun. He died early in adolescence with no artistic or bony evidence of congenital deformity. He underwent a rushed mummification, and the presence of a shaved head indicates that the ancient Egyptian physicians may have queried a head pathology in addition to other injuries, although absolute evidence of direct head trauma does not exist. In short, the peri-cranium and cranium seem intact, but one cannot rule out the possibility of soft tissue

and organic brain disease in this context (see below) with skull X-rays revealing the pouring of resin into the skull at two different perpendicular angles. The intracranial fragment is consistent with the embalming process. The posterior fossa skull thinning and calcification are of unknown significance and can be within normal limits; also, the sella turcica is normal.

Considering other familial diseases, he does not fulfill the classical criteria for the diagnosis of Marfan's disease [12] (despite suggestions of this disease in Tutankhamun [58] and Akhenaten [46,47]). There are depictions of Tutankhamun later in his rule that depict gynecomastia and adiposity consistent with an adult onset feminization syndrome. Nevertheless, Tutankhamun is the 4th pharaoh in a row to die suddenly from an unknown cause, and interestingly, there are depictions of Tutankhamun requiring walking sticks as there were an unusually large number of walking sticks in Tutankhamun's tomb.

The removal of his ribs and sternum is unusual for mummification, as even in a heavy trauma this usually remains structurally steadfast, even in the presence of fractures. His sternum on depictions reveals neither pectus carinatum nor excavatum. Although previous studies have considered Klippel–Feil disease, his cervical X-rays are consistent with the normal embalming process, and his physical depictions are not classical with those of this disease. His skeleton has close similarities to that of the mummified body of KV55 (likely Akhenaten or possibly Smenkhkare), particularly the skull, which is characteristic but not pathologic.

A recent genetic study of Valley of King (KV) mummy tombs applying partial Y-chromosomal information on the amount of autosomal half-allele sharing and family triolikelikelihood calculation reveals that Tutankhamun (KV62) was the son of male KV55 (likely Akhenaten or maybe Smenkhkare) and female KV35YL (likely Nefertiti); the latter two being consanguineous, who in turn were the offspring of Amenhotep and Tiye (also both found in KV35). Tiye was in turn the offspring of male Yuya (KV46) and female Thuya (KV46). Tutankhamun likely fathered two fetuses (KV62) who may have been mothered by female KV21A (possibly Ankhnesenamun) [12]. There is genetic evidence that he suffered from malaria, [92] a condition that would have been widespread throughout the Egyptian population of the time and the association of leiomyomata are highly unlikely within this context).

7. A new unifying theory

We can now summarize a medical historical pattern that includes the lives and deaths of these pharaohs — Tuthmosis IV, Amenhotep III, Akhenaten, Smenkhkare and Tutankhamun. The latter three pharaohs died an untimely death — Akhenaten in his early-thirties, Smenkhkare in his mid-twenties and Tutankhamun in his mid-to late-teens; the causes of which we are still unsure. Historically, Tuthmosis IV is considered to be between 40 and 50 years old at the time of his death, although X-ray evidence suggests an age of between 30 and 35 years. Medical care in the early XIXth dynasty was such that royalty of this era, for example Ramses II, lived to over 85 years (both himself and his son survived a history of ankylosing spondylitis). It is therefore unexpected that their antecedents of the immediately preceding late XVIIIth dynasty (from Thutmose I to Amenhotep III) died in their 20s and 30s. In fact, the total reign of the late XVIIIth dynasty pharaohs is comparable to the singular reign of Ramses II.

If we were to contemplate the non-medical causes of death, such as assassination, we would have to entertain the possibility of a massive socio-political upheaval that would allow assassination of four consecutive generations of pharaohs. Although this may be a possibility, it is unlikely and not corroborated by the historical record.

Addressing the medical complaints of these four pharaohs, one can see a trend that they are all at some point were represented to have gynecomastia in late adolescence and adulthood. Neither Akhenaten nor Tutankhamun fit classically into the picture of Marfan's skeletal abnormalities (pectus excavatum, pectus carinatum, scoliosis, high narrowly

arched palate, tall stature, long arms, long fingers — arachnodactily, pes planus and typical facies). As an autosomal dominant condition, its characteristics are not represented in other family members.

Akhenaten is remembered as having an extreme religious zeal for introducing the monotheistic cult of the Aten. He is noted to recount powerful visions of light from the rays of the sun-disk god. Furthermore, his grandfather Tuthmosis IV is also known for a famous religious vision regarding his future as king. This is described in the Dream Stele, which had him gripped by a vision in the middle of day, when he found himself requiring sleep.

Given the recurrence of gynecomastia in adulthood for the majority of the pharaohs in question and the pattern of early deaths, we can consider an inheritance pattern of pathology, possibly with some degree of genetic anticipation as with each generation, the pharaohs die at an increasingly early age. Acquired diseases such as bilharziasis [37] in four consecutive generations would be unlikely. Furthermore, although there is a strong possibility of an inherited condition, it must be noted that there is no evidence of childhood dysmorphic features in any of these pharaohs and, indeed, the evidence of Akhenaten and Tutankhamun in youth demonstrates physically normal individuals. Tutankhamun has been hypothesized to have had cervical spine deformities such as Klippel–Feil disease, although on subsequent analysis this has been discarded. Furthermore, his tomb reveals the coffin of the two female fetal mummies with deformities [79,91]; they may not necessarily be Tutankhamun's offspring and furthermore they may have been fetuses that were mal-developed and aborted, naturally consistent with miscarriage rates of the time.

The possibility of familial hypogonadism syndrome such as Klinefelter's syndrome is untenable as it is accepted that Akhenaten is renowned as having numerous offspring, notwithstanding Smenkhkare and Tutankhamun as two of them. Other forms of primary inherited hypogonadism would be more prominent earlier in childhood, and although we may consider both infective causes of hypogonadism such as bilateral mumps orchitis or secondary (central) hypogonadism that includes neoplastic causes including pituitary adenomas (prolactinoma) and craniopharyngiomas, we may discount these if we consider that the early deaths of these pharaohs were from an underlying inherited pathology since familial forms of these conditions are rare. Furthermore, the mummies do not have abnormal sella turcicas, which is sometimes found in patients with pituitary disease.

Familial multiple endocrine neoplasia type 1 (FMEN1) is an inherited disorder that affects the endocrine glands and could be an example of this. However, the pharaohs in question do not exhibit any of the other signs and symptoms of these conditions among which include low fertility and abnormally thin skeletal structure.

Although Akhenaten has been described as suffering from Babinski–Frölich's adiposogenital syndrome, this is not a clear cut case, and there is no strong evidence for Tuthmosis IV, Amenhotep III, Smenkhkare or Tutankhamun suffering from this, as they were not fat or short and did not exhibit delayed skeletal maturation. Hepatic disorders such as Wilson's disease have also been hypothesized to account for possible ascites and secondary gynecomastia. This is unlikely as there is no evidence of dystonic facies, posturing or Kayser–Fleischer rings on Tutankhamun's gold sarcophagi.

A possible disease candidate could be myotonic dystrophy. This has previously been considered as pathology for Akhenaten [10], but never before for the whole latter half of the family line. This is a progressive neuromuscular disease where weak and wasted muscles are slow to relax after contraction. There is an autosomal dominant inheritance that generally presents between the ages of 10–30. It is characterized by a long, expressionless face with ptosis, wasting in the forearms and calves, frontal balding, cataracts, low IQ, constipation, testicular atrophy, skin disorders and abnormal shuffling gait. Akhenaten's depictions may thus be interpreted to be demonstrating many of the static physical signs described, which is further reinforced as the disease does exhibit anticipation (earlier onset in each subsequent generation), and in rare

cases includes hypogonadism and gynecomastia. Therefore, for the first time, I suggest the possibility of disease anticipation, particularly in the latter three male family members, with the following ages of death in succeeding pharaohs Tuthmosis IV (35–45 years), Amenhotep III (40–45 years), Akhenaten (30–35 years), Smenkhkare (20–25 years), Tutankhamun (18–20 years).

Although this theory has many merits, the anticipations noted in these diseases are usually via maternal inheritance and therefore unlikely in this case (Fig. 2). Furthermore, although it seems that Akhenaten may well reflect the signs of this disease, this is not so clear-cut in the other pharaohs either in their mummies or their sculptures. In actuality, although disease onset may be early, age of death averages from mid-forties to normal in the absence of treatment, and any application of such a theory would have to recognize similar ages of death for Tuthmosis IV with Amenhotep III and Smenkhkare with Tutankhamun, which is not the case.

8. Hypothesis

If we consider Akhenaten's extreme religious change 4–5 years into his pharaohship, in addition to its socio-political intimations, one may also be able to ascribe a bio-pathological element to this. Epilepsy and religion have been associated together for over two and a half millennia [95–97], with temporal lobe epilepsy being particularly recognized as stimulating and promoting visual hallucinations associated with deep religious experiences. It has been further argued that a number of famed religious individuals experienced this condition, for example, the story of St. Paul's conversion to Christianity may be secondary to a temporal lobe epileptic seizure that resulted in his final religious conviction that allowed his spiritual transformation [98,99].

I propose that Akhenaten may have suffered from this condition, explaining his sudden extreme religious conviction to the monotheistic Aten, the known Egyptian god that had been venerated by his father, albeit to a much smaller extent. An experience associated with temporal lobe epilepsy (complex partial seizures) may have released such a strong religious feeling in Akhenaten that finally led him to become monotheistic, changing the whole cultural and political landscape of his empire in favor of his new beliefs. The extent of this cannot be exaggerated as in a few years Akhenaten attempted to rid his empire of thousands of years of religious and cultural history, banning other gods, their temples, and their socio-economically powerful priest class. The existence of a diseased king ruling over a nation is well documented in Ancient Egypt, [1,58,87] particularly as each pharaoh was considered divine and was politically buffered from direct government through the priest and military classes.

If one now also considers the dream of Tuthmosis IV, where he documented a religious vision that occurred at midday, then the possibility arises that this revelation may have also been secondary to a temporal epileptic episode. The episode is consistent with a photic-induced seizure secondary to sunlight, a well-documented trigger for temporal lobe epilepsy [100,101]. Furthermore in the context of likely inherited disease, a familial temporal epileptic syndrome may account for both Akhenaten and Tuthmosis IV symptoms.

Temporal lobe epilepsy is a condition that has physical, psychic, somatosensory and phenomenal characteristics. Classification of complex partial seizures is largely identified with the International League Against Epilepsy (ILAE), where seizures are associated to some extent with impairment of consciousness [102]. I propose a hypothesis that pharaohs Tuthmosis IV, Amenhotep III, Akhenaten, Smenkhkare and Tutankhamun suffered from temporal lobe epilepsy. This form of epilepsy can have complex auras and wide-ranging somatosensory patterns including all the senses, with symptoms of hallucinations, out-of-body experiences (autoscopy), religiosity and religious phenomena.

Temporal lobe epilepsy is the most common form of adult epilepsy, and most patients have this condition as a result of secondary hippocampal sclerosis with causes including infection, trauma and neoplasms

[103]. The psychiatric assessment of patients with epilepsy has been notoriously difficult in view of the various assessment criteria used to assess pathology. However, it has been shown that patients with temporal lobe epilepsy are at increased risk of psychopathology, with figures ranging between 10 and 60% when compared to 6% in the general population [104]. Fewer studies quote proportions of temporal lobe epilepsy patients with hyper-religiosity or strong religious experiences, however of those, it has been quoted that ictus-related religious experiences occur for 0.99–2.2% of patients with temporal lobe epilepsy, and post-ictal psychosis-related hyper-religious episodes occur for 23.3–27.3% of patients [105].

Taking into account the sequentially early deaths of the cases in question, my hypothesis extends logically to allude to the fact that if the pharaohs of the late XVIIIth dynasty were all closely related, which seems likely (Fig. 2), then they may all have suffered from a common inherited form of the disease. A familial temporal lobe epilepsy could be the cause for this, as in addition to accounting for the symptoms of religiosity, could also be the cause of the familial endocrinopathy and seizure-related accidents that may have affected these pharaohs and ultimately been the cause of their downfall.

If we are to ascribe such a condition to all these rulers, then consideration of the anatomical consequence of temporal epileptic disease, particularly the hypothalamo–pituitary–gonadal and temporolimbic–gonadal axes, is highly relevant. The temporolimbic system is known to have projections to the hypothalamus at its dorsomedial and lateral regions. These in turn relay hormonally to the pituitary–gonadal axis and also to the intermediolateral column of the thoracic spinal cord that provides sympathetic innervation of the testes. In addition, the temporolimbic system projects on to the dorsal motor nucleus of the autonomic vagus nerve that in turn supplies parasympathetic innervation of the testes. In the male, these systems regulate the release of intermediaries such as GnRH, LH and testosterone that may affect endocrine reproductive effects. Indeed, it has been shown in males with temporal lobe epilepsy that they can indeed suffer from an altered reproductive endocrine function that results in hypogonadism [106].

This may therefore account for the consistent and likely familial hypogonadism and gynecomastia shown in the pharaohs, being most extreme in Akhenaten's case, as demonstrated by his characteristic representations. In addition to the temporal lobe-related causes of his hypogonadism, the presence of psychosocial stress encountered by Akhenaten likely resulting from his significant socio-cultural upheavals in the face of known epileptic seizures may also have accounted for his exaggerated hypogonadism, possibly more than his relatives. The numerous abnormal sculptures at the time therefore may well have been anatomically accurate.

If these pharaohs suffered from a familial temporal lobe epilepsy syndrome, these early deaths may not be so surprising as on average, patients with epilepsy have a 2–3 times higher mortality than the general population, with some studies revealing a 9-fold increased probability. Although deaths due to brain neoplasms are increased among patients with epilepsy, in those with chronic epilepsy, seizure-related deaths may account for up to 39% of mortality [107,108]. These include accidents, status epilepticus and sudden unexpected deaths (SUD). Although we do not actually know the cause of deaths of the pharaohs in question, a cause has been shown in at least one depiction where either Smenkhkare or the chariot-keen Tutankhamun is seen as limping. Furthermore, there is the finding of a large number of walking sticks in Tutankhamun's tomb that may reflect a history of recurrent accidents. This may be similar to the possible higher incidence of road vehicle accidents and accidental deaths in patients with epilepsy [109], and could also be considered as a potential source of death in this case. The recent discovery of a left femoral fracture noted on CT scans for Tutankhamun is also in keeping with this theory as fractures at this site are among the most common found in the epilepsy population [110]. Furthermore, recent radiological and pathological cues from the Tutankhamun CT scans have led some researchers to postulate an infective cause of death

secondary to knee trauma [90] (Table 3), a finding which corresponds well with a history of epilepsy. It should be emphasized, however, that although neither suicide nor homicide can be discarded as putative sources of death, these would be rare and highly conspicuous, particularly for consecutive generations of pharaohs such as this.

Although the medical knowledge at the time did have a certain understanding of head trauma and neurological disease largely documented in The Edwin Smith Surgical Papyrus [111], a familiarity with seizures is still controversial and uncertain. Indeed, although there had been initial theories that the Ebers Papyrus described epilepsy, it is now more accurately accepted to be a description of a dermatological complaint [112]. The fact that Tutankhamun may have died secondary to a neurological complaint with a possible disease associated with his head may have guided the physicians at his time to logically treat a head disease the best they knew how, thus explaining his shaven head without direct evidence of cranial trauma.

Modern genetic analysis has clarified some initial mechanistic steps in familial temporal lobe epilepsy. Mutations in the leucine-rich, glioma-inactivated 1 gene (LGI1), otherwise known as epitempin, have been linked to autosomal dominant temporal lobe epilepsy (ADTLE). Although the function of LGI proteins is still largely unknown, they have been shown to be expressed strongly in the temporal region of the brain, with the gene having been located on human chromosome 10q24 [113]. This gene or others could therefore have been responsible for familial temporal lobe epilepsy in the XVIIIth dynasty pharaohs.

The evidence does not rule out an autosomal inheritance (Fig. 2), but more importantly, as we already have the known body of Tutankhamun, we are now in a position to investigate him and his likely mummified relatives with current and future genetic tests to identify the possibility of familial disease.

9. Conclusion

In conclusion, it is interesting to note the complex familial interrelationships of the pharaohs — Tuthmosis IV, Amenhotep III, Akhenaten, Smenkhkare and Tutankhamun. A complete analysis of all the data available to date, which include historical, artistic and medical sources, reveals a pattern of early deaths and disease in these XVIIIth dynasty rulers of ancient Egypt which may be due to a familial temporal epilepsy syndrome. Further understanding of this disease process in these rulers may elucidate their early demise, unique actions and characteristic body morphology.

References

- [1] Hawass Z. Tutankhamun and the golden age of the pharaohs: official companion book to the exhibition sponsored by National Geographic. Washington: National Geographic Society; 2005.
- [2] Harris JE, Wente EF. An X-ray atlas of the royal mummies. Chicago: University of Chicago Press; 1980.
- [3] Bryan BM. The reign of Thutmose IV. Baltimore: The Johns Hopkins University Press; 1991.
- [4] Smith GE. The royal mummies; 1912 [Cairo].
- [5] Harris JE, Weeks KR. X-raying the pharaohs. London: Macdonald and Co; 1973.
- [6] Wente EF. Who was who among the royal mummies, 144. The Oriental Institute News and Notes; 1995.
- [7] Paulshock BZ. Tutankhamun and his brothers. Familial gynecomastia in the Eighteenth Dynasty. *JAMA* 1980;244:160–4.
- [8] O'Connor D, Cline EH. Amenhotep III: perspectives on his reign. Ann Arbor: University of Michigan Press; 1998.
- [9] Risse GB. Pharaoh Akhenaten of ancient Egypt: controversies among Egyptologists and physicians regarding his postulated illness. *J Hist Med Allied Sci* 1971;26:3–17.
- [10] Cattaino G, Vicario L. Myotonic dystrophy in ancient Egypt. *Eur Neurol* 1999;41:59–63.
- [11] Montserrat D. Akhenaten: history, fantasy and ancient Egypt. London: Routledge; 2000.
- [12] Hawass Z, Gad YZ, Ismail S, et al. Ancestry and pathology in King Tutankhamun's family. *JAMA* 2010;303:638–47.
- [13] Hornung E. The rediscovery of Akhenaten and his place in religion. *J Am Res Cent Egypt (JARCE)* 1992;29:43–9.
- [14] Mariette AÉ. Séance du 5 Juin 1859. *Bull Inst Egypt* 1859;1:29–36.
- [15] Maspero GCC. Histoire Ancienne des Peuples de l'Orient; 1878. p. 211–3.
- [16] Lefebvre EJB. Sur différents mots et noms Egyptiens: Khunaten et son nom. *Proc Soc Biblical Archaeol* 1890–91;13:470–83.
- [17] Strachey J. Preliminary notes on the problem of Akhenaten. *Int J Psychoanal* 1939;20:33–42.
- [18] Sobhy GPG. Description d'un crâne trouvé dans une tombe à Tel-el-Amarna. *Bull Inst Franc Archeol Orient* 1918;14:65–7.
- [19] Quercy MAP. Le Pharaon Amenophis IV, sa mentalité. Fut-il atteint de lipodystrophie progressive? *Rev Neurol* 1920;36:448–62.
- [20] Ruffer MA. Pathological note on the royal mummies of the Cairo Museum. In: Moodie RL, editor. Studies in the paleopathology of Egypt. Chicago: University of Chicago Press; 1921. p. 175–6.
- [21] Sobhy GPG. Notes and News. *J Egypt Archaeol* 1923;9:117.
- [22] Weigall AEPB. The life and times of Akhenaten, pharaoh of Egypt. New York: G.P. Putnam's Sons; 1923.
- [23] Smith GE. The diversions of an anatomist in Egypt. *Camb Univ Med Soc Mag* 1926;4:34–9.
- [24] Dawson WR. Artificial deformation of the skull: a suggestion as to the origin of the custom. *Lancet* 1927;213:1001.
- [25] Dawson WR. Artificial deformation of the skull. *Lancet* 1927;213:1166.
- [26] Derry DE. Artificial deformation of the skull. *Lancet* 1927;213:1376.
- [27] Newberry PE. Akhenaten's eldest son-in-law 'Ankhheperure'. *J Egypt Archaeol (JEA)* 1928;14:3–9.
- [28] Smith GE. The Pharaoh Akhenaten—a problem in medical diagnosis, 4. The Broad Way, or Westminster Hospital Gazette; 1928. p. 25–8.
- [29] Porter B, Moss RLB. Topographical bibliography of ancient Egyptian hieroglyphic texts, reliefs, and paintings. II. Theban Temples 2 edn. Oxford: Griffith Institute; 1972.
- [30] Chevrier H. Rapport sur les travaux de Karnak (1929–1930). *Ann Serv Antiq Egypt (ASAE)* 1930;30:159–73.
- [31] Sobhy GPG. The persistence of ancient facial types among modern Egyptians. *J Egypt Archaeol* 1930;16:3.
- [32] Derry DE. Note on the skeleton hitherto believed to be that of King Akhenaten. *Ann Serv Antiq Egypt (ASAE)* 1931;31:115–9.
- [33] Proskauer F. Zur Pathologie der Amarnazeit. *Zeits Agypt Sprach Altertums (ZÄS)* 1932;68:114–9.
- [34] Guest EM. Pathology and art at El Amarna, 18. *Ancient Egypt East*; 1933. p. 81–8.
- [35] Freud S. Moses and monotheism, translated from the German by Katherine Jones. New York: Vintage Books; 1939.
- [36] Snorason E. Cranial deformation in reign of Akhenaten. *Bull Hist Med* 1946;20:601–10.
- [37] Ghalioungui PA. A medical study of Akhenaten. *Ann Serv Antiq Egypt (ASAE)* 1947;47:29–46.
- [38] Smith WS. The art and architecture of ancient Egypt. Baltimore, MD: Penguin Books; 1958.
- [39] Martí-Ibáñez F. The sun queen, 2. *MD Med Newsmag*; 1958. p. 1–3.
- [40] Aldred C, Sandison AT. The Pharaoh Akhenaten. A problem in Egyptology and pathology. *Bull Hist Med* 1962;36:293–316.
- [41] Wells C. Bones, bodies, and disease; evidence of disease and abnormality in early man. London: Thames and Hudson; 1964.
- [42] Kindler W. Artificial cranial deformation throughout the ages, 1. *Sandorama: The Physician's Panorama*; 1964. p. 10–6.
- [43] Tomas V. From what disease did the pharaoh Akhenaten suffer? In: Blaser RH, Buess H, editors. Proceedings of the XIXth international congress on history of medicine 1964. Basel & New York: S. Karger; 1966. p. 177–84.
- [44] Harris JR. Nefertiti Rediviva. *Acta Orient (Ediderunt)* 1973;35:5–13.
- [45] Harris JR. Akhenaten or Nefertiti. *Acta Orient (Ediderunt)* 1977;38:7–10.
- [46] Burrigge A. Did Akhenaten suffer from Marfan's syndrome?, 3. Akhenaten Temple Project Newsletter; 1995.
- [47] Brier B. The murder of Tutankhamen: a 3000-year-old murder mystery. London: Weidenfeld & Nicolson; 1998.
- [48] Ismail AAA, Barth JH. Endocrinology of gynecomastia. *Ann Clin Biochem* 2001;38:596–607.
- [49] Rossbach HC, Letson D, Lacson A, Ruas E, Salazar P. Familial gigantiform cementoma with brittle bone disease, pathologic fractures, and osteosarcoma: a possible explanation of an ancient mystery. *Pediatr Blood Cancer* 2005;44:390–6.
- [50] Braverman IM, Redford DB, Mackowiak PA. Akhenaten and the strange physiques of Egypt's 18th dynasty. *Ann Intern Med* 2009;150:556–60.
- [51] Miller WL. Did Akhenaten have the Antley-Bixler syndrome? *Ann Intern Med* 2009;151:892 [author reply 892].
- [52] Cavka M, Kelava T, Cavka V, Busic Z, Olujic B, Brkljacic B. Homocystinuria, a possible solution of the Akhenaten's mystery. *Coll Antropol* 2010;34(Suppl. 1):255–8.
- [53] Retief FP, Gilliers L. Akhenaten, a unique pharaoh. *S Afr Med J* 2011;101:628–30.
- [54] Connolly RC. Kinship of Smenkhkare and Tutankhamen affirmed by serological micromethod. Microdetermination of blood group substances in ancient human tissue. *Nature* 1969;224:325.
- [55] Harris JR. Göttinger Miszellen, 4; 1973. p. 15–7.
- [56] Filer JM. The KV 55 body: the facts. *Egypt Archaeol* 2000;17:13–4.
- [57] Harrison RG, Connolly RC, Abdalla A. Kinship of Smenkhkare and Tutankhamen demonstrated serologically. *Nature* 1969;224:325–6.
- [58] Doherty PC. The mysterious death of Tutankhamun. London: Constable & Robinson; 2002.
- [59] Boyer RS, Rodin EA, Grey TC, Connolly RC. The skull and cervical spine radiographs of Tutankhamen: a critical appraisal. *AJNR Am J Neuroradiol* 2003;24:1142–7.
- [60] Egyptian_Supreme_Council_of_Antiquities. Press release: Tutankhamun CT scan. Cairo: Egyptian Ministry of Culture; 2005.

- [61] Rühl FJ, Alt KW. Non-invasive examination methods of ancient bone and mummies. In: Grupe G, McGlynn G, Peters J, editors. *Limping together through the ages - Joint afflictions and bone infections (Documenta Archaeobiologiae [DOAB 6])*. Rahden, Westf.: DE; 2008. p. 119–25 [ISBN 978-3-89646-621-1].
- [62] Rühl FJ, von Waldburg H, Nielles-Vallespin S, Boni T, Speier P. Clinical magnetic resonance imaging of ancient dry human mummies without rehydration. *JAMA* 2007;298:2618–20.
- [63] Carter H, Mace AC. *The tomb of Tut-Ankh-Amen*, vol. 3. London: Cassell; 1923–33.
- [64] Mace AC. The Egyptian expedition. *Bull Metr Mus Art (BMMMA)* 1992;(Part 2): 5–11 [December].
- [65] Weigall AEPB. *Tutankhamen and other essays*. London: Butterworth; 1923.
- [66] Derry DE. Report upon the examination of Tutankhamun's mummy. In: Carter H, Mace AC, editors. *The tomb of Tut-Ankh-Amen*, vol. 2. London: Cassell; 1923.
- [67] Harrison RG, Batrawi A, Mahmoud MS. An anatomical examination of the pharaonic remains purported to be Akhenaten. *J Egypt Archaeol (JEA)* 1966;52:95–119.
- [68] Harrison RG, Abdalla AB. The remains of Tutankhamun. *Antiquity* 1972;46:8–14.
- [69] Harrison RG. Post-mortem of two Pharaohs. Was Tutankhamun's skull fractured? *Buried Hist* 1972:18–25.
- [70] Harrison RG. Tutankhamun's postmortem. *Lancet* 1973;1:259.
- [71] Leek FF. *The human remains from the tomb of Tut'ankhamun Number 5 Tut'ankhamun's Tomb Series*. Oxford: Griffith Institute; 1972.
- [72] Aldred C. *Tutankhamen's Egypt*. New York: Scribner's Sons; 1972.
- [73] Weller M. Tutankhamun: an adrenal tumour. *Lancet* 1972;2:1312.
- [74] Walshe JM. Tutankhamun: Klinefelter's or Wilson's? *Lancet* 1973;1:109–10.
- [75] Swales JD. Tutankhamun's breasts. *Lancet* 1973;1:201.
- [76] Gray JE. Tutankhamun's postmortem. *Lancet* 1973;1:259.
- [77] Czeizel E. Life and death of Tutankhamun from the viewpoint of human genetics. *Orv Hetil* 1974;115:97–102.
- [78] MacQuitty W. *Tutankhamun – the last journey*. New York: Crown Publishers; 1976.
- [79] Harrison RG, Connolly RC, Ahmed S, Abdalla AB, El-Ghawaby M. A mummified foetus from the tomb of Tutankhamun. *Antiquity* 1979;53:19–21.
- [80] Czeizel A. Life and death Tutankhamun from human genetic aspects. *Ther Hung* 1980;28:40–3.
- [81] Timmons CF. Genetics of the eighteenth dynasty. *JAMA* 1981;245:1525.
- [82] Reeves N. *The complete Tutankhamun*. London: Thames and Hudson; 1990.
- [83] Dodson A, Ikram S. *The mummy in ancient Egypt*. London: Thames & Hudson; 1998.
- [84] Forbes DC. *Tombs, treasures, mummies: seven great discoveries of Egyptian archeology*. Sebastopol: KMT Communications; 1998.
- [85] Farag TI, Iskandar A. Tutankhamun's paternity. *J R Soc Med* 1998;91:291–2.
- [86] El-Mahdy C. *Tutankhamen: the life and death of a boy king*. London: Headline Book Publishing; 1999.
- [87] King MR, Cooper GM. *Who killed King Tut*. New York: Prometheus Books; 2004.
- [88] Gandon S. The curse of the pharaoh hypothesis. *Proc R Soc Lond B Biol Sci* 1998;265:1545–52.
- [89] Nelson MR. The mummy's curse: historical cohort study. *BMJ* 2002;325:1482–4.
- [90] Egarter-Vigl E, Gostner P. *Alto Adige*; 2006.
- [91] Kozma C. Skeletal dysplasia in ancient Egypt. *Am J Med Genet A* 2008;146A:3104–12.
- [92] Timmann C, Meyer CG. Malaria, mummies, mutations: Tutankhamun's archaeological autopsy. *Trop Med Int Health* 2010;15:1278–80.
- [93] Pays JF. Tutankhamun and sickle-cell anaemia. *Bull Soc Pathol Exot* 2010;103: 346–7.
- [94] Hawass Z, Saleem SN. Mummified daughters of King Tutankhamun: archeologic and CT studies. *AJR Am J Roentgenol* 2011;197:W829–36.
- [95] Devinsky O. Religious experiences and epilepsy. *Epilepsy Behav* 2003;4:76–7.
- [96] Zanchin G. Considerations on “the sacred disease” by Hippocrates. *J Hist Neurosci* 1992;1:91–5.
- [97] Todman D. Epilepsy in the Graeco-Roman world: hippocratic medicine and Asklepien temple medicine compared. *J Hist Neurosci* 2008;17:435–41.
- [98] Dewhurst K, Beard AW. Sudden religious conversions in temporal lobe epilepsy. *Br J Psychiatry* 1970;117:497–507.
- [99] Asheim Hansen B, Brodtkorb E. Partial epilepsy with “ecstatic” seizures. *Epilepsy Behav* 2003;4:667–73.
- [100] Benbadis SR, Gerson WA, Harvey JH, Luders HO. Photosensitive temporal lobe epilepsy. *Neurology* 1996;46:1540–2.
- [101] Fisher RS, Harding G, Erba G, Barkley GL, Wilkins A. Photic- and pattern-induced seizures: a review for the Epilepsy Foundation of America Working Group. *Epilepsia* 2005;46:1426–41.
- [102] Sirven JI. Classifying seizures and epilepsy: a synopsis. *Semin Neurol* 2002;22: 237–46.
- [103] Sloviter RS. The neurobiology of temporal lobe epilepsy: too much information, not enough knowledge. *C R Biol* 2005;328:143–53.
- [104] Gaitatzis A, Trimble MR, Sander JW. The psychiatric comorbidity of epilepsy. *Acta Neurol Scand* 2004;110:207–20.
- [105] Ogata A, Miyakawa T. Religious experiences in epileptic patients with a focus on ictus-related episodes. *Psychiatry Clin Neurosci* 1998;52:321–5.
- [106] Herzog AG. Altered reproductive endocrine regulation in men with epilepsy: implications for reproductive function and seizures. *Ann Neurol* 2002;51:539–42.
- [107] Jallon P. Mortality in patients with epilepsy. *Curr Opin Neurol* 2004;17:141–6.
- [108] Gaitatzis A, Sander JW. The mortality of epilepsy revisited. *Epileptic Disord* 2004;6:3–13.
- [109] Tomson T, Beghi E, Sundqvist A, Johannessen SI. Medical risks in epilepsy: a review with focus on physical injuries, mortality, traffic accidents and their prevention. *Epilepsy Res* 2004;60:1–16.
- [110] Sovereign PC, Webb DJ, Petri H, Weil J, Van Staa TP, Egberts T. Incidence of fractures among epilepsy patients: a population-based retrospective cohort study in the General Practice Research Database. *Epilepsia* 2005;46:304–10.
- [111] Veith I. The medical world of King Tutankhamun. *Perspect Biol Med* 1982;26: 98–106.
- [112] Leitz C. Epilepsie im Alten Ägypten? *Schriftenr Dtsch Ges Gesch Nervenheilkd* 2001;7:149–55.
- [113] Turnbull J, Lohi H, Kearney JA, et al. Sacred disease secrets revealed: the genetics of human epilepsy. *Hum Mol Genet* 2005;14(Spec No. 2):2491–500.
- [114] Chapman PH. Case seven of the Smith Surgical Papyrus: the meaning of TP3W. *J Am Res Cent Egypt (JARCE)* 1992;29:35–42.
- [115] ten Berge RL, van de Goot FR. Seqenenre Taa II, the violent death of a pharaoh. *J Clin Pathol* 2002;55:232.
- [116] Feldtkeller E, Lemmel EM, Russell AS. Ankylosing spondylitis in the pharaohs of ancient Egypt. *Rheumatol Int* 2003;23:1–5.