About the emergence and spreading of smallpox in the Ancient Near East – did it reach us from camels or from cattle?[1]

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In 1997 I began to examine cuneiform texts concerning the history of medicine which colleagues already had work on before 40 years for the last time. It concerned to me less the complete philological revision of these texts, but rather the statement that these texts – among other things – necessarily did not contain a connected enumeration of disease symptoms, complaints and hardly defined diseases after today's terms, without one had made the attempt to identify with the existing term one or more certain diseases. These texts appeared to me despite their initial unintelligibility so interesting that I considered that it would be wise to get in touch with a medical consultant.

Right off it resulted that the symptoms of an infection are described here. Beyond that it was not difficult to join these symptoms and the associated surrounding field to a disease picture that concerns smallpox. Then, a kind of a check list (i.e. a pattern of epicrisis) was set up, which contained all medically substantial. With the assistance of such a pattern of epicrisis the medical contents of these texts could be described and understood clearly. In order to clarify the coherences, I list it up again:

The pattern of epicrisis:

1. The cause of the illness (at that time unknown, deity, daemon),
2. Origin of the illness (sky),
3. Carrier (lambs, kids, humans),
4. Age of the carriers (young animals, infants),
5. Symptoms (high-feverish illness with infestation of the skin),
6. Guiding syndrome (typical skin rashes),
7. Cure (symptomatic medical treatment),
8. Process (typical, spontaneous healing or death),
9. Illness type (suggested by simultaneous
   disease outbreak of several animals and humans (epidemic)),
10. Missing specification relating humans and animals.

Here we have still to make the following note: this investigation concerns the first recognisable written records about smallpox in Mesopotamia at all. They date back to the beginning of the 2nd Millennium BC. and originate from Māri, a city in eastern Syria at the today's border to Iraq.

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[1] Cf. Diamond, J., Evolution, consequences and future of plant and animal domestication, Nature 418, 700 – 707 (08 August 2002); doi: 10.1038 / nature 01019.

Worldwide there are some few other records from the pre-Christian time beyond, which however date later.

Only 5 years ago one could have been proud to have found a further component in the emergence of infections, not only concerning the region of the Ancient Near East, but relevant to the geo-pathological period and localisation in a wider sense.

Also molecular biologists might be able to take appreciatively note of these philological results; philologists however must accept that their conceptions concern completely different periods. Thus a small excursion into molecular biology becomes evenly necessary. I am neither a molecular biologist nor a genetic scientist. Therefore I can only rely myself on my own school knowledge and the realizations of my medical advisors. It might be sufficient however, in order to understand at least in general terms, the scientific coherence.

The same which applies to the emergence, development and spreading of the human genotype applies also to the genotype of bacteria and viruses. The individual chromosomes are carriers of the individual genes. These genes again are carriers of the so-called genetic code, which becomes written from four chemically exactly defined substances, the purin bases, briefly and sufficiently called DNA, comparably as with four letters A, B, C and D. According to the rules of the combinatorial mathematics 3 letters would be enough, to make from 20 other substances the correct selection. And these 20 other substances are the amino acids, which are to be arranged in correct sequence and frequency to proteins. How it works and what it means in details is of no interest for us here.

Only some few remarks: these letter sequences, which are called DNA sequences, are so specific that one can identify criminals with its assistance also. Their task is however to code the appearance and the functions of a human and animal cell, i.e. to specify.

Billions of combinations of these four letters, or with other words of these DNA molecules must to be produced, steered and passed on during their reproduction in the correct order. But 'accidents' are possible, i.e. errors of the encoding of these molecules, which later on will have their results in deformities.

These 4 letters, these now well-known DNA molecules are lying in form of long chains or threads in the chromosomes and are forming the helix, respectively the double helix, which allows passing the genotype on to the next cell.

Thus: the gene is with its DNA ropes the material unit of the genotypes. By the term 'genome' today one understands concerning viruses, bacteria, animals and also humans the whole of the existing genes. The fact that viruses do not possess chromosomes on those their genes could sit, but only consist of simple nucleic acid ropes, is insignificant in this context here. The human genome uses in its double helix, 3.2 billion instructions after those the mentioned amino acids are to be arranged. Unfortunately nature was not content with it. It permits millions of deviations from the

basic pattern. Just this genetic variability keeps us still far from a complete decoding, but gives us the possibility of limiting the age of a gene.

In the last 2 years molecular biologists found out that determined well locatable sections of a gene are subjected changes as a function of their age. These changes are subject to certain laws, which can be seized mathematical-statistically. Thus the age of a gene respectively the development of its encoding can be calculated in good approximation. Thereby it does not depend on a few 1000 years of course. Molecular biologists conducted by M. Gardener from the Institute of Genomic Research, Rockville, MD, USA, now have calculated that the genome of the malarial parasite (plasmodium falciparum), a bacteria, and by the way also that of its carrier, the mosquito anopheles gambiae, must have come into being during a period between 180,000 and 100,000 years ago, thus in a time, to which after the opinion of G. Bräuer of the Institute of Human Biology of the university of Hamburg, the "late archaic homo sapiens" (200,000 – 120,000) dates.

Based on the studies of J. Mu from the Laboratory of Malaria and Vector Research, National Institutes of Health, Bethesda, Maryland, USA, about the genome of the malaria parasite, one may hope that in a similar way the age of the smallpox virus can be limited. The smallpox virus with its size nevertheless approaches to light-microscope dimensions. It possesses a doubled-helix DNA genome, whose structure is already well investigated.

While the time of origin of the malaria parasite plasmodium falciparum dates back 100,000 to 180,000 years by the help of the single nucleotide polymorphism (SNP), no such investigations for the smallpox virus are still present. However it appears daring to assume a similar time of origin of the smallpox virus.

These dating correspond to the findings of Singa in East-Africa, which date to 150,000. From the Ancient Near East we only possess some few findings of the homo sapiens from these early times yet. They are excavated in caves of the Nahal Me'arot of Mount Carmel: 1 female skeleton from the Tabun cave, dated to about 120,000 years ago and 14 skeleton from the Mugharet es-Squl V[2] cave, dated to about 100,000 years ago. Moreover the excavations of the cave of Qafzeh also in Israel, where i.a. 1 female skeleton together with her child (dated by the electron spin resonance method to 120,000 –100,000) was found, who already belonged to the Proto-Cro-Magnon population and of the cave of Zawi Chemi Shānīdār, from where we possess the oldest records of human life in Iraq so far, are of anthropological significance. The findings of human bones originate homo pithecanthropus and homo neandertaliensis from Shānīdār date around 70,000 – 40,000.

S. Tishkoff, from the Department of Biology at the university of Maryland, USA, meanwhile speculates that malaria only became a major health problem after the development of agriculture, because sunlit pools in clearings suddenly provided an ideal habitat for the mosquito that transmits the disease.

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[2] McCown, T. D. - A. Keith, The fossil remains from the Levalloiso-Mousterian, The Stone Age of Mount Carmel, vol. II, The Claredon Press, Oxford, 1939.

The above-mentioned methodology is evenly launched. At the Institute for Microbiology of the university of Göttingen conducted by G. Gottschalk, the genome of the clostridium tetanus pathogen was just determined, although computations of its emergence are not present yet.

I have to supplement not to have found any test results concerning the age of the smallpox genome in the still completely recent literature. With the present general interest in smallpox virus this might be however only a question of time. In each case the molecular-biological age determination shows with the malarial parasite, what modern scientific research can achieve. Nevertheless one may suppose that in analogy to the genome of the smallpox virus the same applies to the malaria bacteria.

On the part of bio-archaeologists the opinion is taken, that at the end of the ice age, thus at the end of the Pleistocene about 11,000 to 10,000 years BC. all substantial processes of emergence were absolutely final in the development of mankind and the animated nature. It is the beginning of becoming settled and of producing food.

The bio-archaeology represents a completely new research discipline, which among other things clears up the phylogenetic coherence by DNA analyses of outlasted protein molecules in bones and mummified tissues. Today with the same method one starts to limit the date of emergence of the human genome. But that is another topic.

Scientists of Ancient Near Eastern studies have surely no reason for resignation, but however have to recognise that their own original research results concerning cuneiform sources relevant for medical-historical research become thrust into the background from the molecular-biological point of view as to determinations of time.

Nevertheless they still fit in however with the scientific concept and give information about the local spreading of certain viruses, what is hardly to be determined molecular-biologically. In addition it comes that the philological records make a contribution to be able to recognise, how ancient humans got along under their conditions with individual illnesses, which now one can determine more precisely.

Thus the attempt to explain and to date the emergence of infections, their pathogenic agents, their spreading to the human population, has a cultural and mankind-historical significance. J. Diamond, one of the leading scientists on the fields of human genetics and phylogenetics approaches this problem, by basing the domestication of plants and animals in their evolution.

His conclusions are the following:

"Infections arise with the emergence of the agriculture approximately before 10,000 years. Molecular biology showed that they developed in the animal organism and became to transfer from there to humans."[3]

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[3] Ewald, P.W., Evolution of Infectious Disease, Oxford 1994, 6f.

"The main killers of humans since the advent of agriculture have been acute, highly infectious, epidemic diseases that are confined to humans and that either kill the victim quickly or, if the victim recovers, immunise him/her for life. Such diseases could not have existed before the origins of agriculture, because they can sustain themselves only in large dense populations that did not exist before agriculture, hence they are often termed 'crowd diseases'. The mystery of the origins of many of these diseases has been solved by molecular biological studies of recent decades, demonstrating that they evolved from similar epidemic diseases of our herd domestic animals with which we began to come into close contact 10,000 years ago. Thus, the evolution of these diseases depended on two separate roles of domestication: [4]

1) The development of closer human populations.
2) A much more frequent transmission of animal illnesses of our domestic animals than of hunted wild animals.

We have to consider, that the AIDS-virus was developed in a special monkey species somewhere in Africa, but only 1959 was dawn on us. The same is to be said about the SARS virus developed in a special Asian cat species.

As mentioned above J. Diamond equates the emergence of epidemic infections with the beginning of agriculture, thus with the Neolithic arising of the cultures (ca. 9000 BC.) of i.a. Qal'at Ğarmo[5] (Iraq), Haçilar (Anatolia), Ali Koš (Iran), Jericho (Israel), Çatalhüyük (Anatolia).

Agriculture makes an increase and a compression of the population possible and creates thus the conditions for 'crowd diseases'. J. Diamond refers to the molecular-biological investigations at our domesticated herd animals, with which we came into contact before approximately 10,000 years. Thus measles and tuberculosis were transferred by pasture live-stock (pasture sheep: *immer rīti/supūri*, *emmer adrê, laḫru muššuštu*, pasture goat: *enzu(m), ṣēnu(m)*, pasture cow/bull/ox: *alap rīti, lītu(m), puṭāru(m)*, pasture animal: *sādīu,* pasture: *pargānu*, *rītu(m)*, pasture land/area: *gabību, nawû(m)*, only to mention some akkadian lexems) to humans and influenza by pigs (*šaḫû(m)*) and ducks (*paspasu, ūsu(m)*). These are – without exceptions – exciters, which were developed from animal diseases and paradoxically are – so J. Diamond – in most cases to humans only limited and to other animals only poorly pathogen.

The origin of the smallpox however is completely open. As their carriers again pasture livestock and above all camels (*gammalu*, *ibilu, udru*) are discussed. Considerations of this

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[4] Diamond, J., Evolution, consequences and future of plant and animal domestication, Nature 418, 700 - 707 (08 August 2002); doi: 10.1038 / nature 01019.

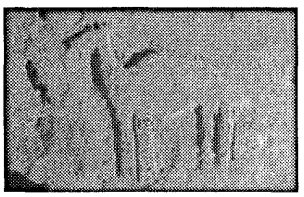
[5] At the beginning of the 7th Millennium BC. one can prove that meanwhile in Qala't Ğarmo were present onager, gazelle, wild goat, house goat, sheep, a kind of cattle, deer, roe deer, pig, bear, wolf, fox, leopard, cat, badger, marten and turtle.

kind refer however in the actual sense to the propagation of existing exciters in the human population and not to the emergence of the pathogen.

Thus a clarification of the origin of the smallpox is still pending, and we have approached the actual important question, which already J. Diamond has asked:

"For instance, measles and tuberculosis arose from diseases of cattle, influenza from a disease of pigs and ducks. An outstanding mystery remains the origins of smallpox: did it reach us from camels or from cattle?" Or by any other kind of pasture livestock?

It is for certain that sheep, goats and also camels respectively dromedaries existed already at the end of the last ice age, thus at around 10,000 BC. We possess findings of bones coming from Sihi at the south coast of the red sea, which can be dated by a radio-carbonic analysis to 8200 BC. It has also been proved that sheep and goats were the first pasture animals, which were domesticated. The knowledge about camels however can be set in after picture documents only with approximately 2500 BC. We possess with a relief found on the island of Umm an-Nar (Oman) besides numerous camel bones the oldest representation of a camel.



Not yet domesticated camel on a relief
from Umm an-Nar, Oman, ca. 2,500 BC.

However no signs are to be recognized as for headgear, which could suggest that it had already concerned a domesticated animal. Also the remains of camel bones from there and from Ras Ghanada at the gulf-coast of the United Arabian Emirates, which can be dated to the end of the 3rd Millennium do not supply evidence for domestication. The accompanying findings rather verify, that those animals were hunted.

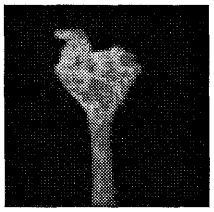
Records from Mesopotamia however cannot be proved seriously from the 3rd Millennium so far. Archaeological and bio-archaeological proofs for the domestication of camels we only possess from the end of the 2nd Millennium and then not only from Umm an-Nar.

Only the records of camel dung and spun camel hair in connection with camel bones found in Jericho, the coast regions around the Arabian Peninsula and in Šar-i-Soqta in East-Iran possibly supply domestication. R.W. Bulliet from the Columbia University, New York, points out:

"To be sure, one or two representations of camels from early Mesopotamia have been alleged, but they are all either doubtfully camelline, as the horsy looking clay plaque from the third dynasty of

Ur (2345–2308 BC.), or else not obviously domestic and hence possibly depictions of wild animals, as in the case with the occasional Ubaid and Uruk period (4000–3000 BC.) examples".[6]

"There are no sound grounds for doubting Albright's contention that camel domestication first became a factor of importance in the Syrian and north Arabian deserts around the eleventh century BC. and, as will be seen, there is much to support the contention besides the absence of camelline remains in Holy Land archaeological sites of earlier date, which was Albright's primary datum. On the other hand, this date need not be taken as the beginning date of camel domestication in an absolute sense. Closer attention to the process of domestication indicates that the camel was actually domesticated long before the year 1100 BC. ..."[7]



Axe head decorated with a camel,
from Qurab, ca. 1,500 BC.

The first cuneiform records – as references to the domestication of camels – date since 1500 BC. when the west-Semitic Arameans invaded Syria and Mesopotamia riding on camels. Dromedaries survived only domesticated, while there exist remainders of wildly living camels. Thus i.a. a cuneiform text from Ugarit (West-Syria) exists, quoted by A. Salonen[8], which gives: „anše-[a]-⌜ab⌝-ba", translated by W.G. Lambert as: „donkey of the sea = dromedary". He points out: "There can be no dispute that these lexical texts from Ugarit go back eventually to Old Babylonian originals from Southern Mesopotamia".[9] "Here then is evidence that the dromedary was known in Southern Mesopotamia in Old Babylonian times." "Perhaps then East Arabia is the region to which we should look for the domestication of the camel."

Point 3 of the above-mentioned pattern of epicrisis lists – concerning cuneiform texts – as pasture livestock: sheep and goats. From the outgoing old-Babylonian period an incantation remains, which after pre-working by others A. Goetze has presented as "An incantation against diseases". From this incantation different text duplicates exist as well as a neo-

6 Bulliet, R.W., The Camel and the Wheel, Columbia: 1990 (orig. ed. 1975), p.46.

7 Bulliet, R.W., p. 36.

8 Salonen, A., Eine lexikalische und kulturgeschichtliche Untersuchung über die Zug-, Trag- und Reittiere, Hippologica Accadica, Helsinki 1955.

9 Lambert, W.G., The Domesticated Camel in the Second Millennium. Evidence from Alalakh and Ugarit, BASOR 160 (1960), pp. 42-43.

Babylonian version. Supplementing a further incantation exists, which is published by A. Cavigneaux (Nr.15289, tablet catalogue of Māri) and treats the same topic.[10]

On this cuneiform incantation tablet a disease is described and exorcised, which for both, humans and animals (lambs, kids, animals of the steppe, no camels respectively dromedaries) was understood obviously as the same illness, as smallpox. It goes without saying that aethiological causes and coherences were not yet known at that time.

If thus from the scientific side the question is still open whether it were goats, sheep or camels, respectively dromedaries, in which the smallpox virus was developed and then changed over to other animals and humans, our philological findings nevertheless permit certain approaches. Of course we do not know, what actually took place before the beginnings of agriculture. In any case we meet in our early cuneiform texts goats and lambs and definitely no camels or dromedaries.

If one follows the considerations J. Diamonds, which were described above, then the findings support the thesis that the smallpox virus originated in the pasture livestock, as there were sheep and goats in early Mesopotamia. They may have been developed wherever, but their emergence as a human infection could be reduced much rather to pasture livestock as to camels.

Conclusion:

If one summarises the scattered references, then in the 2nd Millennium BC. an infectious disease might have been described at different places of the world, which – in all probability – concerns smallpox. G. Seifert[11] sees the spreading of smallpox as follows:

"So one can draw the conclusion with certain caution that the origin of smallpox lies in central Asian areas, perhaps, as Wu Lien-teh[12] accepts, not far from the Caspian Sea. One can assume that they were spread from here over the southern way to India, on the eastern way to Mongol trunks and from them to China, and on the western way over Persia and Arabia to Europe. The smallpox would then have moved similar ways as the plague."

In addition, G. Seifert remarks that all these references are to be evaluated for the most diverse reasons with restraint. The same caution applies to the present. It is therefore of certain importance that in the cultural area of the Ancient Near East cuneiform texts were found, which permit clearer statements concerning the emergence and spreading of smallpox by required critical restraint.

If one refrains from some first working on, which took place in the run-up to these textual analyses, both A. Goetze and A. Cavigneaux identified in these texts only an undifferentiated lining up of different diseases and made the etymological analysis of the individual relevant word to a greater

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10 A detailed study is presented by Th.R. Kämmerer, in UF 27, Neukirchen-Vluyn 1995, p. 129-168.

11 G. Seifert – Du Dscheng – Hsing, Zur Geschichte der Pocken und Pockenimpfung, in Arch. Gesch. Med., Bd.30, Heft 1, Leipzig 1937, S.26-34.

12 Dr. Wu Lien-teh (1879 – 1960), a Chinese physician who studied in Cambridge and fought successfully in 1910 in Manchuria against the pneumonia plague.

extent independently of the whole context. Thus one had probably unconsciously ignored however the train of thought, to understand the given cuneiform records not evenly as different diseases but as symptoms of the same disease. The picture changes, if one tries to subject the contents of these cuneiform sources to a holistic view.

The following diagnosis can be given:

1. Symptoms are described, which are to be added to the smallpox disease.
2. Symptoms arise with animals, which are similar to those with humans.
3. The disease symptoms arise with animal and humans at the same time.
4. They indicate an infection.
5. Obviously a bridge exists between animal and humans.
6. The occurrence of the symptoms (here diseases) in the medically correct order is described.

The molecular-biological antedating of the emergence of the smallpox virus, which is still pending, is the one thing, the proof of their actual occurrence and spreading among humans and animals the other. Anyhow, it would concern periods, from which written certifications may hardly have remained.

As the example of the malaria genome shows, the pathogen and its transmitter, the anopheles mosquito, already existed without the carrier of the disease. Thus the presence of pathogens is not necessarily bound to the existence of its later disease victim. Only many times later the disease with the occurrence of its substrate, the humans, step out of the secrecy and forms with its symptoms a reproducible disease picture. And then as a next step the concerned people must perceive this disease picture. To find out the coherences is the task of the medicine historian.

Altogether one will be depend on written sources. These exist only since the end of the 4th Millennium BC. at all, when the technology of writing on clay tablets gradually took the first place and supplied finally lasting documents. These texts written in Sumerian or Akkadian language finally supply the medicine-historically experienced scientists of Ancient Near Eastern studies with qualified results.

With this renewed processing of those cuneiform texts concerning smallpox two new criteria can be added to the previous knowledge:

1. The bio-archaeology by decoding the genomes of an exciter succeeds in dating the emergence of a specific genome and thus of the exciter itself, in future also those of the smallpox virus.
2. The analysis of the genomes gives however no evidence about the occurrence of a disease and the perception and classification by humans, who became ill. Therefore the philological elaboration of remained cuneiform sources turns out to be absolutely necessary. – Philology and natural science complement each other.

Suggested scheme of development and transmission of the smallpox virus orthopox variola from wild animals via pasture livestock to humans:

180,000 – 100,000 (bio-archaeological records)	**wild animals** (no evidence for camels or dromedaries in the Ancient Near East)	←	**smallpox virus arises** orthopox variola (variola vera) (variola haemorrhagica)
	↓		
9,000 – 6,000 (bio-archaeological records)	**first domesticated pasture livestock (sheep, goats)** (no evidence for camels or dromedaries in the Ancient Near East)	→	**human adults** (settled farmers, mothers) ↘ ↙ (mortal or immunisation) children
	↓		
3,100 – 2,500 (bio-archaeological records and sumerian cuneiform scriptures)	**first records for domesticated pasture livestock in sumerian cuneiform scriptures** (no written evidence for domesticated camels or dromedaries in the Ancient Near East)	→	**the evaluation of sumerian cuneiform sources is still pending**
2,500 – 1,800 (bio-archaeological and archaeological records, sumerian and akkadian cuneiform scriptures)	**first records for non domesticated camels and dromedaries in art** (camelus dromedarius, camelus bactrianus)	↓	**Umm an-Nar (Oman)** (2,500 BC: relief of a non yet domesticated camel)
1,800 onwards (bio-archaeological and archaeological records, sumerian and akkadian cuneiform scriptures)	**first records for smallpox-infected livestock pasture <u>and</u> humans in akkadian cuneiform scriptures** (no written evidence for any coherence between smallpox-infected humans and domesticated camels or dromedaries in Ancient Near East)	→	**Māri (East-Syria)** (1st half of the 2nd Millennium: old-Babylonian incantations)