Mat goes into me

With literacy arose the industry of ink-making

ANANTHANARAYANAN

he cuneiform is an ancient form of writing, in clay, using a stylus made of reed, which left a wedge-shaped impression hence the word *cuneiform*, which means "wedge-shaped". And there was carving, on seals or temple walls. But the best ancient records are writing with inks, on papyrus, or more commonly in India, on palm leaves.

What this means is that some ancient writing has been preserved for over 2,000 years. This is more than we can say of most of the records we create today. And it speaks of the sophistication of ink-making in ancient times. Thomas Christiansen, Marine Cotte, Wout de Nolf, Elouan Mouro, Juan Reves-Herrera, Steven de Meyer, Frederik Vanmeert, Nati Salvadó, Victor Gonzalez, Poul Erik Lindelof, Kell Mortensen, Kim Ryholt, Koen Janssensd, and Sine Larsenj, from the Universities of Copenhagen, Sorbonne, Pierre and Marie Curie, Paris, Antwerp, Catalonia, the National Museum of Denmark and the Synchrotron facility in Grenoble, France, write, in the journal, *PNAS*, of their work with the red and black inks found on Egyptian papyri. While they found that iron and lead were used in the pigments, they worked out that iron was the colourant while lead was for fixing stains.

Black inks were usually made by mixing carbon black with a thickening and adhesive agent, like oils and animal glue. The mixture was then ground and allowed to dry, for moistening when needed for use. The ink was applied with a reed pen and the carbon stayed on the writing surface when the ink dried. The paper in *PNAS* says that examples of writing, with ink on papyrus, have been found in ancient Egypt from more than 5,000 years ago, and the examples are both of black ink, and red ink that was used for headings or emphasis. While soot was the main component of black ink, red ink made use of ochre,

the red oxide of iron. The paper says that different kinds of black ink were developed over the ages, some containing copper or lead, along with carbon, and those have been fairly well studied.



The earliest black ink was carbonbased and invented in China, though it is known as India Ink. This was perhaps because some of the constituents came from India. Nearer home, it is said that the accountants from the Marwar region of Rajasthan had their own method to make black ink. The method involved allowing iron nails to rust in a bath Now, fading of ink is the feature that allows forgeries or changes in writing, carried out after a delay, to be detected. Clients of the accountants of Marwar, however, had a way out

years after they were written. The accountants stored each year's stock of ink in pots buried in a vault below their place of work. When a client who wanted changes came to them, they could pull out the bottle with the ink used when the entries were made, and the new writing would look no different from what was being changed!

if they needed to alter their books even

The nature of red ink, however, has received less attention. The authors of the paper hence undertook detailed analysis of the black, red and pink inks found on a selection of fragments of several manuscripts from the so-called Tebtunis temple library, an institutional library, the only one to survive, of ancient Egypt.

The Tebtunis library was discovered in 1899-1900, during excavations at the site of the ancient city, now the village of Umm-el-baragat, in Egypt, some 100 kms southwest of Cairo. The library was inside the main temple precinct and threw up thousands of fragments of some 500 manuscripts --

blages of papyri unearthed in the sands of Egypt," the paper says, "The papyri selected for analysis were acquired in 1931 to 1938 by the Carlsberg Foundation on (sic) the antiquities market in Cairo. Today they are housed in the Papyrus Carlsberg Collection at the University of Copenhagen."

Earlier analyses of the red and pink inks had shown that they had iron and lead compounds, and ochre, the oxide of iron had been identified, but none of the methods used had provided information about the nature of the lead-based compounds, the paper says. The use of lead compounds to produce pigments was also documented, but those compounds had not been found in papyri. While the compound, red lead, had been used in some applications, its use in pigments was much later. The present investigation was hence directed to pinning down the iron and lead compound found in the writing on papyri. And to this end, the authors went back to papyrus fragments in the Carlsberg Collection.

Detailed analyses, with high energy X-ray probes, generated at the particle accelerator at Grenoble, to reveal the structure, and analysis of infra-red absorption to reveal the chemical bonds, were used to study the elements and chemical composition of the tiniest grains of the pigment material. With 12 samples and two colours, there were 24 samples in



all, and variations in the papyrus and the thickness of the ink had to be factored in, with statistical analysis to arrive at reliable estimates of the composition.

The results were that almost all the red samples contained iron and lead, aluminium, sometimes with magnesium, silicon and potassium. The elements in the red samples corresponded to the ores of iron, notably the oxide, ochre, with clay and sand intermixed. The composition of the lead content was also made out, with it forming rings around specks of ochre, in the red pigment and in the papyrus.

Lead was found to be present in both the red and black samples. The lead compounds, however, were not the forms that were later documented for use with pigments. This observation, that the lead compounds would not contribute to colour and that they

were found in the black ink as well as the red ink, suggests that they were not there for colour, but for other properties, like enabling drying. The paper refers to other records of the paint recipes of master painters in later centuries, and close chemical analysis, to conclude that the lead content was only for drying the pigment and added at the time of preparation.

Considering the volume of the manuscripts and the writing, it is not likely that the temple priests mixed their own inks, they must have relied on specialised workshops, the paper says. "The results presented in this article have provided valuable information on the preparation and composition of red and black inks in ancient Egypt and Rome some 2,000 years ago," the paper concludes.

The writer can be contacted at

MORE SUSCEPTIBLE

Here's why men may have a worse response to Covid-19 than women

MEGHAN E REBULI

f you ask most women about how their male relatives, partners and friends respond to being sick, they'll often tell you with an accompanying eye roll, "He's such a baby." "He's extra whiny." Or "he exaggerates so much." But there may be a biological explanation for this behaviour.

Dubbed the "man flu," this phenomenon has been validated in a review of previously published, large epidemiological studies, as well as in studies of influenza in animals. In these studies, males were sick longer, with more severe symptoms and had a weaker response to vaccination. Laboratory tests with animals infected with the influenza virus also underscore that there are sex-based differences in immune response that influence outcomes observed in humans. But are these more severe symptoms and outcomes unique to

cold and flu? As a respiratory toxicologist and researcher investigating sex differences in the respiratory system, I was intrigued to read a recent study on sex-specific responses to Covid-19 that suggest that men are, actually, more vulnerable and suffer more from this disease.

Sex differences in Covid-19

These findings may apply to other respiratory viruses like Sars-CoV-2, which causes Covid-19. For example, reports of Sars-CoV-2 infection rates are similar between males and females, but male sex is a significant risk factor for more serious Covid-19 disease and death. In fact, one study revealed that men are 2.4

times more likely to die from Covid-19. I find it interesting that higher death rates in men also occurred in other coronavirus diseases like severe acute respiratory syndrome, caused by Sars-CoV, and Middle East respiratory syndrome.

Based on data from the Centers for Disease Control and Prevention as of 5 October 2020, the risk of death from Covid-19 in men 30-49 years old was also found to be more than twice that of females. In other age groups, the risk of Covid-19-related death in males was also higher than the same female age cohort. But it was not as high as in the 30 to 49-year-old age group.

This contrasts with almost equal rates of Sars-CoV-2 infection in those same age groups, leading scientists to wonder why males might be more susceptible.

Study identifies why men may be more susceptible to Covid-19

The recent report published in Nature explores how males and females respond differently to Covid-

19.

This study examined samples including nasal swabs, saliva, and blood, which were either collected from healthy individuals or Covid-19 patients. These samples were used to better understand what the immune response to the infection looks like and how it differs in people with more severe disease.

Similar to CDC data on infection rates, no sex difference in the concentration of virus or the amount of virus present was observed in either the nasal swab or the saliva. There were also no differences in antibody levels -



virus – detected in infected men and

Males with Sars-CoV-2 show greater inflammation

However, the authors identified major sex differences during the early immune response that occurs soon after someone is infected with the Sars-CoV-2 virus.

The blood samples were analysed for a variety of cytokines some of the first signalling molecules that help immune cells respond to pathogens. The levels of these signals rise and fall to provide an adequate response to fight an invading pathogen. But large quantities of these molecules can severely damage the body. This is the case in a cytokine

The authors of the Nature report observed sex differences in the strength of the cytokine response. Men showed higher levels of cytokines that trigger inflammation, like IL-8 and IL-18, than women. Higher quantities of these cytokines are linked to more severe disease. In severe cases of Covid-19, fluid builds up in the lungs, reducing the oxygen available in the body for normal functions. This can lead to tissue damage,

- a signal the body had identified the shock and potentially the failure of ing large gatherings and ignoring multiple organs.

Females with Sars-CoV-2 are better prepared to eliminate the

In addition to sex differences in cytokine levels, the authors also found sex differences in the function of immune cells.

Compared to men, women had a higher number of T cells – essential for eliminating the virus – that were activated, primed and ready to respond to the Sars-CoV-2 infection. Men with lower levels of these activated T-cells were more likely to have severe disease.

Thus, there are several aspects of the human immune response to Sars-CoV-2 that differ between men and women. Understanding these differences can inform how doctors treat patients and can help researchers develop sex-specific therapies.

Increased Covid-19 susceptibility in men is likely biological

These results contradict speculation that male susceptibility to Sars-CoV-2 infection is due to more risky behaviours. Those include downplaying the seriousness of the virus, joinsocial distancing guidelines, as well as lower rates of hand-washing and wearing masks. Instead, rates of infection are similar between males and females, while males are more at risk of serious Covid-19 disease, suggesting biological differences in response to infection.

This paper is one of the first of its kind to delve into mechanisms of susceptibility sex differences. With greater innate biological risk for severe disease and death in men, this suggests that males might need to be hypervigilant about social distancing,

hand-washing and mask-wearing. Greater adherence to infection prevention protections, especially in men, would not only reduce their risk of infection, but also combat their increased risk of severe disease and death from Covid-19.

The take-home message of this new paper is that researchers need to consider strategies to ensure treatments and vaccines are equally effective for both women and men, especially when one is more susceptible than another.

The writer is assistant professor of paediatrics, University of North Carolina at Chapel Hill, US. This article first appeared on www.theconversation.com

PLUS POINTS

Transmission numbers

Reopening schools following coronavirus lockdowns is linked to a surge in transmissions within a month, according to the first study to look at the impact of lifting restrictions on the R

R represents the average number of people each person with Covid-19 goes on to infect. When the figure is above one, an outbreak can grow exponentially.

Children's return to classrooms was followed by an average 24 per cent rise in the R transmission number, University of Edinburgh researchers found after analysing data from 131 countries. The only other measure linked to a higher increase in the rate is lifting a ban on groups gathering, which led to a 25 per cent rise in R. To create their models, the authors linked data on country-level R estimates from the London School of Hygiene & Tropical Medicine with information about non-pharmaceutical interventions from the Oxford Covid-19 government response tracker.

Reopening schools was associated with a 24 per cent increase in R after 28 days, although the researchers cautioned they were unable to account for different precautions some countries implemented for reopening schools, such as limiting class sizes, social distancing, cleaning, personal hygiene, face masks, and temperature checks.

"We found an increase in R after reopening schools but is not clear whether the increase is attributable to specific age groups, where there may be substantial differences in adherence to social distancing measures within and outside classrooms," said Harish Nair, professor of paediatric infectious diseases at the University of Edinburgh. "Furthermore, more data are needed to understand the specific role of schools in increased Sars-CoV-2 transmission through robust contact tracing."

The study, published in The Lancet Infectious Diseases journal, also created models of the impact combinations of measures had on the R rate when introduced. They found a comprehensive package of restrictions including public



events bans, school closures, a ban on gatherings of 10 or more people, widespread home-working, and stay-athome orders was linked to the biggest fall in R rate. Transmissions fell by 52 per cent within four weeks when those measures were all introduced.

The least comprehensive package of measures – a ban on public events and gatherings of more than 10 people -- would reduce R by 29 per cent by day 28, the study concluded. Looking at the measures individually, a ban on public events was associated with the greatest reduction in R, amounting to a 24 per cent reduction after 28 days.

Nair said, "Our study can inform decisions on which measures to introduce or lift, and when to expect to see their effects, but this will also depend on the local context -- the R number at any given time, the local healthcare capacity, and the social and economic impact of measures."

The researchers also analysed Google mobility data, modelling visits to workplaces and time spent in residential areas. Results indicated that people took some time to adapt their behaviour to comply with workplace closures and stay-at-home requirements, which was like the delay between the measures and the effects seen on R of between one and three weeks. Researchers suggested the delay was possibly due to the population taking time to modify their behaviour to adhere to measures.

They said some of the greatest effects on R were seen for measures that were more easily enforceable by law, like schools reopening and public events bans. This may have been because their effects were more immediate and compliance was easier to ensure, the researchers added.

Chris Bauch, a professor of applied mathematics at Canada's University of Waterloo and who was not involved in the research, said the study "could be highly valuable for optimising a country's" coronavirus rules as its findings "tell us that non-pharmaceutical interventions work and which ones work best".

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