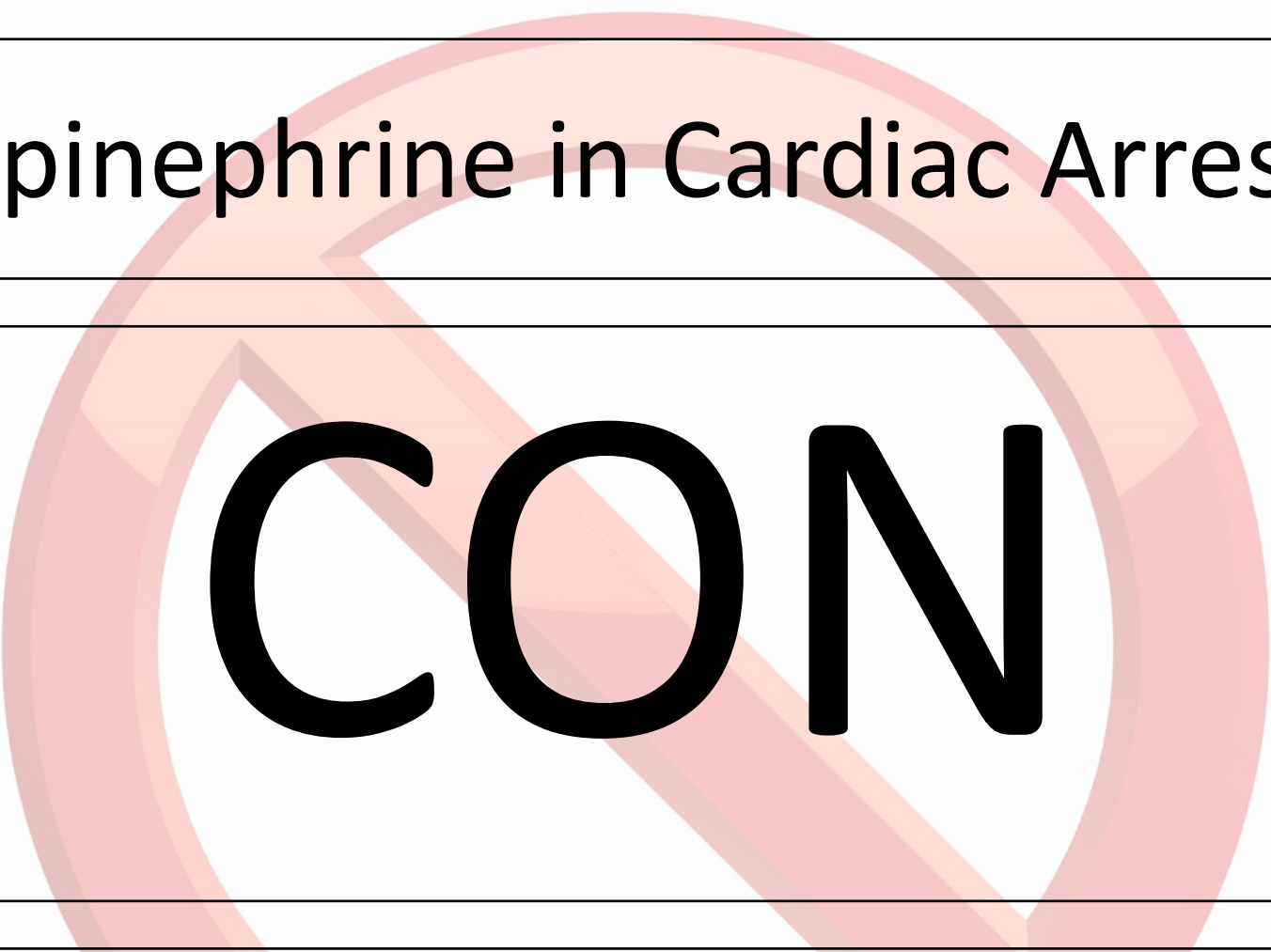
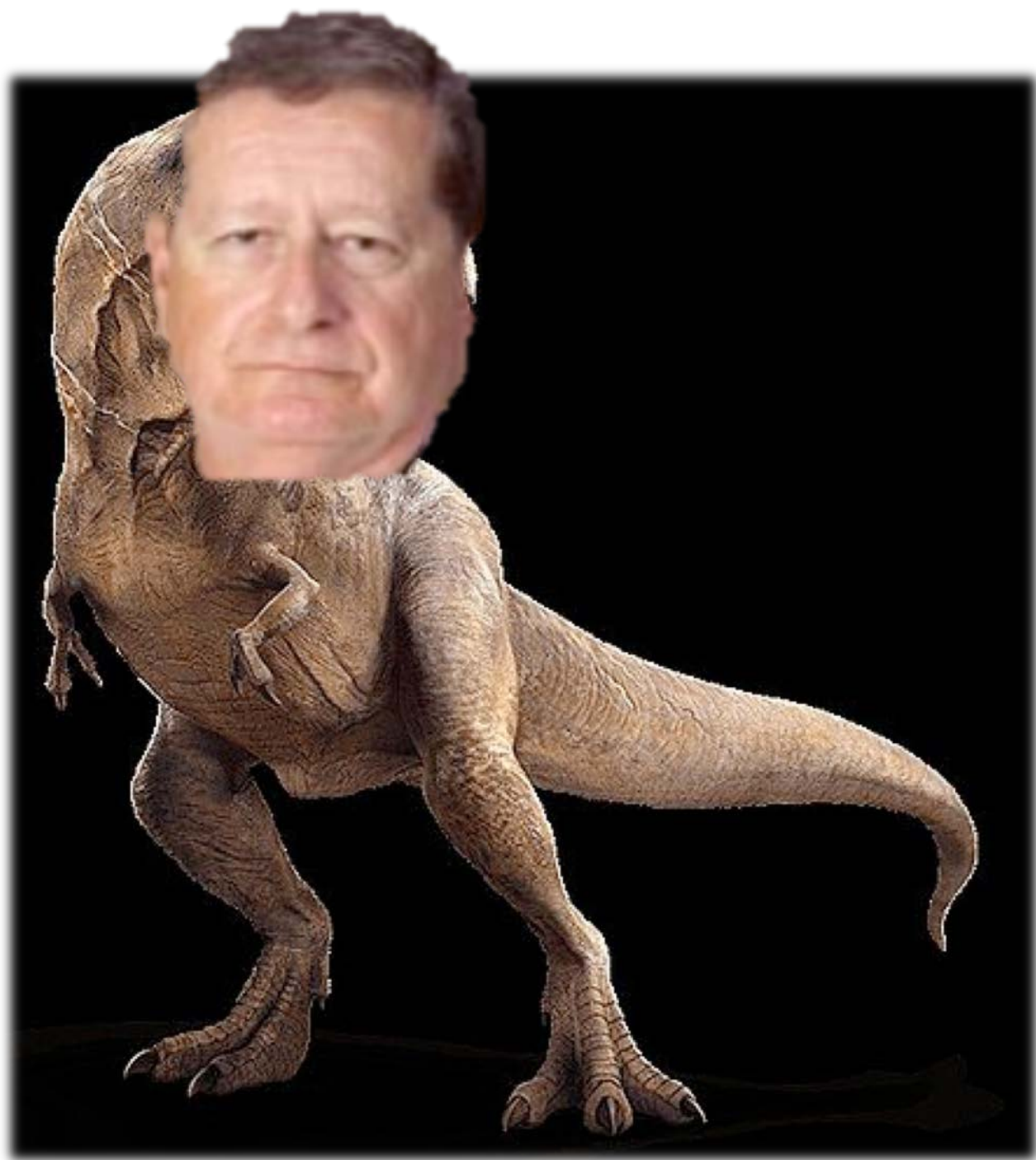


Epinephrine in Cardiac Arrest



CON

Ray Fowler, MD, FACEP, FAEMS
Professor and Chief, Division of EMS
James M. Atkins Professor of EMS
University of Texas Southwestern







Epinephrine...what do we know?

Observational studies involving more than 500,000 patients have reported higher rates of return of spontaneous circulation but **worse neurologic outcomes** in patients who were treated with epinephrine. The interpretation of these findings has been limited by conflicting results and the influence of unmeasured confounders.

For Example...



JAMA. 2012 Mar 21;307(11):1161-8. doi: 10.1001/jama.2012.294.

Prehospital epinephrine use and survival among patients with out-of-hospital cardiac arrest.

Hagihara A¹, Hasegawa M, Abe T, Nagata T, Wakata Y, Miyazaki S.

DESIGN SETTING AND PARTICIPANTS.

***Hagihara,
2012***

JAMA. 2012 Mar 21;307(11):1161-8. doi: 10.1001/jama.2012.294.

Prehospital epinephrine use and survival among patients with out-of-hospital cardiac arrest.

Hagihara A¹, Hasegawa M, Abe T, Nagata T, Wakata Y, Miyazaki S.

CONCLUSION:

Among patients with OHCA in Japan, use of prehospital epinephrine was significantly associated with increased chance of return of spontaneous circulation before hospital arrival but decreased chance of survival and good functional outcomes 1 month after the event.



...or, more recently



The NEW ENGLAND
JOURNAL of MEDICINE

The ***PARAMEDIC 2*** *Trial*

August 23, 2018

N Engl J Med 2018; 379:711-721

DOI: 10.1056/NEJMoa1806842



The NEW ENGLAND
JOURNAL of MEDICINE

A Randomized Trial of Epinephrine in Out-of-Hospital Cardiac Arrest

METHODS

In a randomized, double-blind trial involving 8014 patients with out-of-hospital cardiac arrest in the United Kingdom, paramedics at five National Health Service ambulance services administered either parenteral epinephrine (4015 patients) or saline placebo (3999 patients), along with standard care. The primary outcome was the rate of survival at 30 days. Secondary outcomes included the rate of survival until hospital discharge with a favorable neurologic outcome, as indicated by a score of 3 or less on the modified Rankin scale (which ranges from 0 [no symptoms] to 6 [death]).



The NEW ENGLAND
JOURNAL of MEDICINE

A Randomized Trial of Epinephrine in Out-of-Hospital Cardiac Arrest

RESULTS

At 30 days, 130 patients (3.2%) in the epinephrine group and 94 (2.4%) in the placebo group were alive (unadjusted odds ratio for survival, 1.39; 95% confidence interval [CI], 1.06 to 1.82; $P=0.02$). There was no evidence of a significant difference in the proportion of patients who survived until hospital discharge with a favorable neurologic outcome (87 of 4007 patients [2.2%] vs. 74 of 3994 patients [1.9%]; unadjusted odds ratio, 1.18; 95% CI, 0.86 to 1.61). At the time of hospital discharge, severe neurologic impairment (a score of 4 or 5 on the modified Rankin scale) had occurred in more of the survivors in the epinephrine group than in the placebo group (39 of 126 patients [31.0%] vs. 16 of 90 patients [17.8%]).



The NEW ENGLAND
JOURNAL of MEDICINE

A Randomized Trial of Epinephrine in Out-of-Hospital Cardiac Arrest

*“...more survivors had
severe neurologic impairment
in the epinephrine group...”*

(Funded by the U.K. National Institute for Health Research and others; Current Controlled Trials number, [ISRCTN73485024](https://www.clinicaltrials.gov/ct2/show/study?term=ISRCTN73485024).)

*Is that
so surprising?!?*

Epinephrine in Cardiac Arrest

Epinephrine (adrenaline) has potentially beneficial effects in cardiac arrest through the constriction of arterioles mediated by α -adrenergic receptors. Such constriction increases aortic diastolic pressure during CPR, thereby augmenting coronary blood flow and increasing the chance of a return of spontaneous circulation.

“Epinephrine might in fact exacerbate the condition of suboptimal exchange of oxygen and carbon dioxide associated with progressive hypoxemia and hypercarbia observed during asphyxia cardiac arrest.”

G. Ristagno, 2007

“Unsuccessful outcomes after successful CPR are in part caused by impaired cerebral function caused by ischemic brain injury, and we therefore believe that it would be appropriate to reevaluate epinephrine as the drug of first choice for cardiac resuscitation, especially under the particular condition of asphyxia cardiac arrest. ”

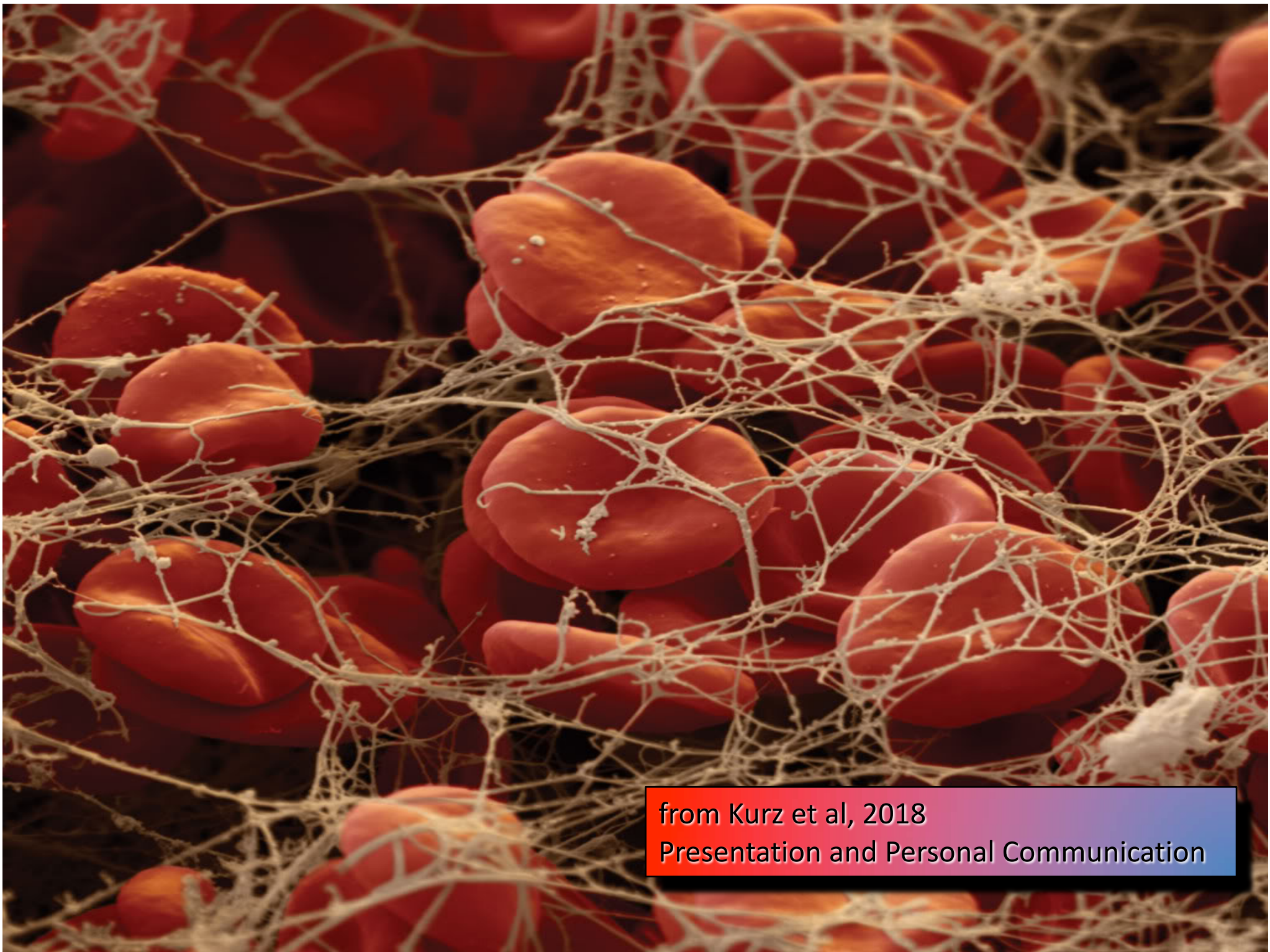
G. Ristagno, 2007



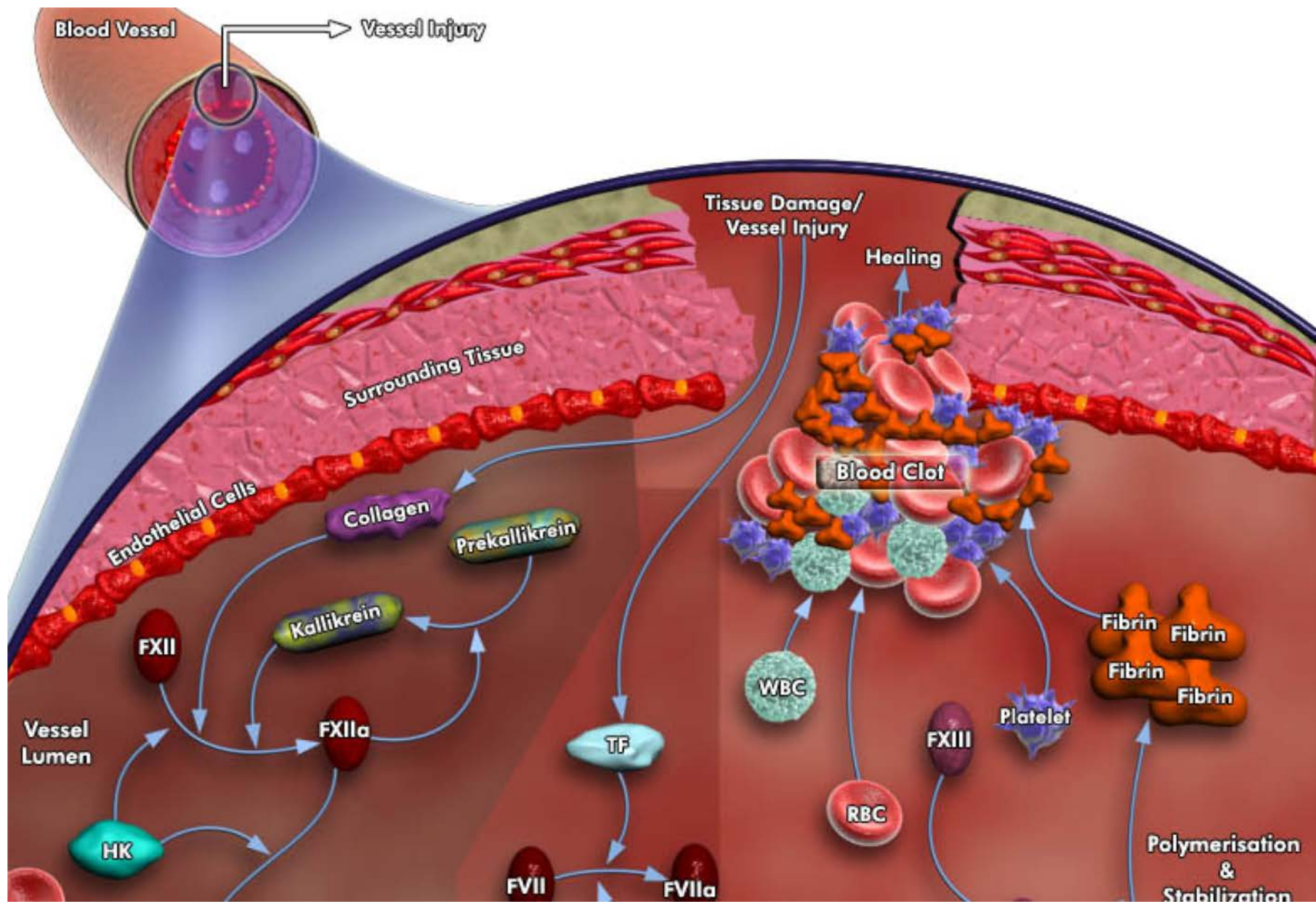
*But what else
about the heart stopping?*

Epinephrine in Cardiac Arrest

α -adrenergic stimulation causes platelet activation, which promotes thrombosis and impairs the microvascular blood flow in the cerebral cortex

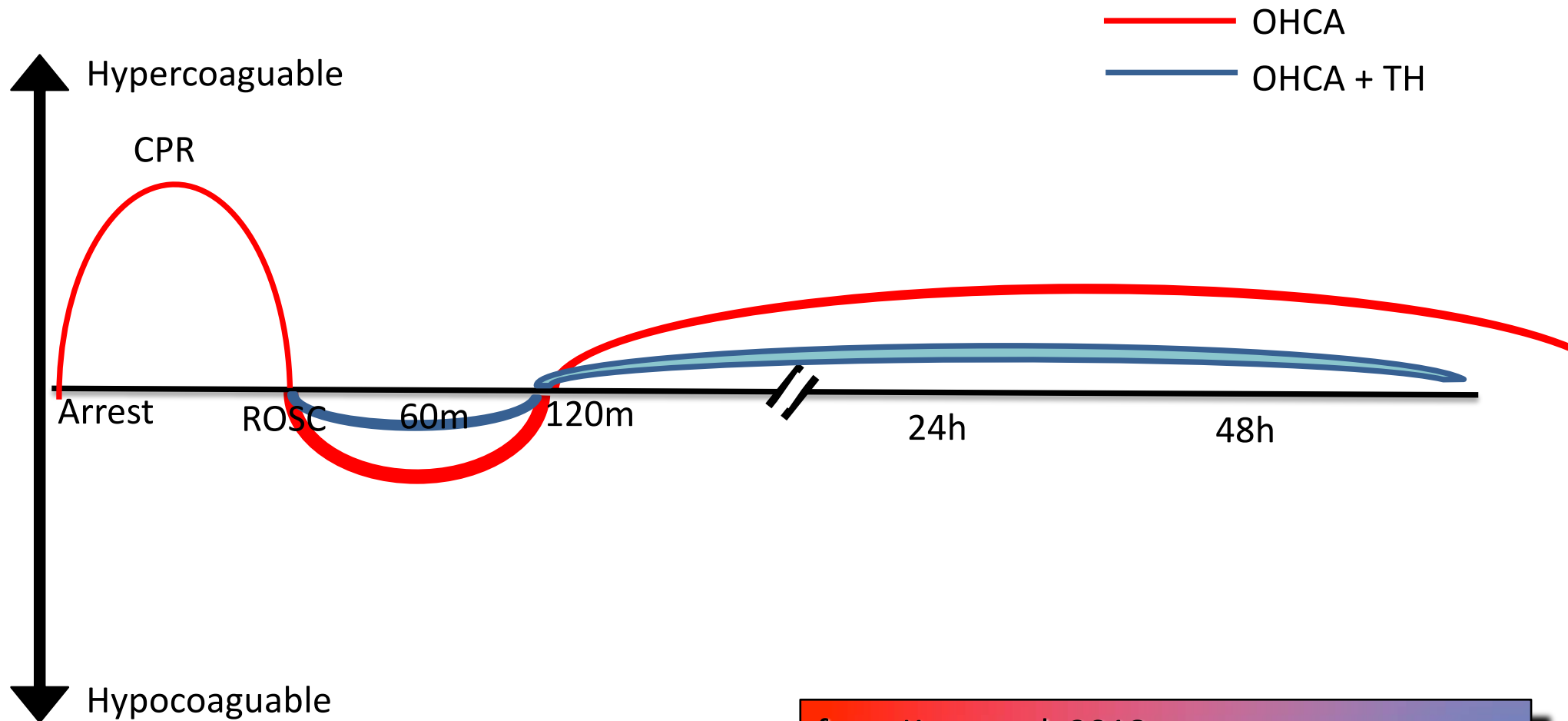


from Kurz et al, 2018
Presentation and Personal Communication

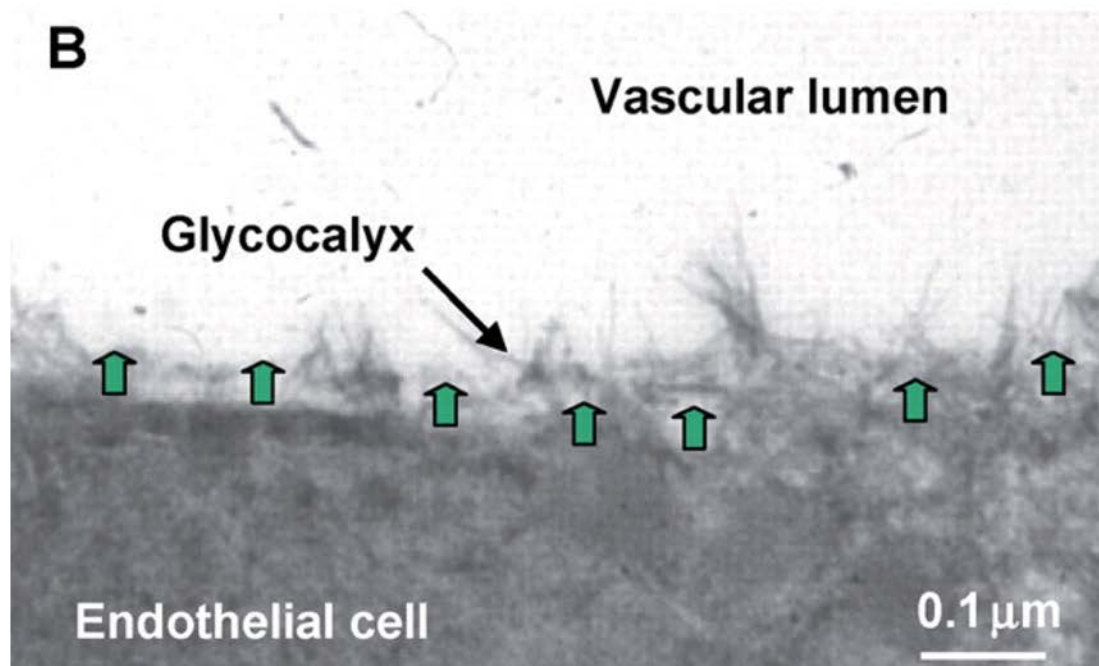
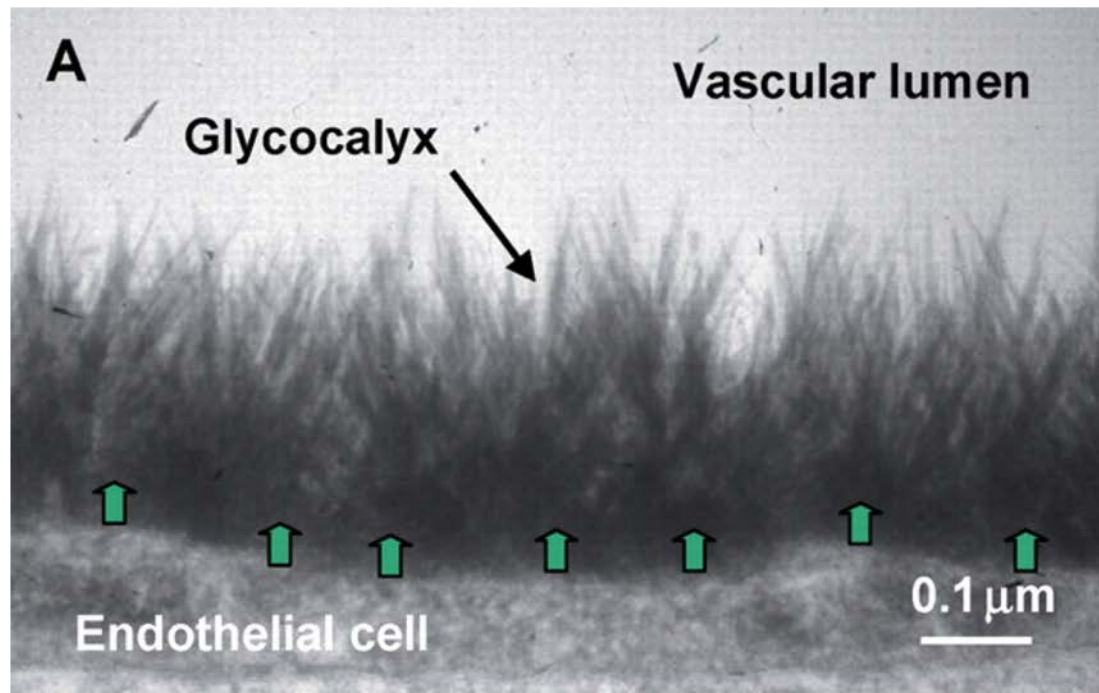


from Kurz et al, 2018
Presentation and Personal Communication

The trajectory of coagulation following OHCA...



from Kurz et al, 2018
Presentation and Personal Communication



from Kurz et al, 2018 Presentation and Personal Communication

*Is this a
new finding?*

AN EXPERIMENTAL
CITATION

By GEORGE W. CRILE
(From the Laboratory of

RESUSCITATION
ETICS

M.D.
Medical School,

Crile
1906

©-H. S. J. 1906
CHICAGO



AN EXPERIMENTAL RESEARCH INTO THE RESUS-
CITATION OF DOGS KILLED BY ANESTHETICS
AND ASPHYXIA.

By GEORGE CRILE, M.D., AND DAVID H. DOLLEY, M.D.

*(From the Laboratory of Surgical Physiology, Western Reserve Medical School,
Cleveland.)*





ANNALEN DER PHYSIK.

BEGRÜNDET UND FORTGEFÜHRT DURCH
F. A. C. GREY, L. W. GILBERT, J. C. POGGENDORFF, G. UND E. WIEDEMANN.

VIERTE FOLGE.

BAND 17.

DER GANZEN REIHE 322. BAND.

KURATORIUM:

F. KOHLRAUSCH, M. PLANCK, G. QUINCKE,
W. C. RÖNTGEN, E. WARBURG.

UNTER MITWIRKUNG

DER DEUTSCHEN PHYSIKALISCHEN GESELLSCHAFT

UND INSBESONDERE VON

M. PLANCK

HERAUSGEGEBEN VON

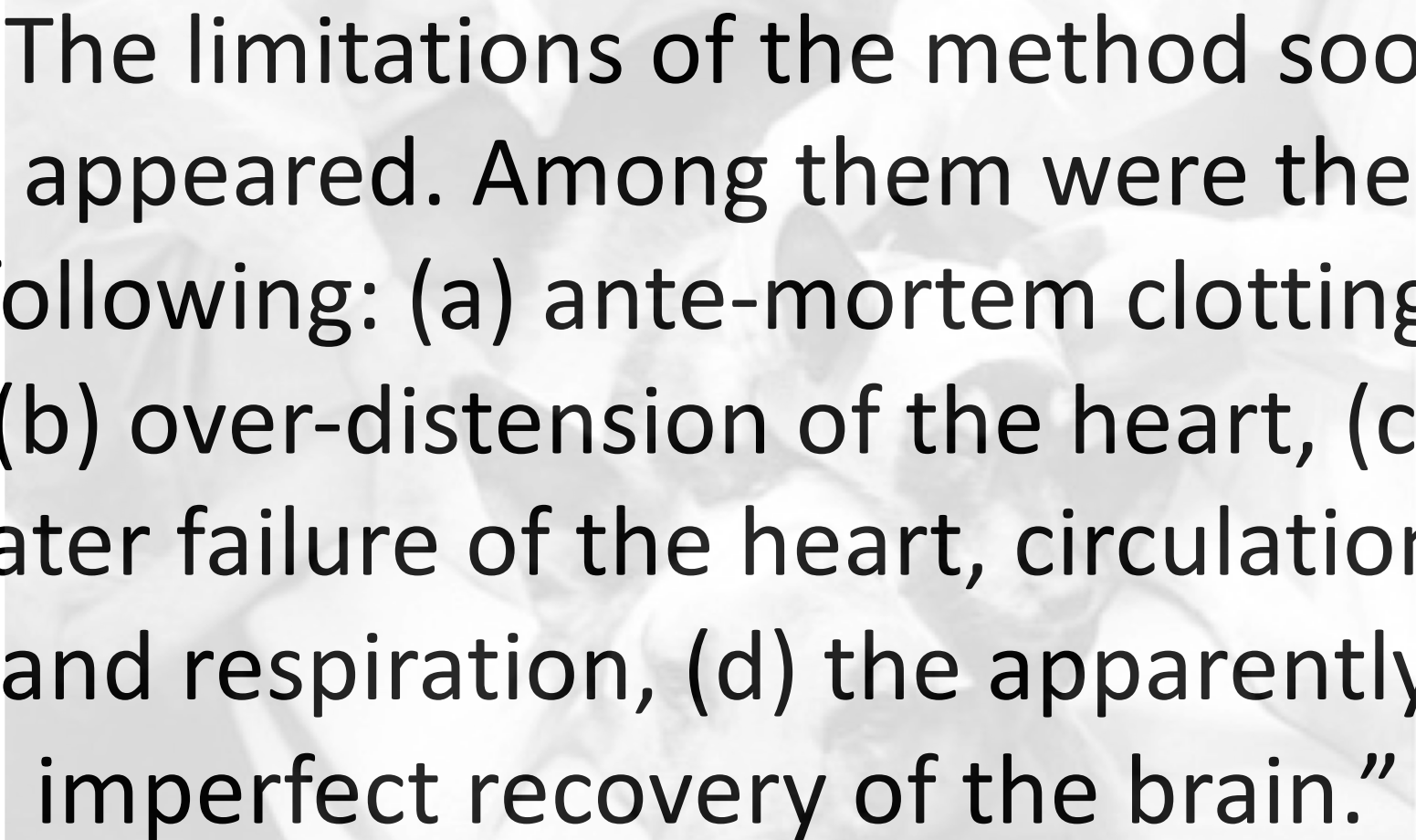
PAUL DRUDE.

MIT FÜNF FIGURENTAFELN.



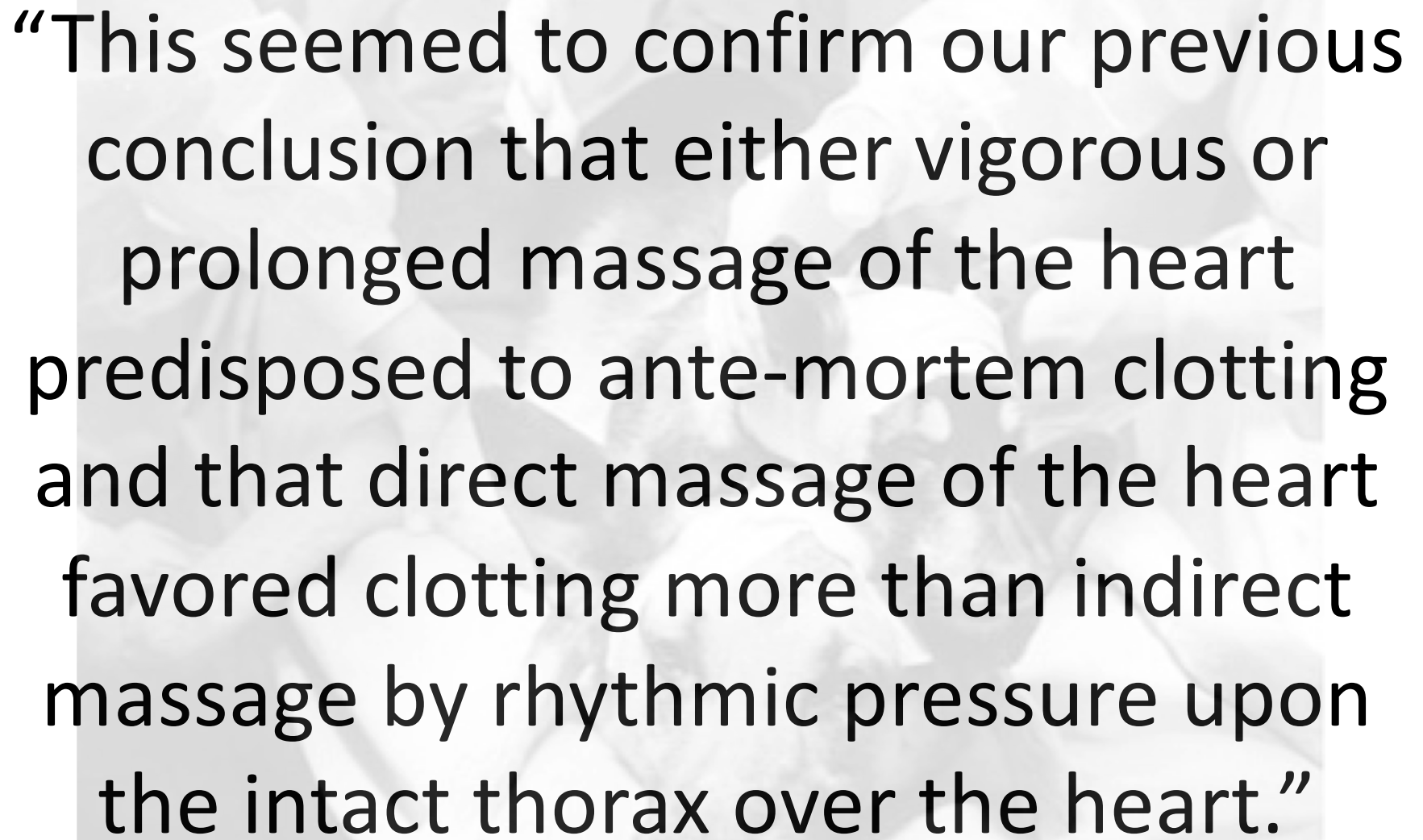
LEIPZIG, 1905.

VERLAG VON JOHANN AMBROSIOUS BARTH.



“The limitations of the method soon appeared. Among them were the following: (a) ante-mortem clotting, (b) over-distension of the heart, (c) later failure of the heart, circulation, and respiration, (d) the apparently imperfect recovery of the brain.”

Crile, 1906



“This seemed to confirm our previous conclusion that either vigorous or prolonged massage of the heart predisposed to ante-mortem clotting and that direct massage of the heart favored clotting more than indirect massage by rhythmic pressure upon the intact thorax over the heart.”

Crile, 1906

“We also observed what on *a priori* grounds we supposed to be true, namely, that a tendency to clotting was increased in a direct ratio with the lapse of time. When clotting occurred resuscitation was practically always impossible. The heart would beat for a short time, but the beat would soon fade away.”

Crile, 1906

Some Summary Thoughts

What did we learn 112 years go?

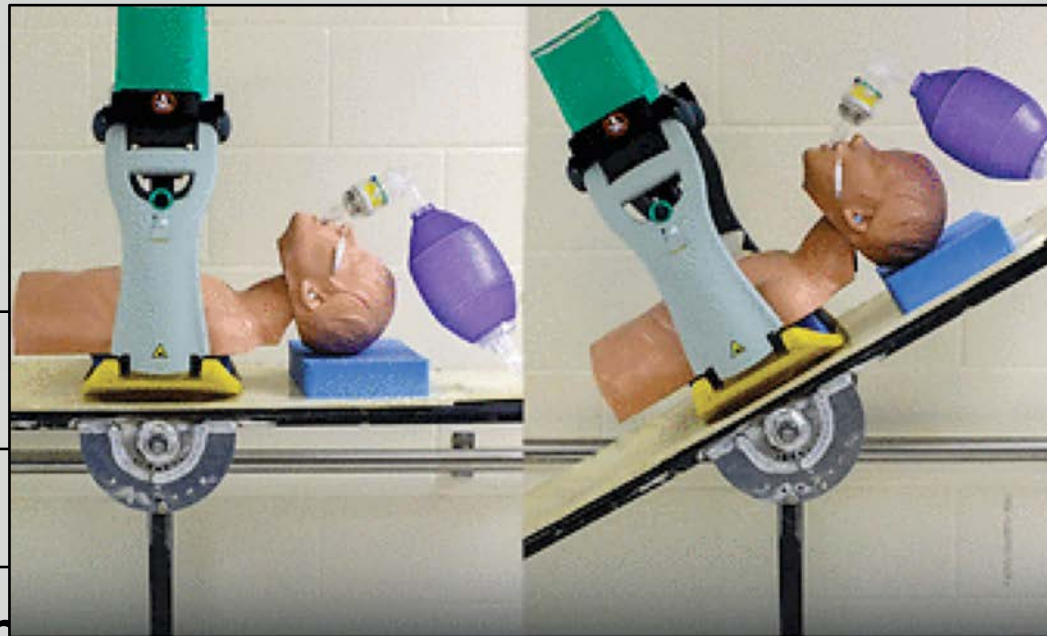
- Animals after death from chloroform, ether, or asphyxia up to five minutes were uniformly and readily resuscitated
- After twenty-three minutes in adult dogs and thirty-five minutes in puppies complete return of the circulation was not accomplished.
- After death from chloroform and ether animals were more readily resuscitated than after death from asphyxia.

What did we learn 112 years go?

- Resuscitation, if successful, occurred within one minute after the administration of adrenalin in the majority of instances ; it rarely occurred after an interval greater than three minutes.
- The greatest difficulty to be overcome was clotting. The probability of clotting increased in direct ratio with the lapse of time after death. Cardiac trauma predisposed to clotting.
- The younger the animal, up to certain limits, the more readily it was resuscitated.

What did we learn 112 years go?

- The probable success of resuscitation is greater in inverse relation to the lapse of time after death; a rapid rise in the arterial pressure is attained by arterial infusion with a therapeutic dose of adrenalin, together with good artificial respiration and the avoidance of unnecessary cardiac trauma by massage.



- Body isn't pressure
- A more optimiz

AND THE DEAD SHALL RISE

Head-up CPR & the revolutionary research model used to develop it

By **Ralph J. Frascione, MD, FACP, FAEMS**

What do the high rises in Seoul, South Korea, have to do with the hemodynamics of CPR? You'll be amazed. Seoul has a very dense population and many of their apartment buildings are 40 stories or more, with very small elevators that have always presented challenges to EMS crews. In fact, the elevators are so small that when a cardiac arrest occurs, the patient can't be loaded and transported in a flat position. Instead, the patient must be put in the elevator diagonally with the head up or down.

On a visit to the Twin Cities, Sung Do Shin, a

physician from Seoul, told Keith Lurie, MD—a highly respected cardiac arrest researcher and inventor of the active compression-decompression CPR (ACD-CPR) device ResQPUMP® and the impedance threshold device (ITD) ResQFPOD®—that he thought the best position for the patient's head while taking the elevator to ground floor should be down. Lurie immediately replied that the patient's head should be up and that he would prove it.

Although Lurie is a lifelong, dedicated researcher who has been working on the hemodynamics of CPR nearly his entire career, he'd

never worked on this specific question. In the lab, he put pigs in a flat position and then treated them on a tilt table with a mechanical chest compression device performing CPR and with an ITD. Coronary and cerebral perfusion pressures were measured along with blood flow in the heart and brain.

The measurements were recorded with the pigs positioned at 30 degrees head down, upright and 30 degrees head up. (See Figure 1, p. 34.) The results were remarkably consistent. (See Figure 2, p. 34, and Figure 3, p. 35.) All four parameters were significantly improved with the pig's heads up at 30 degrees. More striking, the pigs started to gasp spontaneously when in the head-up position.

Although it was clear that the pigs did better with their head up, it wasn't clear what the ideal elevation should be. Therefore, the same parameters were measured at 0, 20, 30, 40 and 50 degrees. All parameters improved linearly as the elevation increased. (See Figure 4, p. 36.) Thirty degrees appeared to have the best balance between decreased intracranial pressure (ICP), increased cerebral flow and aortic pressure.

Now Lurie faced the challenge of proving this in humans.

Hemodynamic trials are extremely cumbersome and difficult to study in cardiac arrest—especially prehospital trials.



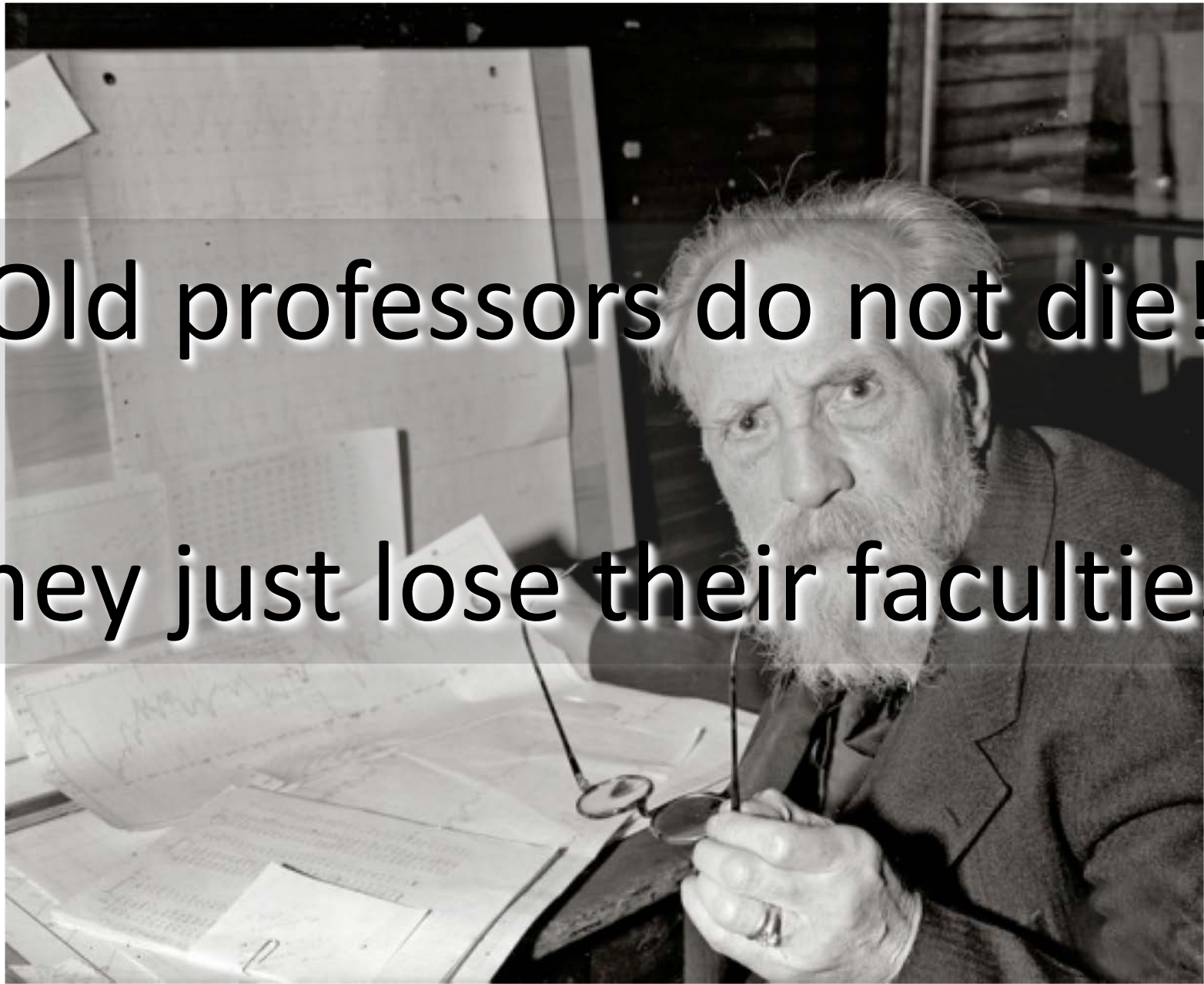




Terry, Terry, Terry!!!
Come INTO the 21st Century!!!



Old professors do not die!
They just lose their faculties!



A photograph of a large, light-colored stone sign for the UT Southwestern Medical Center. The sign features the 'UT' logo and the text 'SOUTHWESTERN MEDICAL CENTER'. Above the main text, the number '5323' is visible. The sign is set in a landscaped area with green grass, pink flowers, and trees. In the background, a multi-story building is visible under a clear blue sky.

Thank you!

www.rayfowler.com