



From Hippocrates to HUGO and back again - humanistic lessons from hi-tech science

Linn Getz, MD PhD





OUTLINE OF LECTURE

- I. Hippocrates, HUGO, Hi-tech and Humanistic -
- II. A very brief history of the 'mindset' of scientific medicine, illustrated by Helena, a woman with many problems, including high blood pressure

Meta-analysis 1: "Once the rockets are up...."

Meta-analysis 2: "Rough God"

Meta-analysis 3: "The healing game"

- III. *Ad fontes (back to the origins):*
Medicine is a moral enterprise, - it is about helping.
Science provides essential tools, but not the aims

Hippocrates of Cos (ca. 460 BC – 370 BC)

Founder of modern scientific medicine in the age of Classical Athens

HUGO Humane Genome Project (ca. 2001)

Complete sequencing of the human DNA

Hi-tech representing ‘the cutting edge’ of natural science medical research

Humanism “a rational philosophy informed by science, inspired by art, and motivated by compassion”.



The brains (or minds?) behind the meta-analyses



Tom Lehrer (b. NY 1928)
Harvard mathematician and songwriter



Van Morrison (b. Belfast 1945)
“a painfully introverted figure who rarely gives interviews and is often at a loss to explain his own lyrics.”

- *The Rolling Stone Encyclopedia of Rock & Roll*, 2001

The dawn of scientific, medical thinking



Antiquity (400 B.C) : Diseases natural, but under environmental influence. Healing powers of nature.

“.... no one disease is either more divine or more human than another, ... no one (disease) arises without a natural cause.”

*Source: The Corpus. On Airs, Waters and Places.
In: Hippocratic Writings; Kaplan Classics of Medicine 2008:139*



Ancient Greek understanding of disease and the role of the physician

Of the Epidemics, Section III. The Corpus. Hippocratic Writings, 2008: 159

“1. With regard to diseases, the circumstances from which we form a judgement on them are, - by attending to the general nature of all, and the peculiar nature of the individual, - to the disease, the patient and the applications, - to the person who applies them, as that makes a difference for better or for worse, - to the whole constitution of the season, and particularly to the state of the heavens, and the nature of each country; to the patient's habits, regimen and pursuits; - to his conversation, manners, taciturnity, thoughts, sleep, or absence of sleep, and sometimes his dreams, what and when they occur; - to his picking and scratching; to his tears; - (*to... here follows a long list of physical symptoms and signs incl. urine/ sputum/ vomitings/ sweat/ rigor,.....*) - from these, and their consequences, we must form our judgement.”

The roots of modern biomedicine

1600- The scientific revolution and enlightenment. Dualism; the human body as a physical object. Laws of the natural sciences. Progress!



....Vesalius (The humani corporis fabrica), Galileo, Harvey (circulatory system), Descartes, Newton, Boerhave.... Pasteur, Koch....

“The greatest benefit to mankind...”

Vaccines
Antibiotics
Anaesthesiology
Surgical techniques
Intensive care
Cortisol, insulin, thyroxin...
Antihypertensives
Imaging techniques
Transplants, ...

equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

¹ Young, F. B., Gerrard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1920).

² Longuet-Higgins, M. S., *Mon. Not. Roy. Astro. Soc., Geophys. Supp.*, **5**, 255 (1949).

³ Von Atz, W. S., Woods Hole Papers in Phys. Oceanogr. Meteor., **11** (3) (1950).

⁴ Ekman, V. W., *Arkiv. Mat. Astron. Fysik. (Stockholm)*, **2** (11) (1905).

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A proper description of their publication in this axis, (1) V X-ray the atomic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β -D-deoxy-ribofuranose residues with 3',5' linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furburg's² model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furburg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis.

is a residue on each chain every 3.4 Å. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 Å. The distance of a phosphorus atom from the fibre axis is 10 Å. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position

1953

the DNA double helix...

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally^{3,4} that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data^{3,4} on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at



- > Membership
- > News
- > GP Training
- > Revalidation
- > Knowledge Resources
- > Professional Development
- > Courses & Events
- > Policy
- > Patient Information
- > International
- > Special Interests

History & Chronology

The Coat of Arms



The College received the letters patent for the Coat of Arms in 1961. The symbols have three main themes

- those traditionally used showing medicine's ancient lineage
- those symbolising wide knowledge
- those conveying the doctor's caring and healing relationship with patients.

Motto

Scientific knowledge applied with compassion.





Life in general practice

Helena (54), married with two grown-up children. Low education. Her new GP finds these long-standing problems in her medical record:

Hypertension, ←

Diabetes type 2,

Overweight (BMI 29),

Asthma

Chronic widespread pain,

Depression with anxiety,

Periodically high use of addictive drugs.

Low bone density

She still smokes, despite advice.





ARTERIAL HYPERTENSION AND ISCHAEMIC HEART DISEASE

PREVENTIVE

Report of an E

1. Introduction
2. Prevention and control of arteri
 - 2.1 Terminology and classificati
 - 2.2 Methodology of blood pres
 - 2.3 Diagnosis
 - 2.4 Stages of essential hyperten
 - 2.5 Renal hypertension
 - 2.6 Preventive and therapeutic
 - 2.7 Research aspects
3. Prevention and control of ischa
 - 3.1 Terminology and classificati
 - 3.2 Diagnostic criteria
 - 3.3 Preventive and therapeutic
 - 3.4 Research aspects
4. Summary and conclusions . .
- Annex 1. Methodology of renal inve
- Annex 2. Differential diagnosis of

WORLD HEALTH

GEN

15

2.6.1 *Clinical aspects*

p. 11

2.6.1.1 *Essential hypertension*

The problems of preventive therapy, as defined above, will first be discussed in relation to the three stages of essential hypertension.

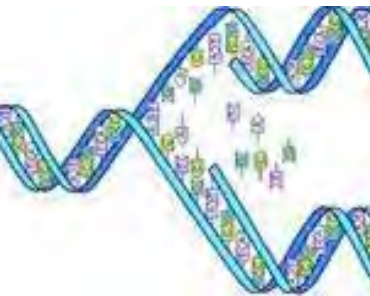
Stage 1. The Committee feels that different factors may contribute to the hypertension at this stage. Thus in some patients nervous or emotional stress appears to be of major importance. There is evidence that in such cases change of environment may lead to a fall in the blood pressure level, and to the relief of associated symptoms. A return to the stressful environment is, however, often associated with reappearance of hypertension. The role of environmental stress may vary in different age-groups. It is generally agreed, therefore, that what may be described as "common sense psychotherapy" (WHO 1978 p.41) Prolonged adverse psychological and social factors have not

with a change in ex
Apart from sedatio
ineffective.

been proved to contribute to blood pressure elevation...



A turning point in modern medicine?



Ca 2001 HUGO: The culmination of reductionist thinking in scientific medicine?
Identifiable genes and biological risk factors cause specific diseases

Desktop Medicine

Jason Karlawish, MD

CONCEPTS OF DISEASE ARE ESSENTIAL FOR DEFINING medicine. By the 20th century, the dominant concept was pathology in an individual, the foundation for the bedside model of medicine. Bedside medicine organizes the patient-physician relationship around the chief concern, which guides the focus of the history taking and physical examination; medical training that emphasizes laboratory-based sciences and a physical diagnosis; and a bedside presentation.

Today, however, a new model has emerged: desktop medicine. This term describes how a desk with a networked computer is transforming medical science and, in turn, medical practice. The desktop is the space in which researchers discover risk factor–based diseases and where physicians and patients go to gain information to diagnose and treat diseases. In developed nations, desktop diseases such as dyslipidemia occupy a substantial portion of a physician's practice, are leading causes of morbidity and mortality, and have attracted the attention of policy makers. Medicare will soon require an annual personalized health risk assessment.¹

Desktop diseases are discovered when studies show a factor (eg, blood pressure) is associated with a negative health outcome (eg, stroke), and then a clinical trial shows that an intervention affecting that risk factor reduces the risk of that outcome event.² Key technologies are networked computers that perform rapid multivariate analyses of large data sets. These sciences and technologies enable researchers to discover the characteristics of persons at risk and to create

trate this. A physician enters data about the patient and receives the patient's medical history and then determines the chief concern.

Desktop medicine transforms how physicians diagnose and treat disease. Physicians compete with signs and symptoms of disease, a relatively milder state of disease is transformed into a disabling cognitive dysfunction. Concepts of disease are transforming the way we cover from a bedside to a desktop, focusing on other diseases (eg, for cancer).³

The salience of diagnosis, and treatment, suggests that the medical college admission Test should measure skills in probabilistic reasoning and decision making, thereby encouraging students to major in desktop medicine. The core of desktop medicine is the US Medical edge of epidemiology. The core of desktop medicine is a focused laboratory-based probability to calculate risk.

The desktop role of the patient encounter (TABLE 1) approach called performing a risk assessment as the chief concern.



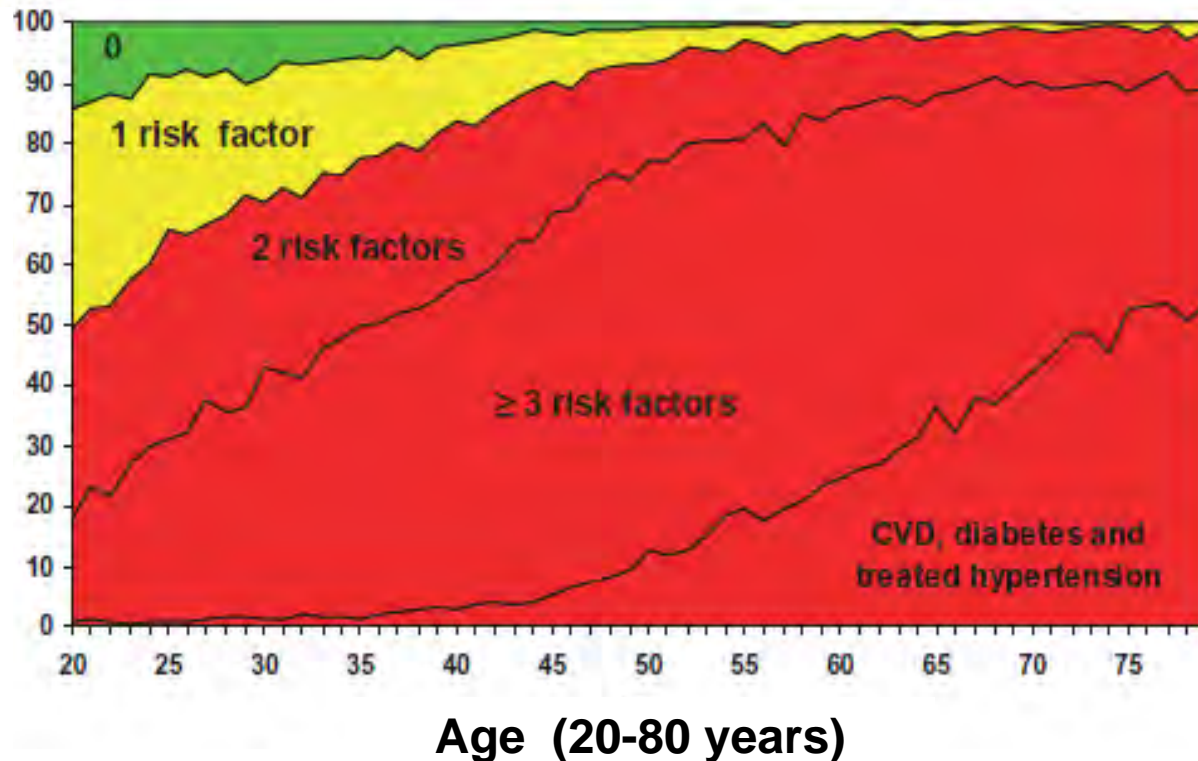
“Run the numbers first”

- Risk factor levels
- Gene tests

How many people at risk?

Norwegian context: cardiovascular disease (incl. diabetes) and CVD risk factors in the general population (> 60.000 persons)

% of individuals with diagnosis or risk factor(s) according to EBM guidelines



Petursson, Getz, Sigurdsson, Hetlevik. J Eval Clin Pract 2009



Meta-analysis 1: The moral responsibility of scientists

illustrated by the case of rocket scientist Wernher von Braun



*Don't say that he's hypocritical,
Say rather that he's apolitical.*

***"Once the rockets are up,
who cares where they come down?
That's not my department,"
says Wernher von Braun.***

- Tom Lehrer, 1965



The Challenge of Multiple Comorbidity for the US Health Care System

Anand K. Parekh, MD, MPH

Mary B. Barton, MD, MPP

future of health care reform is uncertain, Congress has drafted legislation that includes experimental and pilot approaches to realigning such incentives and payments. Even if these necessary reforms were enacted, the effects of the legislation in improving health outcomes would remain uncertain. The challenge is to ensure that the individual components of the reform are coordinated and that the overall system is able to deliver the best possible care to patients.

etc...

**Musculo-
skeletal**

Asthma

Rheumatic

Obesity

Depression

Osteoporosis

COPD

CVD

Diabetes

Hypertension

The “silo approach” to chronic disease

(Parekh & Barton, JAMA, 2010)

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etc...

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Expert
communities

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**EBM
Guidelines**

**EBM
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Guidelines**

**EBM
Guidelines**

**EBM
Guideline**

Helping Helena on the basis of science?

Helena (54), married with two grown-up children. Low education. Her new GP finds these long-standing problems in her medical record:

Hypertension, ←

Diabetes type 2,

Overweight (BMI 29),

Asthma,

Chronic widespread pain,

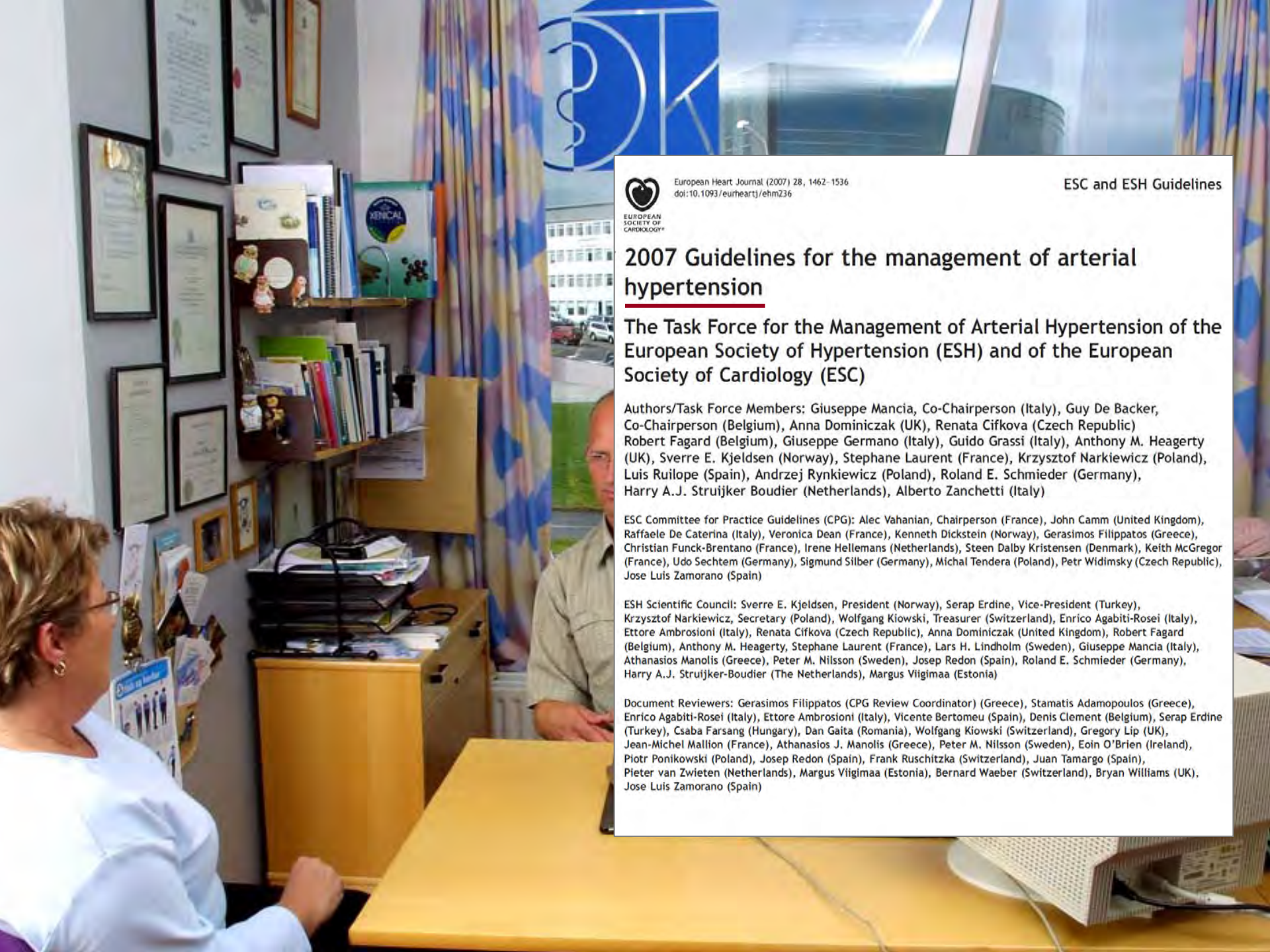
Depression with anxiety,

Periodically high use of addictive drugs.

Low bone density

She still smokes, despite advice.





European Heart Journal (2007) 28, 1462–1536
doi:10.1093/eurheartj/ehm236

ESC and ESH Guidelines

2007 Guidelines for the management of arterial hypertension

The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

Authors/Task Force Members: Giuseppe Mancia, Co-Chairperson (Italy), Guy De Backer, Co-Chairperson (Belgium), Anna Dominiczak (UK), Renata Cifkova (Czech Republic), Robert Fagard (Belgium), Giuseppe Germano (Italy), Guido Grassi (Italy), Anthony M. Heagerty (UK), Sverre E. Kjeldsen (Norway), Stephane Laurent (France), Krzysztof Narkiewicz (Poland), Luis Ruilope (Spain), Andrzej Rynkiewicz (Poland), Roland E. Schmieder (Germany), Harry A.J. Struijker Boudier (Netherlands), Alberto Zanchetti (Italy)

ESC Committee for Practice Guidelines (CPG): Alec Vahanian, Chairperson (France), John Camm (United Kingdom), Raffaele De Caterina (Italy), Veronica Dean (France), Kenneth Dickstein (Norway), Gerasimos Filippatos (Greece), Christian Funck-Brentano (France), Irene Hellemans (Netherlands), Steen Dalby Kristensen (Denmark), Keith McGregor (France), Udo Sechtem (Germany), Sigmund Silber (Germany), Michal Tendera (Poland), Petr Widimsky (Czech Republic), Jose Luis Zamorano (Spain)

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Document Reviewers: Gerasimos Filippatos (CPG Review Coordinator) (Greece), Stamatis Adamopoulos (Greece), Enrico Agabiti-Rosei (Italy), Ettore Ambrosioni (Italy), Vicente Bertomeu (Spain), Denis Clement (Belgium), Serap Erdine (Turkey), Csaba Farsang (Hungary), Dan Gaita (Romania), Wolfgang Kiowski (Switzerland), Gregory Lip (UK), Jean-Michel Mallion (France), Athanasios J. Manolis (Greece), Peter M. Nilsson (Sweden), Eoin O'Brien (Ireland), Piotr Ponikowski (Poland), Josep Redon (Spain), Frank Ruschitzka (Switzerland), Juan Tamargo (Spain), Pieter van Zwieten (Netherlands), Margus Viigimaa (Estonia), Bernard Waeber (Switzerland), Bryan Williams (UK), Jose Luis Zamorano (Spain)

Open Access

Halfdan Petursson^{*1}, Linn Getz², Johann A Sigurdsson¹ and Irene Hetlevik²

* Corresponding author

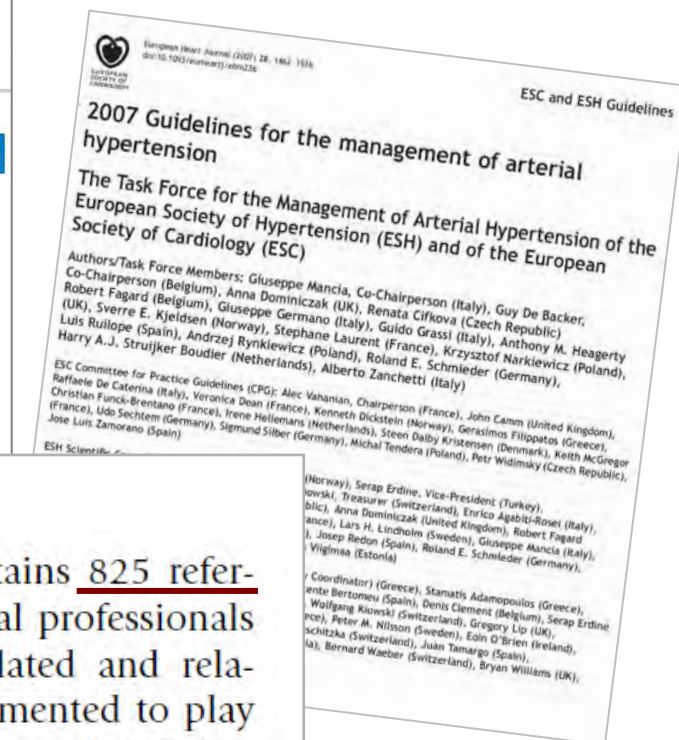
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Conclusion: The potential to destabilise the healthcare systems of nations, by international companies, regarded as scientifically sound, sustainability and social determinants.

The 2007 guideline's evidence-base contains 825 references. None of these discuss how medical professionals may address societal, political, work-related and relational factors, which have all been documented to play significant roles in CVD aetiology and prognosis [47,48].

The **workload** associated with the 2007 guidelines could destabilise the healthcare system in Norway, one of the world's most long- and healthy living nations...

... neither scientifically sound nor ethically justifiable



Immune Function of Caregivers of Alzheimer's Disease Patients¹

Amanda K. Damjanovic,^{*} Yinhua Yang,^{*} Ronald Glaser,^{2,†} Janice K. Kiecolt-Glaser,^{3,†} Huy Nguyen,^{*} Bryon Laskowski,³ Yixiao Zou,^{*} David Q. Beversdorf,¹ and Nan-ping Weng^{2*}

Caregivers of Alzheimer's disease patients endure chronic stress associated with a decline of immune function. To assess the psychological and immunological changes of caregivers, we compared depressive symptoms, PBMC composition, in vitro activation-induced proliferation and cytokine production, and 41 age- and gender-matched controls. We found that caregivers had higher levels of depressive symptoms ($p < 0.001$). Correspondingly, caregivers had cytokines (TNF- α and IL-10) than controls in replicative lifespan and found that caregivers respectively, $p < 0.05$ with similar shortening not due to an increase of shorter telomere p in PBMC and T cells was significantly higher cells to compensate the excessive loss of telomere.

Quality of child-parent attachment moderates the impact of antenatal stress on child fearfulness

K. Bergman¹, P. Sarkar², V. Glover¹, and T.G. O'Connor²

¹Institute of Reproductive and Developmental Biology, Imperial College London, UK; ²Department of Psychiatry, University of Rochester Medical Center, Rochester, NY, USA

Background: Animal studies have shown that prenatal stress has perinatal effects on sex of offspring development, more recent studies show that this effect may be eliminated by rearing. Human studies of perinatal anxiety/stress are now also beginning to show antenatal stress/anxiety and behavioural and cognitive development of the child on human evidence as to whether the early caregiving environment moderates

Antenatal maternal stress and long-term effects on child neurodevelopment: how and why?

Nicole M. Tolj,^{1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000}

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Early life experiences on b

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the glucocorticoid re

s with childhood ab

3, Sergiy Dymov³, Benoit Labonté^{1,4}

Abstract

Stories are used extensively

a fundamental part of our

made progress in uncovering

summarizes the current neuro

this information with the pro

the possible interaction betw

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a number of avenues for futu

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Abstract

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Sammendrag

Bakgrunn. Mennesket er terende, meningssøkende og målrettet organisme. ordne og videreutvikle k hvordan erfaringer knytt vissthet, relasjoner og ve bidra til utvikling av hels er en stor medisinteoret

Materiale og metode. Vi teoriveiledet syntese av r lig kunnskap fra flere fag dert epigenetikk, psykon krinoimmunologi, stress systembiologi, basert på kjente tidsskrifter og fag utvalgt for å gi innsikt i s mellom eksistensielle be forstand (biografi) og bio forhold i kroppen (biolog

Resultater. Forskning vi neskeorganismen boksta inkorporerer biografisk l informasjon, som omfatti

The human biology – saturated with experience

Summary

Background. Human beings are reflective, meaning-seeking, relational and purposeful organisms. Although experiences associated with such traits are of paramount importance for the development of health and disease, medical science has so far failed to integrate these phenomena into a coherent theoretical framework.

Material and method. We present a theory-driven synthesis of new scientific knowledge from a number of disciplines, including epigenetics, psycho-neuro-endocrino-immunology, stress research and systems biology, based on articles in recognised scientific journals and other academic works. The scientific sources have been deliberately chosen to provide insight into the interaction between existential conditions in the widest sense (biography) and biomolecular processes in the body (biology).

Results. The human organism literally incorporates biographical information

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University of Iceland

Anna Luise Kirkengen

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University of Tromsø
and
Centre for Health Promotion
Akershus University Hospital

Elling Ulvestad

Department of Microbiology
Haukeland University Hospital
and
The Gade Institute
University of Bergen

Material and method

Many disciplines, including evolutionary biology, ecology, embryology and physiology, have investigated variable traits of organisms. For a long time this fragmented research resulted in differing views on the organism's significance. In recent years, more emphasis has been put on understanding the integrity of the organism as a living whole, be it a bacterium or a human being (3). With this integrative understanding as our starting point, we present knowledge that reveals the interaction between the human body (biology) and life experience (biography) in the broadest sense.

The reference works we have selected substantiate the notion that the human organism is integrated with its surroundings and relational in its nature. We include studies from epidemiology, somatic and psychiatric clinical medicine, genetics, microbiology, immunology and neuroscience. We also include works from new, overarching disciplines

PubMed, 64 refs.

psycho- well as es, evolutionary biology, theory of science and philosophy. The complexity and breadth of the subject did not allow for systematic literature searches.

Human beings have unique characteristics that distinguish them from all other known



Neuroscience, Molecular Biology, and the Childhood Roots of Health Disparities

Building a New Framework for Health Promotion and Disease Prevention

Jack P. Shonkoff, MD

W. Thomas Boyce, MD

Bruce S. McEwen, PhD

ADVANCES IN DEVELOPMENTAL biology are building an increasingly persuasive case for a new way of thinking about health promotion and disease prevention that focuses on the origins of persistent disparities in morbidity and mortality in the early years of life. Central to this framework is an increasing interest in the extent to which early experiences and

A scientific consensus is emerging that the origins of adult disease are often found among developmental and biological disruptions occurring during the early years of life. These early experiences can affect adult health in 2 ways—either by cumulative damage over time or by the biological embedding of adversities during sensitive developmental periods. In both cases, there can be a lag of many years, even decades, before early adverse experiences are expressed in the form of disease. From both basic research and policy perspectives, confronting the origins of disparities in physical and mental health early in life may produce greater effects than attempting to modify health-related behaviors or improve access to health care in adulthood.

JAMA. 2009;301(21):2252-2259

www.jama.com

in early childhood may be a more effective way to reduce disparities in health outcomes.

“ The two cultures in science”



Natural sciences

conceptualize the human body as physical **matter**:

Genetics & genomics, neuroscience, psycho-neuro-endocrino-immunology, medical imaging, etc.

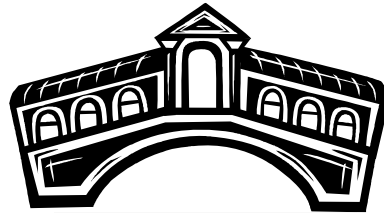
Humanities

deal with systems of values, **meaning** and **subjective experience**:

Philosophy and ethics, sociology, phenomenology, theology, history, linguistics, fine arts, etc.

New knowledge – bridging concepts

Complexity theory, Systems biology, Narrative medicine, Evolutionary theory, Developmental biology, Psych-Neuro-Endocrino-Immunology, Telomere research, Epigenetics, Allostatic load,



Natural sciences

conceptualize the human body as physical **matter**:

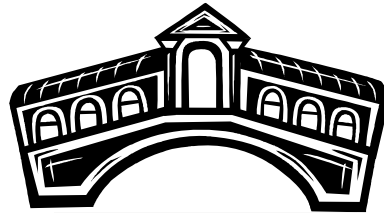
Genetics & genomics, neuroscience, psycho-neuro-endocrino-immunology, medical imaging, etc.

Humanities

deal with systems of values, **meaning** and **subjective experience**:

Philosophy and ethics, sociology, phenomenology, theology, history, linguistics, fine arts, etc.

Complexity theory, Systems biology, Narrative medicine, Evolutionary theory, Developmental biology, Psych-Neuro-Endocrino-Immunology, Telomere research, Epigenetics, Allostatic load,



Natural sciences

conceptualize the human body as physical **matter**:

*Genetics & genomics
neuroscience, psych
neuro-endocrino-
immunology, medical
imaging, etc.*

Humanities

deal with systems of values, **meaning** and **subjective experience**:

*Philosophy and ethics,
sociology, phenomenology,
theology, history,
lingusitics, fine arts, etc.*

Epigenetics

the organism's experience regulates genomic function
without changing the DNA sequence

Evolution
selects the basic
gene **sequence**
(DNA)



Individual history
opens and locks
gene **expression**
(epigenetics)

Richard M. Millis

“... and back again”?
Rediscovering complex aetiology
with hi-tech methods

Indeed, one of the challenges of 21st century medicine may be to identify common factors in disease events and to educate the public about avoiding the environmental and lifestyle stressors that adversely bias the expression of genes and increase human predilections for chronic diseases such as essential hypertension.

specific cause. It seems to occur with higher frequency in certain ethnicities and families, thereby suggesting a genetic component to the disease [1]. As biotechnology has made advancements and changed our capabilities for gene detection and mapping, views of genetic diseases have changed. It was first hoped that a small number of "hypertension genes"

The complex, Ancient Greek understanding of disease and the role of the physician

Of the Epidemics, Section III. The Corpus. Hippocratic Writings, 2008: 159

"1. With regard to diseases, the circumstances from which we form a judgement on them are, - by attending to the time of all, and the peculiar nature of the disease, the patient and the applications, to apply them, as that makes a difference for or worse, - to the whole constitution particularly to the state of the heavens, each country; to the patient's habits, his, - to his conversation, manners, his sleep, or absence of sleep, and his dreams, what and when they occur; - to his long list of physical symptoms and signs incl. urine/ sputum/ vomitings/ sweat/ rigor..... - from these, and their consequences, we must form our judgement."

etiology

ous hypertensive



Allostatic overload

**overtaxation of the body's adaptive, physiological systems
in response to a threatened integrity**

Allostasis, Gr: 'stability through change'

HPA axis

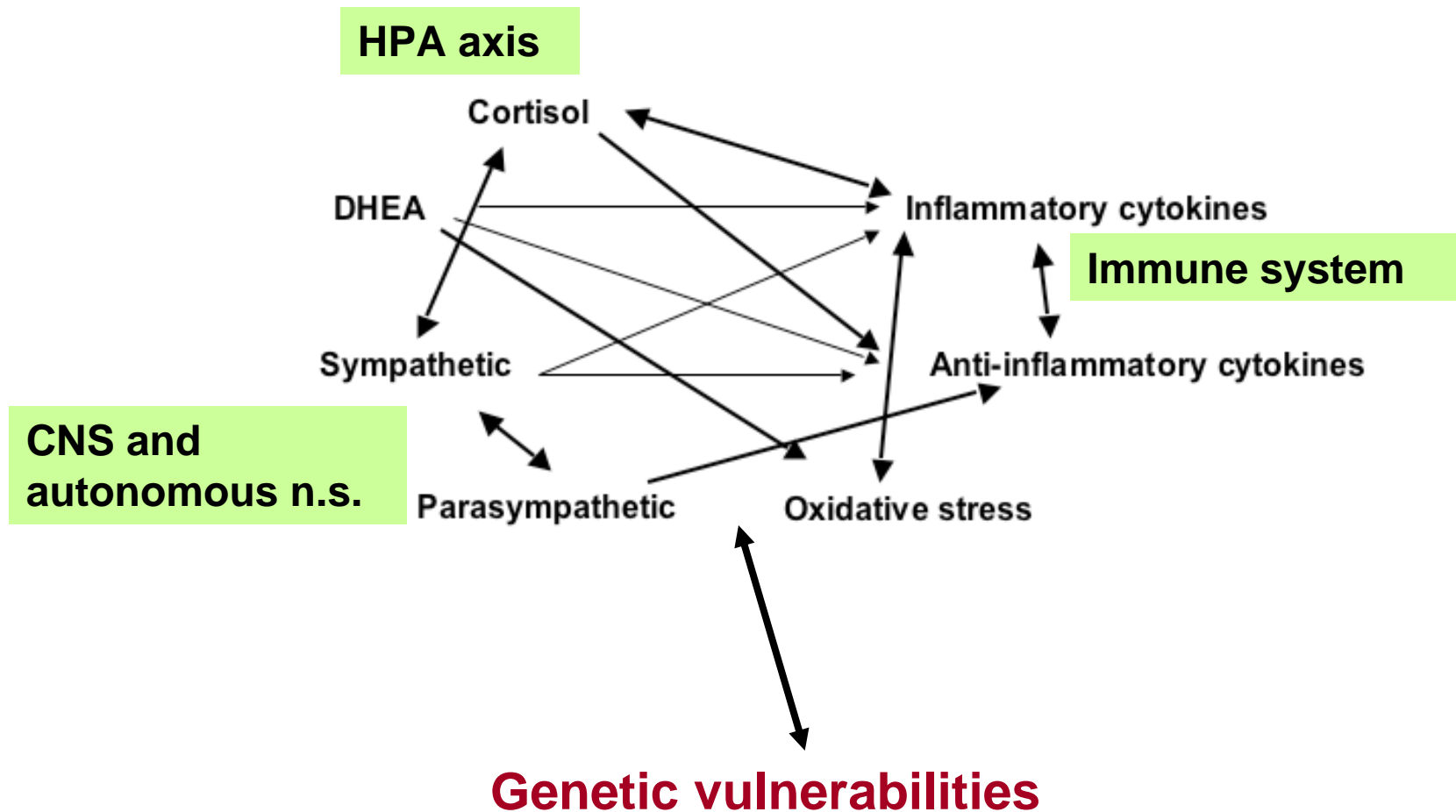
Immune system

**CNS and
autonomous n.s.
(sympaticus and
parasympaticus)**



Allostatic overload

overtaxation of the body's adaptive, physiological systems in response to a threatened integrity





The pathophysiology of **allostatic overload**

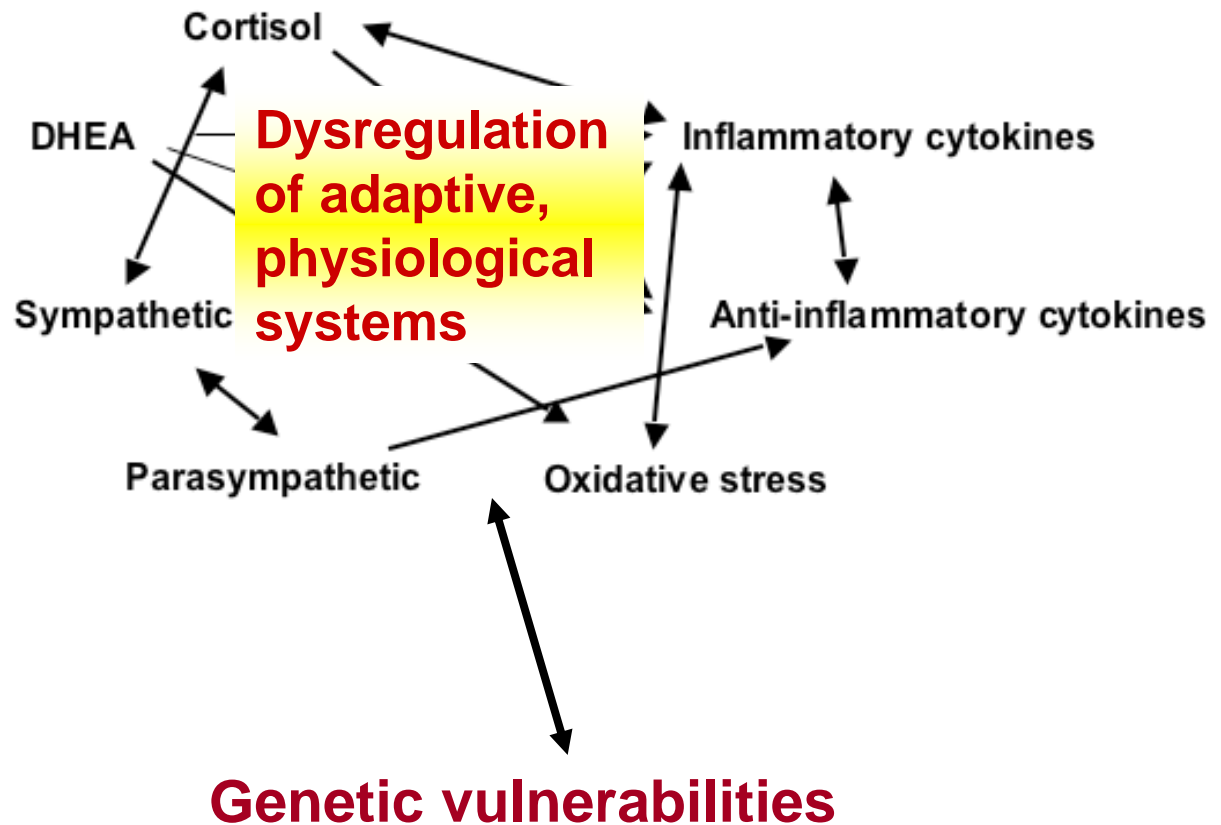
Refs: Bruce S. McEwen and co-workers (PubMed)

Ex: neglect,
unfairness,
poverty,
betrayal...

**Mental
stressors**

**Physical
stressors**

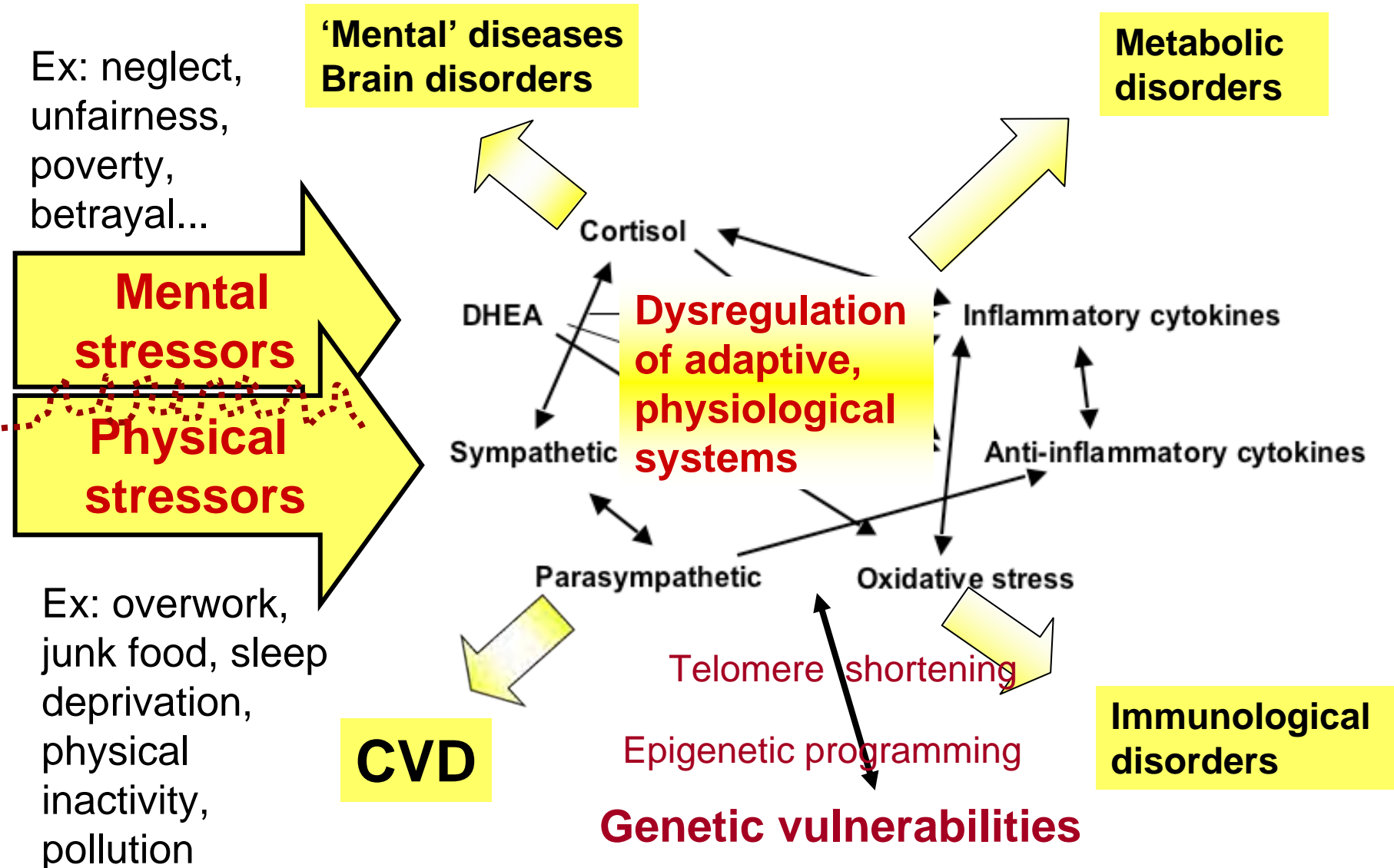
Ex: overwork,
junk food, sleep
deprivation,
physical
inactivity,
pollution





The pathophysiology of **allostatic overload**

Refs: Bruce S. McEwen and co-workers (PubMed)



The Challenge of Multiple Comorbidity for the US Health Care System

Anand K. Parekh, MD, MPH

Mary B. Barton, MD, MPP

future of health care reform is uncertain, Congress has drafted legislation that includes experimental and pilot approaches to realigning such incentives and payments. Even if these necessary reforms were enacted, the effects of the clinicians in improving health outcomes would remain. Individual

etc...

**Musculo-
skeletal**

Asthma

Rheumatic

Obesity

Depression

Osteoporosis

COPD

CVD

Diabetes

Hypertens

Expert
communities

Expert
communities

Expert
communities

Expert
communities

Expert
communities

Expert
communities

Task forces

Task forces

Task forces

Task forces

Task forces

Task force

Patient org.

Patient org.

Patient org.

Patient org.

Patient org.

Patient or

Industrial
Sponsors

Industrial
Sponsors

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Sponsors

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Sponsors

Industrial
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Industrial
Sponsors

**EBM
Guidelines**

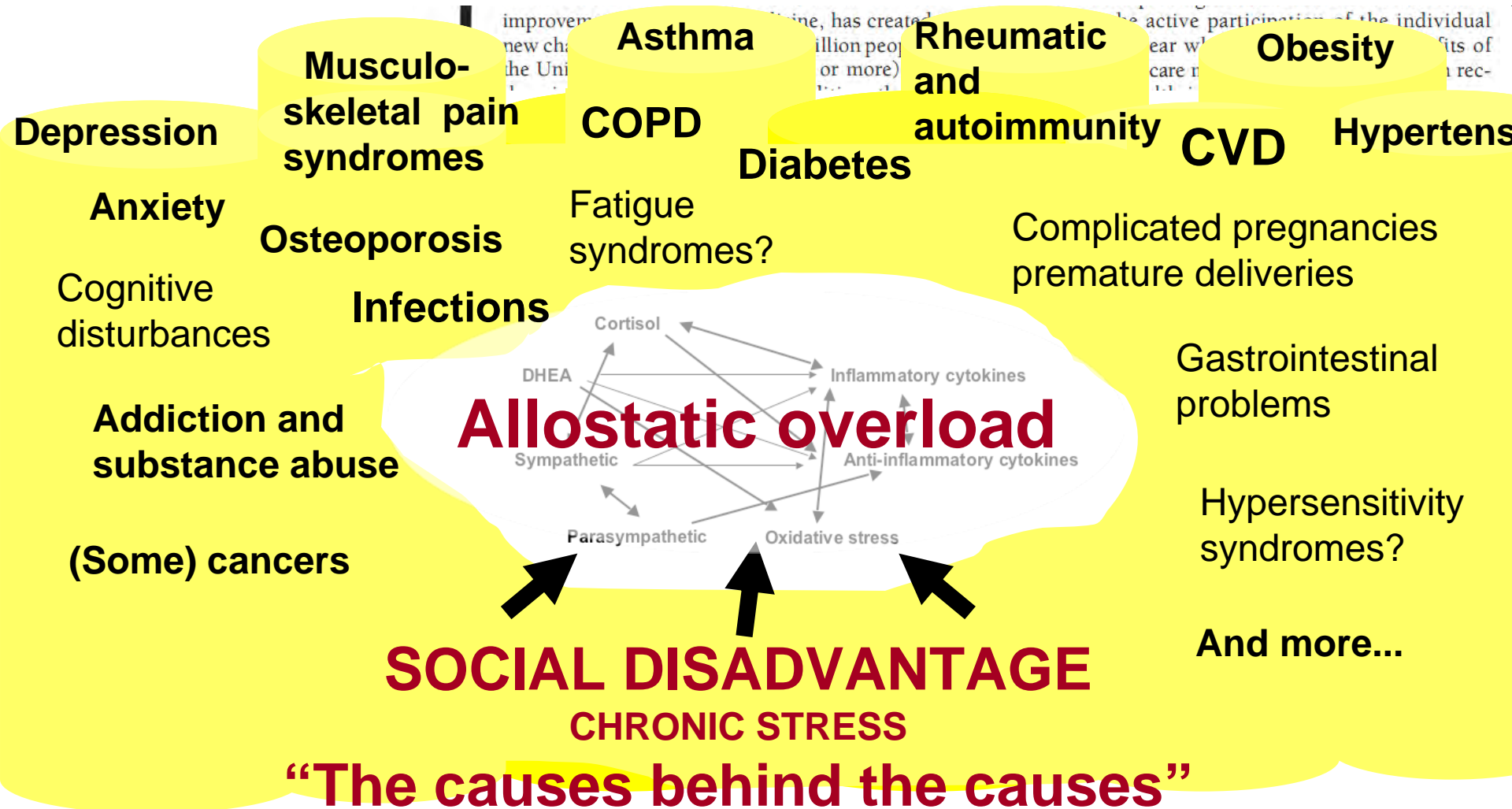
**EBM
Guidelines**

**EBM
Guidelines**

**EBM
Guidelines**

**EBM
Guidelines**

**EBM
Guideline**





A balance of existential ”gains and drains”

Anna Luise Kirkengen: How abused children become sick adults, 2009

Gains (salutogenesis)

Trust

Belonging and nourishment

Respect

Care

Honour and pride

Drains (pathogenesis)

Threat and betrayal

Isolation and neglect

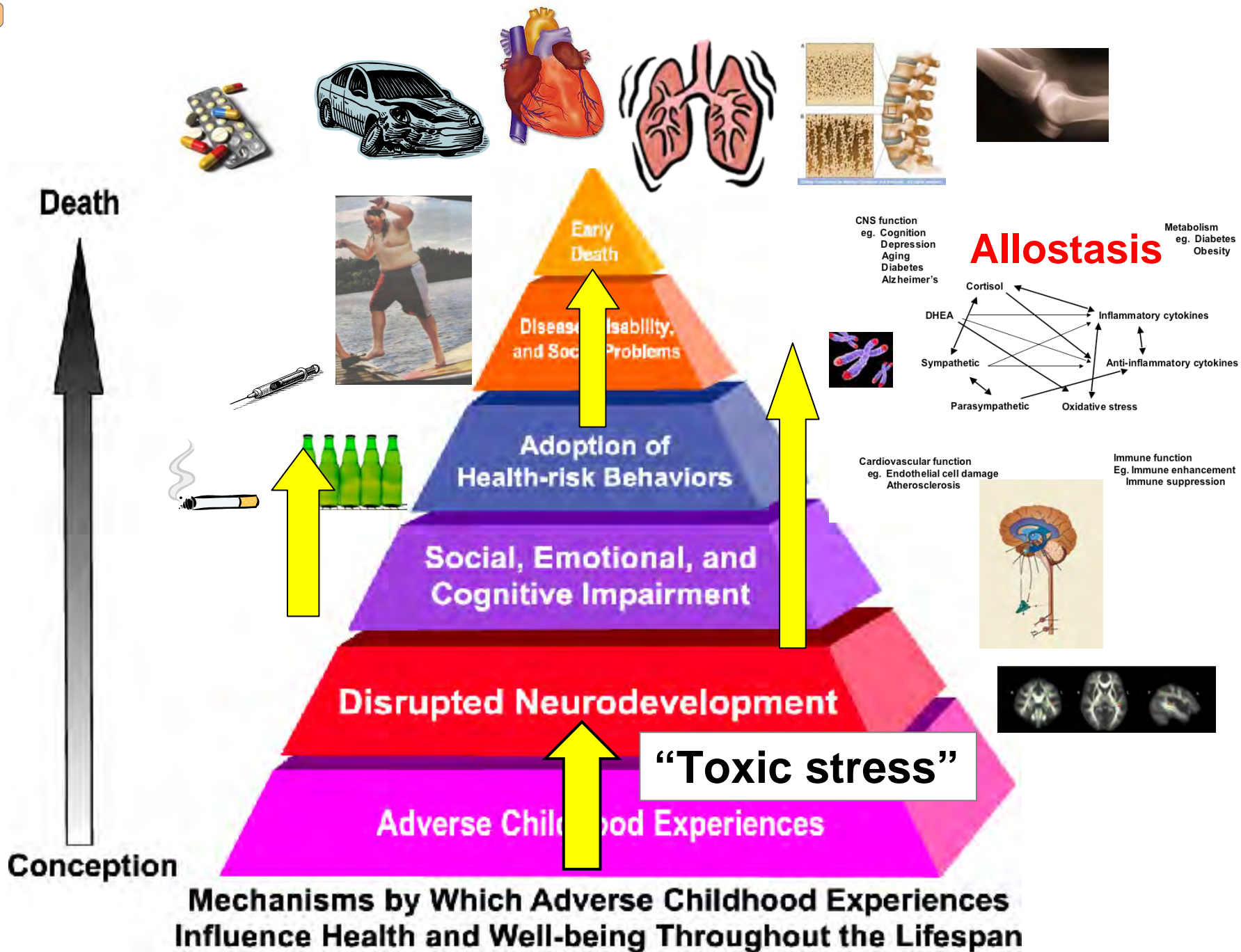
**Humiliation and
integrity violation**

Leaving behind

Guilt and shame

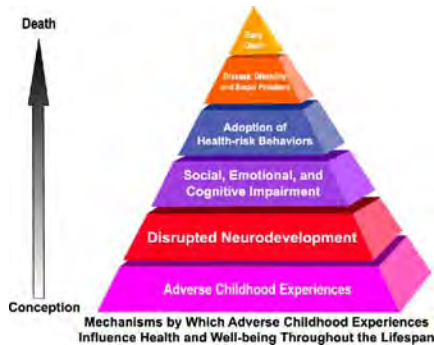
**A healing
physiology of
meaning, belonging
and hope**

**“The biology of
social disadvantage”**



Meta-analysis 2: “The biology of disadvantage”

Van Morrison: Rough God goes riding (1997)



“I was educated by the school of hard knocks”
- Van Morrison (2008)

Oh the mud splattered victims
Have to pay out all along
the ancient highway

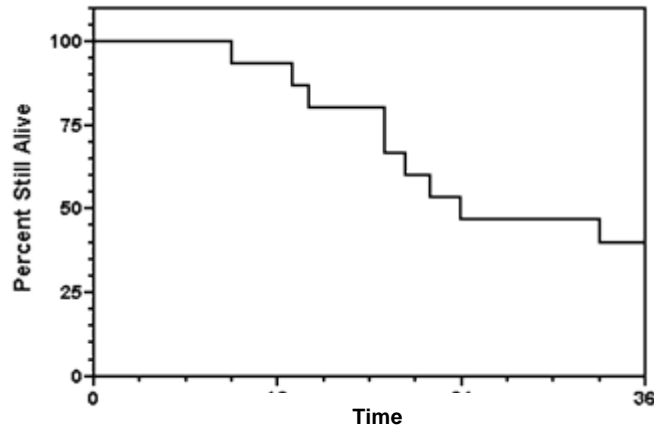
Torn between half truths
and victimisation
Fighting back with counter attacks

It's when that rough God goes riding
When the rough God goes gliding
And then the rough God goes riding
Riding on in...



Continues...

Rough God goes riding (1997) *cont..*



....And it's a matter of ***survival*** when you're born with your back against the wall...

....Won't somebody hand me a Bible, won't you give me that number to call...

Unhealthy food
Overeating
Smoking
Pollution and toxins
Living with threats
Noise
Sleep deprivation
Economic hardship
Unemployment
Lack of exercise
Physical strain

Substance abuse
Bad housing
Abuse or violence
 - physical
 - emotional
 - sexual
Neglect
 - emotional
 - physical
Absent parent(s)
Unresolvable grief
Social isolation
Stigma
Racism
Disorganized family life:
 unpredictable, alcoholism,
 drug abuse, mental disease
Betrayal
Unfairness
Shame
High demand, low control; repeated tough deadlines
Infections, acute and latent



Humanism in medicine

“Humanism in medicine is an enlightened solidarity with the patient as a living, culturally situated human being.”

- Steen Wackerhausen, 2002



Annu Rev Psychol 2010 Structural Plasticity and Hippocampal Function

Benedetta Leuner and Elizabeth Gould

Department of Psychology, Neuroscience Institute, Princeton University, Princeton, New Jersey 08544; email: goulde@princeton.edu

EXPERIENCE MODULATES STRUCTURAL PLASTICITY

Structural plasticity in the hippocampus is sen-

progress in
Neurobiology

(2007) 218–236

www.elsevier.com/locate/neurobiol

from neuroimaging studies of
psychotherapy, and placebo effect

gard a,b,c,d,e,*

Montreal, Montreal (Quebec), Canada
Montreal, Montreal (Quebec), Canada
HEC, Université de Montréal, Montreal (Quebec), Canada

NEUROPSYCHOLOG

Neuropsychologia 42 (2004) 1414–1434

www.elsevier.com/locate/neuropsychologia

Review

The neuropsychology of narrative: story comprehension, story production and their interrelation

Raymond A. Mar*

Department of Psychology, University of Toronto, Sidney Smith Hall, 4th Floor, 100 St. George

Received 23 October 2002; received in revised form 1 May 2003; accepted 2

Abstract

Stories are used extensively for human communication; both the comprehension and production of stories are fundamental parts of our experience. While study of this topic has largely been the domain of literary scholars, recent progress in uncovering the processes underlying these abilities. In an attempt to synthesize the current neuroimaging and patient research pertaining to narrative comprehension and production, (1) summarizes this information with the processes described by the discourse models of cognitive psychology, and (2) attempts to integrate this information with the processes described by the discourse models of cognitive psychology, and (3) uses this information to examine the possible interrelation between comprehension and production. Story comprehension appears to entail a network of frontal, temporal, and cingulate areas that support working-memory and theory-of-mind processes. The specific functions associated with these areas are congruent with the processes proposed by cognitive models of comprehension. Moreover, these same areas appear necessary for story production, and the causal-temporal ordering of selected information may partially account for this common ground. A basic description of comprehension and production based solely on neuropsychological evidence is presented to complement current cognitive models, and a number of avenues for future research are suggested.



THE BIOLOGY OF MEANING AND SUPPORTIVE RELATIONS

James W. Pennebaker and Janine P. Pincus
The University of Texas at Austin



Effect of a psychoneurotherapy on brain electromagnetic tomography in individuals with major depressive disorder

Vincent Paquette^{a,d,*}, Mario Beauregard^{a,b,c,d,*}, Dominic Beaulieu-Prévost^{a,d}

^aCentre de Recherche en Neuropsychologie et Cognition (CERNEC), Département de Psychologie, Université de Montréal, Montréal (Québec), Canada
^bCentre de Recherche, Institut Universitaire de Gériatrie de Montréal (CIRUM), Montréal (Québec), Canada
^cDépartement de Radiologie, Faculté de Médecine, Université de Montréal, Montréal (Québec), Canada
^dCentre de Recherche en Sciences Neurologiques (CRSN), Université de Montréal, Montréal (Québec), Canada
^eCentre de Recherche Fernand-Seguin, Hôpital Louis H.-Jadovance, Montréal (Québec), Canada

Can Meditation Slow Rate of Cellular Aging? Cognitive Stress, Mindfulness, and Telomeres

Elissa Epel,^a Jennifer Daubenmier,^b Judith Tedlie Moskowitz,^b
Susan Folkman,^b and Elizabeth Blackburn^c

^aUniversity of California San Francisco, Department of Psychiatry, San Francisco, California, USA

^bUniversity of California San Francisco, Department of Medicine, San Francisco, California, USA

^cUniversity of California San Francisco, Department of Biochemistry & Biophysics, San Francisco, California, USA

brain-computer
interfaces. The
effects of abnormal

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Key



Social Relationships and Mortality Risk: A Meta-analytic Review

Julianne Holt-Lunstad^{1*}, Timothy B. Smith^{2,3}, J. Bradley Layton³

1 Department of Psychology, Brigham Young University, Provo, Utah, United States of America, **2** Department of Psychology, Brigham Young University, Provo, Utah, United States of America, **3** Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States of America

Decreased mortality (OR)



Figure 6. Comparison of odds (lnOR) of decreased mortality across several conditions associated with mortality. Note: Effect size of

Conclusion (based on 148 studies): Human relationships should be taken as seriously as other risk factors that affect mortality



“Enlightened solidarity with the patient as a living, culturally situated human being”

Contribute and cultivate what you can here

Let your voice be heard to defend the scientific and moral integrity of medicine

Do **not** add to this burden!

Trust

Belonging and nourishment

Respect

Care

Honour and pride

Threat and betrayal

Isolation and neglect

Humiliation and integrity violation

Leaving behind

Guilt and shame

Ad fontes (Lat: go to the sources)



Together with

Ablativus

Knowledge,
insight, science

Nominativus

Love / compassion,
understood in an active and
“doing” sense

“Compassion with scientific knowledge”

—Scientific knowledge applied with compassion?

Meta-analysis 3: Hi-tech 'rediscovery' of ancient wisdom

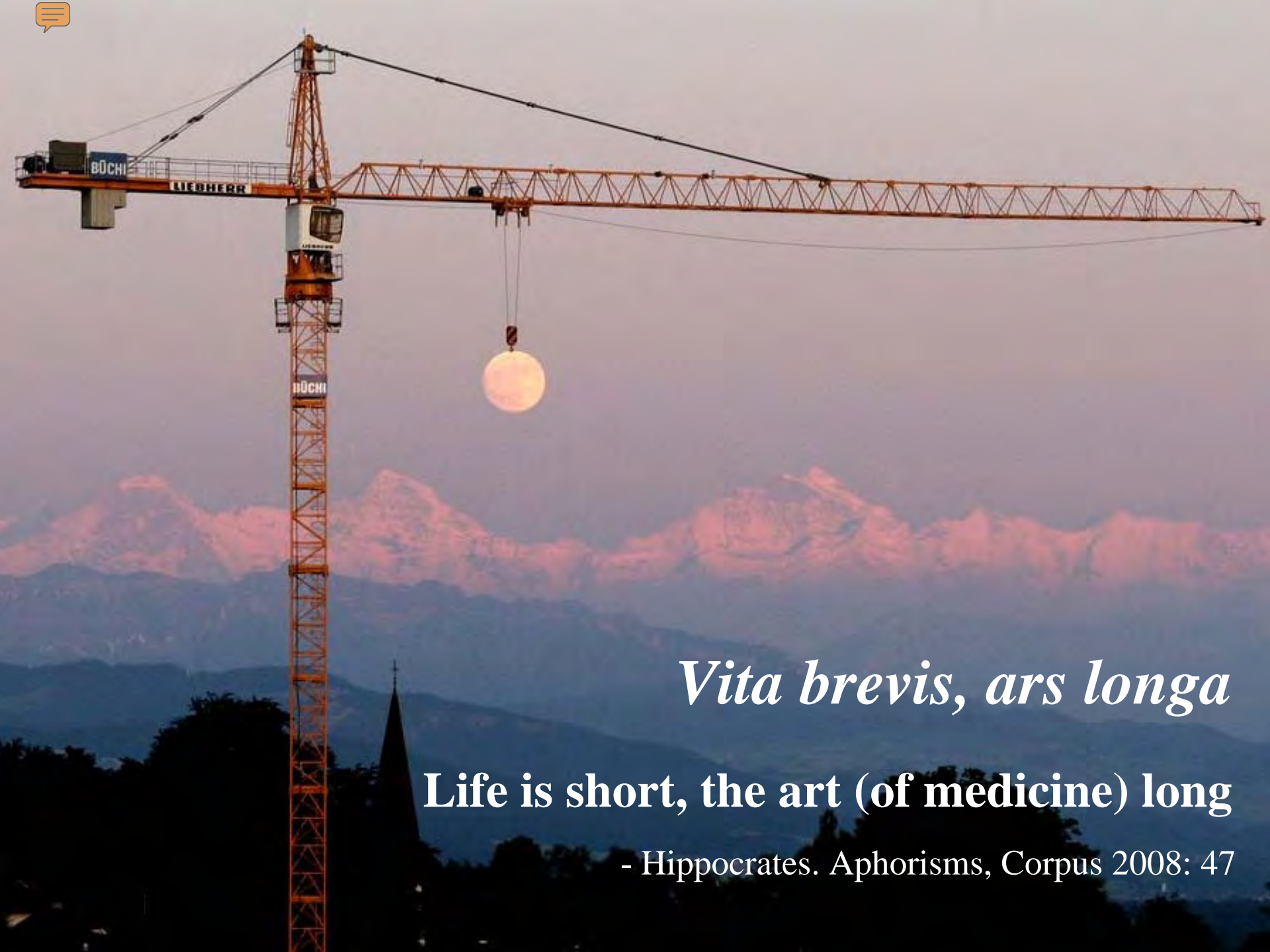


Van Morrison: The Healing Game (1997)

Here I am again
Back on the corner again
Back where I belong
Where I've always been
Everything the same
It don't ever change
I'm back on the corner again
In the healing game...



The temple of Asclepios,
the Greek god of medicine and
healing (Greek physicians
respected the gods whilst
interacting with nature)



Vita brevis, ars longa

Life is short, the art (of medicine) long

- Hippocrates. Aphorisms, Corpus 2008: 47

Thank you