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November, 2019

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American Journal of Epidemiology

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- **1887** Invited Commentary: Is DNA Methylation an Actionable Mediator of Prenatal Exposure Effects on Child Health? Christine Ladd-Acosta and M. Daniele Fallin
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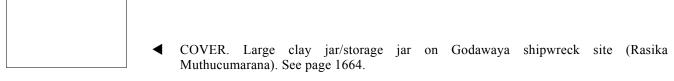
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*Author(s) for correspondence







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Defining a Culture of Health in the Workplace

Safeer, Richard; Allen, Judd

Journal of Occupational and Environmental Medicine. 61(11):863-867, November 2019.

<u>Literature Review of Policy Implications From Findings of the Center for Work, Health,</u> and Well-being

Gómez, María Andrée López; Sparer-Fine, Emily; Sorensen, Glorian; More

Journal of Occupational and Environmental Medicine. 61(11):868-876, November 2019.

<u>Direct and Indirect Cost of Obesity Among the Privately Insured in the United States:</u> <u>A Focus on the Impact by Type of Industry</u>

Ramasamy, Abhilasha; Laliberté, François; Aktavoukian, Shoghag A.; More

Journal of Occupational and Environmental Medicine. 61(11):877-886, November 2019.

Current Issue Highlights

ORIGINAL ARTICLES

Defining a Culture of Health in the Workplace

Safeer, Richard; Allen, Judd

Journal of Occupational and Environmental Medicine. 61(11):863-867, November 2019.

<u>Literature Review of Policy Implications From Findings of the Center for Work, Health, and Well-being</u>

Gómez, María Andrée López; Sparer-Fine, Emily; Sorensen, Glorian; More

Journal of Occupational and Environmental Medicine. 61(11):868-876, November 2019.

BOOK REVIEW

<u>Christoph Scherrer, Katja Radon (Eds.): Occupational Safety and Health Challenges in</u> Southern Agriculture

Laestadius, Jasminka Goldoni

Journal of Occupational and Environmental Medicine. 61(11):e459, November 2019.

PEOPLE AND EVENTS

News Highlights

Journal of Occupational and Environmental Medicine. 61(11):e460, November 2019.

<u>Calendar of Meetings</u> Journal of Occupational and Environmental Medicine. 61(11):e460, November 2019.

Nature

Volume 575 Issue 7781, 7 November 2019

This Week

Editorial

• Editorial | 06 November 2019

Nature at 150: evidence in pursuit of truth

A century and a half has seen momentous changes in science. But evidence and transparency are more important than ever before.

Research

News & Views

News & Views | 09 October 2019

The structure of DNA

In the early 1950s, the identity of genetic material was still a matter of debate. The discovery of the helical structure of double-stranded DNA settled the matter — and changed biology forever.

- Georgina Ferry
- News & Views | 04 November 2019

Detection of a strange particle

In 1947, scientists found a previously unseen particle, which is now called a neutral kaon. This work led to the discovery of elementary particles known as quarks, and ultimately to the establishment of the standard model of particle physics.

- Taku Yamanaka
- News & Views | 22 October 2019

A breakthrough method that became vital to neuroscience

Originally developed to record currents of ions flowing through channel proteins in the membranes of cells, the patch-clamp technique has become a true stalwart of the neuroscience toolbox.

- Alexander D. Reyes
- News & Views | 15 October 2019

Birth of a class of nanomaterial

Nearly 30 years ago, a simple chemical principle was reported that enabled the synthesis of a plethora of porous materials — some of which might enable applications ranging from biomedicine to petrochemical processing.

- Ryong Ryoo
- News & Views | 29 October 2019

How Australopithecus provided insight into human evolution

In 1925, a *Nature* paper reported an African fossil of a previously unknown genus called *Australopithecus*. This finding revolutionized ideas about early human evolution after human ancestors and apes split on the evolutionary tree.

- Dean Falk
- News & Views | 08 October 2019

First exoplanet found around a Sun-like star

In 1995, astronomers detected a blisteringly hot Jupiter-mass planet orbiting closer to its host star than Mercury is to the Sun. This discovery recast our thinking of how planets form and led to a new era of exoplanetary exploration.

- Eliza Kempton
- News & Views | 14 October 2019

Cell identity reprogrammed

The discovery that cell differentiation can be reversed challenged theories of how cell identity is determined, laying the foundations for modern methods of reprogramming cell identity and promising new regenerative therapies.

- Samantha A. Morris
- News & Views | 23 October 2019

The discovery of the Antarctic ozone hole

The unexpected discovery of a hole in the atmospheric ozone layer over the Antarctic revolutionized science — and helped to establish one of the most successful global environmental policies of the twentieth century.

Susan Solomon

News & Views | 04 November 2019

The advent and rise of monoclonal antibodies

A 1975 *Nature* paper reported how cell lines could be made that produce an antibody of known specificity. This discovery led to major biological insights and clinical successes in treating autoimmunity and cancer.

- Klaus Rajewsky
- News & Views | 28 October 2019

The nano-revolution spawned by carbon

In 1985, scientists reported the discovery of the cage-like carbon molecule C₆₀. The finding paved the way for materials such as graphene and carbon nanotubes, and was a landmark in the emergence of nanotechnology.

- o Pulickel M. Ajayan
- News & Views | 04 November 2019

From the archive

Aphorisms by Goethe — the opening article of the first issue of *Nature*, 4 November 1869.

Articles

• Article | 06 November 2019

A small proton charge radius from an electron-proton scattering experiment

A magnetic-spectrometer-free method for electron—proton scattering data reveals a proton charge radius 2.7 standard deviations smaller than the currently accepted value from electron—proton scattering, yet consistent with other recent experiments.

- 。 W. Xiong, A. Gasparian & Z. W. Zhao
- Article | 07 October 2019

Carrier-resolved photo-Hall effect

A carrier-resolved photo-Hall technique is developed to extract properties of both majority and minority carriers simultaneously and determine the critical parameters of semiconductor materials under light illumination.

Oki Gunawan, Seong Ryul Pae & Byungha Shin

Article | 30 October 2019

High-temperature superconductivity in monolayer Bi₂Sr₂CaCu₂O_{8+δ}

Transport and scanning tunnelling microscopy studies of freestanding monolayers of an unconventional layered copper oxide establish that the superconducting properties of copper oxides are not changed in the 2D limit.

- Yijun Yu, Liguo Ma & Yuanbo Zhang
- Article | 06 November 2019

Nanomagnetic encoding of shape-morphing micromachines

A micromachine less than 100 micrometres across, made of arrays of nanomagnets on hinged panels, is encoded with multiple shape transformations and actuated with a magnetic field.

- o Jizhai Cui, Tian-Yun Huang & Laura J. Heyderman
- Article | 30 October 2019

Dry double-sided tape for adhesion of wet tissues and devices

A new strong, biocompatible and biodegradable double-sided tape can adhere to wet tissues and devices through a mechanism involving rapid water removal from the surface, swift hydrogen and electrostatic interactions, and covalent bonding.

- o Hyunwoo Yuk, Claudia E. Varela & Xuanhe Zhao
- Article | 28 October 2019

Seeing mesoatomic distortions in soft-matter crystals of a double-gyroid block copolymer

Slice-and-view scanning electron microscopy tomography is used to characterize a double-gyroid block copolymer, finding mesoatomic distortions that break the symmetry of these soft-matter crystals across multiple scales.

Xueyan Feng, Christopher J. Burke & Edwin L. Thomas

• Article | 06 November 2019

California's methane super-emitters

Emission of methane from 'point sources'—small surface features or infrastructure components—is monitored with an airborne spectrometer, identifying possible targets for mitigation efforts.

- o Riley M. Duren, Andrew K. Thorpe & Charles E. Miller
- Article | 28 October 2019

Human origins in a southern African palaeo-wetland and first migrations

Analyses of mitochondrial genomes from populations in southern Africa provide evidence of a southern African origin of anatomically modern humans and a sustained occupation of the homeland before the first migrations of people appear to be driven by regional climate shifts.

- o Eva K. F. Chan, Axel Timmermann & Vanessa M. Hayes
- Article | 30 October 2019

Quantifying the dynamics of failure across science, startups and security

A model demonstrates that people who eventually succeed and those who do not may initially appear similar, but are characterized by fundamentally distinct failure dynamics in terms of the efficiency and quality of each subsequent attempt to succeed.

- Yian Yin, Yang Wang & Dashun Wang
- Article | 30 October 2019

Hierarchical organization of cortical and thalamic connectivity

Using mouse lines in which subsets of neurons are genetically labelled, the authors provide generalized anatomical rules for connections within and between the cortex and thalamus.

- o Julie A. Harris, Stefan Mihalas & Hongkui Zeng
- Article | 30 October 2019

Allele-selective lowering of mutant HTT protein by HTT-LC3 linker compounds

Compounds that interact with mutant huntingtin and an autophagosomal protein are able to reduce cellular levels of mutant huntingtin by targeting it

for autophagic degradation, demonstrating an approach that may have potential for treating proteopathies.

- Zhaoyang Li, Cen Wang & Boxun Lu
- Article | 23 October 2019 | Open Access

Pan-cancer whole-genome analyses of metastatic solid tumours

The mutational landscape of metastatic cancer genomes is analysed in a large-scale, pan-cancer study of metastatic solid tumours that includes whole-genome sequencing of 2,520 tumour—normal tissue pairs.

- o Peter Priestley, Jonathan Baber & Edwin Cuppen
- Article | 30 October 2019

The clinical KRAS(G12C) inhibitor AMG 510 drives anti-tumour immunity

Treatment of *KRAS*^{G12C}-mutant cancer cells with the KRAS(G12C) inhibitor AMG 510 leads to durable response in mice, and anti-tumour activity in patients suggests that AMG 510 could be effective in patients for whom treatments are currently lacking.

- o Jude Canon, Karen Rex & J. Russell Lipford
- Article | 30 October 2019

Human gut bacteria contain acquired interbacterial defence systems

An interbacterial defence strategy, involving clusters of immunity genes against toxins released by the type VI secretion system of the same or different species, is widespread among Bacteroides species, and transfer of these gene clusters confers resistance to toxins in vitro and in the mammalian gut.

- Benjamin D. Ross, Adrian J. Verster & Joseph D. Mougous
- Article | 16 October 2019

Altered chromosomal topology drives oncogenic programs in SDH-deficient GISTs

Gastrointestinal stromal tumours can be initiated by gain-of-function mutations of the *KIT* or *PDGFRA* oncogenes but also by loss of the metabolic complex succinate dehydrogenase (SDH), which leads to DNA hypermethylation; this study shows that in SDH-deficient tumours, displacement of CTCF insulators by DNA methylation activates oncogene expression, illustrating how epigenetic alterations can drive oncogenic signalling in the absence of kinase mutations.

- o William A. Flavahan, Yotam Drier & Bradley E. Bernstein
- Article | 30 October 2019

Structure of the Fanconi anaemia monoubiquitin ligase complex

The structure of the multiprotein Fanconi anaemia core complex, determined using cryo-electron microscopy and mass spectrometry, shows that the complex adopts an extended asymmetric structure and highlights the structural and functional asymmetry of the RING finger domains.

o Shabih Shakeel, Eeson Rajendra & Lori A. Passmore

Volume 575 Issue 7782, 14 November 2019

This Week

Editorial

• Editorial | 08 November 2019

Cold-war lessons for European science

The fall of the Berlin Wall 30 years ago united Europe's scientists. But continuing fractures in East–West collaboration must be healed.

• Editorial | 13 November 2019

The mental health of PhD researchers demands urgent attention

Anxiety and depression in graduate students is worsening. The health of the next generation of researchers needs systemic change to research cultures.

• Editorial | 12 November 2019

Global lessons from South Africa's rooibos compensation agreement

Indigenous communities must be compensated for their knowledge and treated as equals in research.

Research

News & Views

News & Views | 13 November 2019

How to print multi-material devices in one go

A multi-nozzle system has been devised that allows the 3D printing of objects using several viscous materials, thereby allowing control over the material properties of objects at the submillimetre scale.

- Johannes T. B. Overvelde
- News & Views | 11 November 2019

A genetically tailored education for birds

The ability of birds to learn a song depends not on their genes alone, but also on whether their genetic make-up is well matched to that of their singing teacher. This discovery sheds light on how gene—environment interactions affect learning.

- o Ofer Tchernichovski & Dalton Conley
- News & Views | 30 October 2019

One ring to rule them all

Distant DNA regions are juxtaposed and joined to form diverse immunesystem genes encoding antibodies and T-cell receptors. It seems that both types of gene form by relying on DNA extrusion through a protein ring called cohesin.

- Ferenc Livak & André Nussenzweig
- News & Views | 13 November 2019

Link between antimatter and dark matter probed

Ultrasensitive experiments on trapped antiprotons provide a window onto possible differences between matter and antimatter. Now they could also shed light on the identity of dark matter — the 'missing' mass in the Universe.

- Gianpaolo Carosi
- News & Views | 08 November 2019

Small molecule combats cancer-causing KRAS protein at last

A molecule has now been characterized that acts to inhibit a cancer-causing form of KRAS protein and stimulate the immune system. The inhibitor is one of the first of its kind to show anticancer activity in the clinic.

- Roy S. Herbst & Joseph Schlessinger
- News & Views | 30 October 2019

Metabolic vulnerability in tumours illuminated

A tracer molecule has been used to analyse tumours *in vivo* in mice and to group cancers according to their metabolic characteristics. Such information could have implications for determining how different malignancies are treated.

o Aparna D. Rao & Ralph J. DeBerardinis

Articles

• Article | 13 November 2019

Direct limits on the interaction of antiprotons with axion-like dark matter

Spin-flip resonance data are used to place direct constraints on the interaction of ultralight axion-like particles with antiprotons, improving the sensitivity to the corresponding coupling coefficient by five orders of magnitude.

- o C. Smorra, Y. V. Stadnik & S. Ulmer
- Article | 07 October 2019

Axionic charge-density wave in the Weyl semimetal (TaSe₄)₂I

In the charge-density-wave Weyl semimetal (TaSe₄)₂I, an axion is observed and identified as a sliding mode in the charge-density-wave phase characterized by anomalous magnetoelectric transport effects.

- 。 J. Gooth, B. Bradlyn & C. Felser
- Article | 13 November 2019

A volumetric display for visual, tactile and audio presentation using acoustic trapping

A volumetric display that can simultaneously deliver visual, tactile and auditory content is demonstrated.

- o Ryuji Hirayama, Diego Martinez Plasencia & Sriram Subramanian
- Article | 04 November 2019

Controlled flight of a microrobot powered by soft artificial muscles

Heavier-than-air insect-scale aerial robots powered by soft artificial muscles can hover and also recover from in-flight collisions, illustrating the potential for developing next-generation agile soft robots.

- o Yufeng Chen, Huichan Zhao & Robert J. Wood
- Article | 13 November 2019

Voxelated soft matter via multimaterial multinozzle 3D printing

Voxelated soft matter is designed and fabricated using multimaterial multinozzle three-dimensional printing, which switches between different viscoelastic inks along the same print filament to print multiple materials simultaneously.

- o Mark A. Skylar-Scott, Jochen Mueller & Jennifer A. Lewis
- Article | 30 September 2019

Metal-free directed sp²-C-H borylation

A method for the site-selective C–H borylation of arenes and heteroarenes is described, in which BBr₃ acts as both a reagent and a catalyst.

- o Jiahang Lv, Xiangyang Chen & Zhuangzhi Shi
- Article | 13 November 2019

Large hydropower and water-storage potential in future glacier-free basins

Glacierized regions that are projected to become ice-free in this century could provide substantial water storage and hydroelectric power, according to this worldwide theoretical assessment.

- o Daniel Farinotti, Vanessa Round & Harry Zekollari
- Article | 13 November 2019

Heterogeneity in banker culture and its influence on dishonesty

In contrast to a previous study in which only bankers showed increased dishonesty when reminded of their profession, this study found that such reminders induced some dishonesty in bankers, although the effect was not significant, and that this effect was not unique to bankers.

Zoe Rahwan, Erez Yoeli & Barbara Fasolo

Article | 30 October 2019

Grandmaster level in StarCraft II using multi-agent reinforcement learning

AlphaStar uses a multi-agent reinforcement learning algorithm and has reached Grandmaster level, ranking among the top 0.2% of human players for the real-time strategy game StarCraft II.

- o Oriol Vinyals, Igor Babuschkin & David Silver
- Article | 06 November 2019

Dynamic lineage priming is driven via direct enhancer regulation by ERK

ERK reversibly regulates embryonic stem cell transcription via selective redistribution of co-factors and RNA polymerase from pluripotency to early differentiation enhancers, while leaving transcription factors bound to their enhancers, thus preserving plasticity.

- o William B. Hamilton, Yaron Mosesson & Joshua M. Brickman
- Article | 06 November 2019

Lipid signalling drives proteolytic rewiring of mitochondria by YME1L

Under conditions such as hypoxia or starvation, an mTORC1-lipid signalling pathway initiates mitochondrial proteolysis by YME1L.

- o Thomas MacVicar, Yohsuke Ohba & Thomas Langer
- Article | 23 September 2019

UNC93B1 recruits syntenin-1 to dampen TLR7 signalling and prevent autoimmunity

The interaction of UNC93B1 with syntenin-1 facilitates the sorting of TLR7–UNC93B1 complexes into intraluminal vesicles of multivesicular bodies, and mutations in UNC93B1 that disrupt such interactions lead to enhanced TLR7 signalling and autoimmunity.

- o Olivia Majer, Bo Liu & Gregory M. Barton
- Article | 23 September 2019

Release from UNC93B1 reinforces the compartmentalized activation of select TLRs

The Toll-like receptor TLR9 is activated only after regulated release from its trafficking chaperone UNC93B1, which occurs within endosomes and is required for ligand binding and signal transduction.

- o Olivia Majer, Bo Liu & Gregory M. Barton
- Article | 16 October 2019

The ADP/ATP translocase drives mitophagy independent of nucleotide exchange

A CRISPR—Cas9 genetic screen shows that the adenine nucleotide translocator is required for mitophagy and that this role is independent of its nucleotide translocase activity.

- Atsushi Hoshino, Wei-jia Wang & Zoltan Arany
- Article | 30 October 2019

In vivo imaging of mitochondrial membrane potential in non-small-cell lung cancer

A positron emission tomography imaging tracer is developed to image mitochondrial function in vivo, and application of this tracer to a mouse model of lung cancer identifies distinct functional mitochondrial heterogeneity between tumour cells.

- o Milica Momcilovic, Anthony Jones & David B. Shackelford
- Article | 30 October 2019

Fundamental roles of chromatin loop extrusion in antibody class switching

Chromatin loop extrusion has fundamental mechanistic roles in immunoglobulin heavy chain class switch recombination.

- 。 Xuefei Zhang, Yu Zhang & Frederick W. Alt
- Article | 16 October 2019

HP1 reshapes nucleosome core to promote phase separation of heterochromatin

The *S. pombe* HP1 protein Swi6 couples chromatin compaction to phase separation by dynamically exposing buried histone residues within nucleosomes.

- 。 S. Sanulli, M. J. Trnka & G. J. Narlikar
- Article | 10 October 2019

Structure of the mitochondrial import gate reveals distinct preprotein paths

The high-resolution cryo-electron microscopy structure of the yeast translocase of the outer mitochondrial membrane reveals key features of mitochondrial protein import that are conserved in all eukaryotes.

Yuhei Araiso, Akihisa Tsutsumi & Toshiya Endo

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This Week

Editorial

• Editorial | 20 November 2019

Researchers must unite against US environment agency's attack on scientific evidence

The Environmental Protection Agency must desist from a course that could harm both human and planetary health.

• Editorial | 20 November 2019

Human germline editing needs one message

Science academies and the World Health Organization must act in unison.

• Editorial | 19 November 2019

How California can use its research muscle to keep the lights on

The state's universities can help to design and build a clean and resilient power grid.

Research Highlights

• Research Highlight | 13 November 2019

The meal plan that hinders the gut's recovery from antibiotics

Experiments in mice show that a regimen of low-fibre foods keeps the gut microbiome from bouncing back.

• Research Highlight | 11 November 2019

Viscous water holds the secret to an ice skater's smooth glide

Ice owes its trademark slipperiness to a layer of melt water with surprising properties.

• Research Highlight | 15 November 2019

'Bubble wrap' cushions a cell's nucleus on the move

A network of protein fibres helps to prevent the all-important organelle from being bent out of shape.

• Research Highlight | 07 November 2019

The most extreme rains of today are set to become more commonplace

For every 1 °C of global warming, the frequency of the heaviest rainfalls will nearly double.

• Research Highlight | 11 November 2019

A lethal avalanche's fury is captured in unprecedented detail

Waterlogged ground contributed to the gargantuan debris flow in the Swiss Alps.

• Research Highlight | 14 November 2019

A spy plane's declassified snapshots reveal an ancient city's size

The city of Ur, located in modern-day Iraq, might at some points have covered more than eight times as much ground as previously estimated.

• Research Highlight | 11 November 2019

Move aside, plastic: 3D printing conquers glass

Technique produces an array of transparent objects, including a glass leaf with delicate veins.

Articles

Article | 20 November 2019

Teraelectronvolt emission from the γ-ray burst GRB 190114C

Observations of teraelectronvolt-energy γ -rays starting about one minute after the γ -ray burst GRB 190114C reveal a distinct component of the afterglow emission with power comparable to the synchrotron emission.

- V. A. Acciari, S. Ansoldi & L. Nava
- Article | 20 November 2019

Observation of inverse Compton emission from a long γ-ray burst

A multi-frequency observing campaign of the γ -ray burst GRB 190114C reveals a broadband double-peaked spectral energy distribution, and the teraelectronvolt emission could be attributed to inverse Compton scattering.

- V. A. Acciari, S. Ansoldi & D. R. Young
- Article | 20 November 2019

A very-high-energy component deep in the γ -ray burst afterglow

Very-high-energy γ -rays observed ten hours after the prompt emission of the γ -ray burst 180720B can be attributed to either an inverse Compton or an extreme synchrotron process.

- o H. Abdalla, R. Adam & O. J. Roberts
- Article | 09 October 2019

Large electrocaloric effects in oxide multilayer capacitors over a wide temperature range

High-quality multilayer capacitors of a perovskite oxide show that large electric-field-driven caloric effects could improve solid-state refrigeration technology and challenge today's standard (based on magnetocaloric effects in gadolinium).

- o B. Nair, T. Usui & N. D. Mathur
- Article | 20 November 2019

Skin-integrated wireless haptic interfaces for virtual and augmented reality

Interfaces for epidermal virtual reality technology are demonstrated that can communicate by programmable patterns of localized mechanical vibrations.

- o Xinge Yu, Zhaoqian Xie & John A. Rogers
- Article | 14 October 2019

Real-space charge-density imaging with sub-ångström resolution by four-dimensional electron microscopy

A real-space imaging technique that combines scanning transmission electron microscopy with an angle-resolved pixellated fast-electron detector is used to image the charge distribution in SrTiO₃, BiFeO₃ and the junction between them.

- o Wenpei Gao, Christopher Addiego & Xiaoqing Pan
- Article | 20 November 2019

Geochemical evidence for high volatile fluxes from the mantle at the end of the Archaean

Depletion of Archaean atmospheric xenon in ¹²⁹Xe relative to the modern atmosphere might indicate that a short burst of mantle activity took place around 2.6 to 2.2 billion years ago.

- Bernard Marty, David V. Bekaert & Claude Jaupart
- Article | 06 November 2019

A new Miocene ape and locomotion in the ancestor of great apes and humans

Danuvius guggenmosi moved using extended limb clambering, thus combining adaptations of bipeds and suspensory apes and providing evidence of the evolution of bipedalism and suspension climbing in the common ancestor of great apes and humans.

- Madelaine Böhme, Nikolai Spassov & David R. Begun
- Article | 13 November 2019

High-resolution lineage tracking reveals travelling wave of adaptation in laboratory yeast

A renewable barcoding system reveals the evolutionary dynamics of laboratory budding yeast, showing that fitness changes over time in a travelling wave of adaptation that can fluctuate owing to leapfrogging events.

- o Alex N. Nguyen Ba, Ivana Cvijović & Michael M. Desai
- Article | 13 November 2019

Marine Proteobacteria metabolize glycolate via the β-hydroxyaspartate cycle

Marine Proteobacteria use the β -hydroxyaspartate cycle to assimilate glycolate, which is secreted by algae on a petagram scale, providing evidence of a previously undescribed trophic interaction between autotrophic phytoplankton and heterotrophic bacterioplankton.

- Lennart Schada von Borzyskowski, Francesca Severi & Tobias J. Erb
- Article | 13 November 2019

Bacteriophage targeting of gut bacterium attenuates alcoholic liver disease

In patients with alcoholic hepatitis, cytolysin-positive *Enterococcus faecalis* strains are correlated with liver disease severity and increased mortality, and in mouse models these strains can be specifically targeted by bacteriophages.

- Yi Duan, Cristina Llorente & Bernd Schnabl
- Article | 09 October 2019

Resolving the fibrotic niche of human liver cirrhosis at single-cell level

Single-cell RNA sequencing is used to characterize and compare the functional diversity of cells from liver biopsies of human scarred and normal

liver, and identifies markers for scar-associated macrophages and endothelial cells.

- o P. Ramachandran, R. Dobie & N. C. Henderson
- Article | 30 October 2019

Immunity to commensal papillomaviruses protects against skin cancer

A mouse model of papillomavirus infection reveals that skin colonization with commensal papillomaviruses protects the immunocompetent host against chemical- and UV-induced skin cancer through CD8⁺ T cell immunity.

- o John D. Strickley, Jonathan L. Messerschmidt & Shadmehr Demehri
- Article | 13 November 2019

CDK phosphorylation of TRF2 controls t-loop dynamics during the cell cycle

A phospho-switch is identified in the shelterin subunit TRF2 that regulates transient recruitment of the RTEL1 helicase to, and release from, telomeres, and provides a narrow window during which RTEL1 can unwind t-loops to facilitate telomere replication.

- o Grzegorz Sarek, Panagiotis Kotsantis & Simon J. Boulton
- Article | 13 November 2019

Quantifying secondary transport at single-molecule resolution

Imaging of substrate transport by individual MhsT transporters, members of the neurotransmitter:sodium symporter family of secondary transporters, at single- and multi-turnover resolution reveals that the rate-limiting step varies with the identity of the transported substrate.

- o Gabriel A. Fitzgerald, Daniel S. Terry & Scott C. Blanchard
- Article | 13 November 2019

Cryo-EM structure of the spinach cytochrome b₆f complex at 3.6 Å resolution

A 3.6 Å resolution cryo-electron microscopy structure of the dimeric cytochrome $b_{\theta}f$ complex from spinach reveals the structural basis for operation of the quinol cycle and its redox-sensing function.

- o Lorna A. Malone, Pu Qian & Matthew P. Johnson
- Article | 13 November 2019

Structures of a RAG-like transposase during cut-and-paste transposition

Analysis of multiple structures of the *Helicoverpa zea* DNA transposase Transib, determined by X-ray crystallography and cryo-electron microscopy, reveals the detailed pathway of the transposition reaction and sheds light on the evolution of the RAG recombinase.

- Chang Liu, Yang Yang & David G. Schatz
- Article | 03 October 2019

Architecture of autoinhibited and active BRAF-MEK1-14-3-3 complexes

The autoinhibited and active states of full-length BRAF in complexes with its substrate MEK1 and the 14-3-3 protein are determined by cryo-electron microscopy.

o Eunyoung Park, Shaun Rawson & Michael J. Eck

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This Week

Editorial

• Editorial | 27 November 2019

Protect Italy's new funding agency

Lawmakers must ensure that a much-needed funding agency is independent and autonomous.

• Editorial | 26 November 2019

Egypt stands to benefit from sharing its latest discoveries with all Egyptologists

When the time is right, the country should consider inviting researchers from around the world to study the latest finds from its ancient past.

• Editorial | 27 November 2019

Academics should not need to live in fear for the pursuit of their science

Attacks on scholars are on the rise at the same time as universities find themselves at the centre of student protests.

Research

News & Views

News & Views | 21 October 2019

A powerful cell-protection system prevents cell death by ferroptosis

The discovery of a mechanism that guards against a type of cell death called ferroptosis reveals a system that regenerates a ubiquitous protective component of biological membranes, and might offer a target for anticancer drugs.

- Brent R. Stockwell
- News & Views | 27 November 2019

Molecular catalyst converts carbon dioxide to methanol

A molecular catalyst dispersed on carbon nanotubes has been found to catalyse the electrochemical conversion of carbon dioxide to methanol — a liquid fuel and industrially useful bulk chemical.

- Xin-Ming Hu & Kim Daasbjerg
- News & Views | 06 November 2019

Toxin discovery reveals fresh ammunition for bacterial warfare

A previously unknown bacterial toxin has now been characterized. The protein is secreted into neighbouring cells, depleting them of essential energy-carrying molecules and so leading to the cells' demise.

- Brent W. Anderson & Jue D. Wang
- News & Views | 18 November 2019

Temperature-dependent polarization in a non-polar crystal

A crystal's surface has been found to behave as a distinct material that has temperature-dependent electrical polarization — despite the rest of the crystal being non-polar.

Gustau Catalan & Beatriz Noheda

News & Views | 06 November 2019

A rule from bacteria to balance growth and expansion

Bacteria move along gradients of chemical attractants. Two studies find that, in nutrient-rich environments, bacteria can grow rapidly by following a non-nutritious attractant — but expanding too fast leaves them vulnerable.

- Henry Mattingly & Thierry Emonet
- News & Views | 27 November 2019

Quantum dots realize their potential

Scientists have engineered semiconducting nanocrystals called quantum dots that lack toxic heavy metals and are highly efficient light emitters. These nanostructures might be used in displays, solar cells and light-emitting diodes.

Alexander L. Efros

Articles

Article | 27 November 2019

A wide star-black-hole binary system from radial-velocity measurements

Radial-velocity measurements of a Galactic B-type star show a dark companion that seems to be a black hole of about 68 solar masses, in a widely spaced binary system.

- Jifeng Liu, Haotong Zhang & Xiangqun Cui
- Article | 21 October 2019

A gated quantum dot strongly coupled to an optical microcavity

Strong coupling between a gated semiconductor quantum dot and an optical microcavity is observed in an ultralow-loss frequency-tunable microcavity device.

- o Daniel Najer, Immo Söllner & Richard J. Warburton
- Article | 21 October 2019

Imaging work and dissipation in the quantum Hall state in graphene

Imaging studies show that topological protection in the quantum Hall state in graphene is undermined by edge reconstruction with a dissipation

mechanism that comprises two distinct and spatially separated processes—work generation and entropy generation.

- o A. Marguerite, J. Birkbeck & E. Zeldov
- Article | 27 November 2019

Highly efficient and stable InP/ZnSe/ZnS quantum dot light-emitting diodes

A method of engineering efficient and stable InP/ZnSe/ZnS quantum dot light-emitting diodes (QD-LEDs) has improved their performance to the level of state-of-the-art cadmium-containing QD-LEDs, removing the problem of the toxicity of cadmium in large-panel displays.

- Yu-Ho Won, Oul Cho & Eunjoo Jang
- Article | 27 November 2019

Domino electroreduction of CO₂ to methanol on a molecular catalyst

Individual cobalt phthalocyanine derivative molecules immobilized on carbon nanotubes effectively catalyse the electroreduction of CO₂ to methanol via a domino process with high activity and selectivity and stable performance.

- Yueshen Wu, Zhan Jiang & Hailiang Wang
- Article | 16 October 2019

Concise asymmetric synthesis of (-)-bilobalide

A synthetic route to the *Ginkgo biloba* metabolite (–)-bilobalide is described.

- Meghan A. Baker, Robert M. Demoret & Ryan A. Shenvi
- Article | 27 November 2019

Twofold expansion of the Indo-Pacific warm pool warps the MJO life cycle

Since the 1980s, rapid warming of the Indo-Pacific warm pool has altered global rainfall pattern by changing the residence time of the Madden–Julian Oscillation, decreasing it by 3–4 days over the Indian Ocean and increasing it over the Indo-Pacific by 5–6 days.

o M. K. Roxy, Panini Dasgupta & Daehyun Kim

Article | 20 November 2019

Genetic predisposition to mosaic Y chromosome loss in blood

A genome-wide association study of mosaic loss of chromosome Y (LOY) in UK Biobank participants identifies 156 genetic determinants of LOY, showing that LOY is associated with cancer and non-haematological health outcomes.

- o Deborah J. Thompson, Giulio Genovese & John R. B. Perry
- Article | 06 November 2019

Chemotaxis as a navigation strategy to boost range expansion

Pioneering bacterial cells use chemotaxis along self-generated attractant gradients to facilitate rapid colonization of nutrient-replete environments.

- o Jonas Cremer, Tomoya Honda & Terence Hwa
- Article | 06 November 2019

An evolutionarily stable strategy to colonize spatially extended habitats

To successfully colonize a habitat in the presence of competing chemotactic bacterial populations, the winner is required to expand its range at a speed given by the habitat size and the population doubling time.

- o Weirong Liu, Jonas Cremer & Chenli Liu
- Article | 20 November 2019

NLRP3 inflammasome activation drives tau pathology

The authors show that NLRP3 inflammasome is activated in microglia of patients with fronto-temporal dementia and in a mouse model of tau pathology, and that the loss of NLRP3 inflammasome function decreases tau pathology and improves cognition in mice.

- o Christina Ising, Carmen Venegas & Michael T. Heneka
- Article | 06 November 2019

An interbacterial toxin inhibits target cell growth by synthesizing (p)ppApp

The bacterium *Pseudomonas aeruginosa* attacks competing bacteria using the toxin Tas1, which pyrophosphorylates adenosine nucleotides to generate (p)ppApp, thereby depleting ATP and disrupting multiple cellular functions.

- Shehryar Ahmad, Boyuan Wang & John C. Whitney
- Article | 13 November 2019

Activity of caspase-8 determines plasticity between cell death pathways

Alternative cell death pathways are revealed in the absence of caspase-8-dependent apoptosis and MLKL-dependent necroptosis.

- o Kim Newton, Katherine E. Wickliffe & Vishva M. Dixit
- Article | 20 November 2019

Caspase-8 is the molecular switch for apoptosis, necroptosis and pyroptosis

The enzymatic activity of caspase-8 controls apoptosis, necroptosis and pyroptosis, and prevents tissue damage during embryonic development and adulthood in mice.

- o Melanie Fritsch, Saskia D. Günther & Hamid Kashkar
- Article | 21 October 2019

The CoQ oxidoreductase FSP1 acts parallel to GPX4 to inhibit ferroptosis

A synthetic lethal CRISPR—Cas9 screen identifies ferroptosis suppressor protein 1 as a key ferroptosis-resistance factor, the expression of which correlates with ferroptosis resistance in hundreds of cancer cell lines.

- o Kirill Bersuker, Joseph M. Hendricks & James A. Olzmann
- Article | 21 October 2019

FSP1 is a glutathione-independent ferroptosis suppressor

In the absence of GPX4, FSP1 regenerates ubiquinol from the oxidized form, ubiquinone, using NAD(P)H and suppresses phospholipid peroxidation and ferroptosis in cells.

- Sebastian Doll, Florencio Porto Freitas & Marcus Conrad
- Article | 20 November 2019

Circular ecDNA promotes accessible chromatin and high oncogene expression

Imaging and sequencing approaches are combined to show that extrachromosomal DNA (ecDNA) in cancer is circular and has unique chromatin structure that amplifies oncogene output.

- o Sihan Wu, Kristen M. Turner & Paul S. Mischel
- Article | 20 November 2019

Mechanism of head-to-head MCM double-hexamer formation revealed by cryo-EM

Time-resolved electron microscopy reveals the mechanism by which the origin recognition complex loads pairs of MCM helicases around DNA prior to bidirectional replication.

o Thomas C. R. Miller, Julia Locke & Alessandro Costa

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Heliconius melpomene (left) and H. erato (right) gained protection from predators by evolving similar warning colors, an example of Müllerian mimicry. These species are among 20 sequenced butterfly

genomes that illustrate the importance of hybridization and gene flow in genomic evolution. See pages 570 and 594. Photo: Andrew Neild

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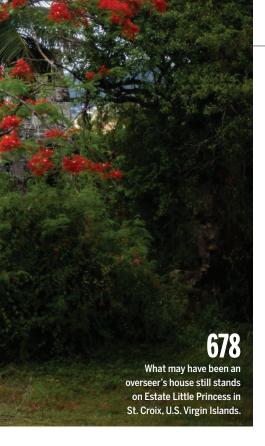
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Time-lapse image of the Roman Colosseum, which symbolizes the power and durability of Rome—one of the largest cities of the ancient world and seat of an empire of ~70 million people. A sample of ancient genomes spanning 12,000

years reveals that, from ~3000 years ago on, Rome had a population of diverse ancestries. Rapid genetic shifts in historical time reflect movements of people as Rome's political connections and trade networks changed. See pages 673 and 708. Credit: Mark Bassett/Alamy Stock Photo

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Stylized view of the cell to illustrate that the nucleus exports RNA messages that are translated into proteins (blue) by ribosomes. Proteasomes and lysosomes degrade and recycle internalized, aberrant, or excess

proteins. The endoplasmic reticulum and Golgi complex package and sort cargoes for transport to other organelles or for export from the cell. Mitochondria provide power to the rest of the cell. For more on cellular quality control, see page 816. Illustration: Nigel Sussman

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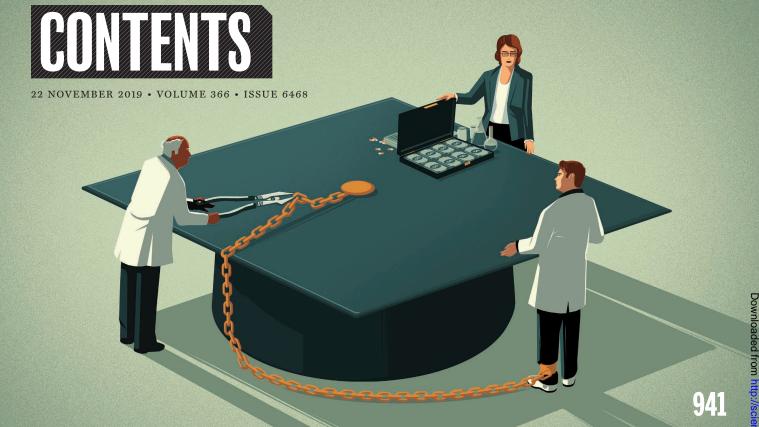
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Onthophagus sagittarius dung beetle with prominent horns on its head and thorax. The thoracic horn, an evolutionary novelty whose origin has been a long-standing mystery, is derived from

the same serially reiterated tissues that gave rise to wings in the more posterior thoracic segments. By textbook definition, evolutionary novelty requires the absence of homology, yet thoracic horns, considered a classic example of this phenomenon, appear to have originated by relying deeply on their homology to wings. See pages 946 and 1004. Photo: Alexander Wild

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Nerve cells from the mouse brain, densely reconstructed in this volume. For a century, neuron reconstruction in the cerebral cortex showed only ~1 in 1000 nerve cells (black); now researchers can use

3D electron microscopy and Al-based image analysis to reconstruct all of them (gray). The connectivity matrix between thousands of axons and dendrites can be measured, yielding insights about the formational patterns of brain circuits and possible imprints of learning in the neuronal network. See page 1093. *Image: V. Altounian/Science; Data: A. Motta* et al., Science **366** eaay 3134 (2019)

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Muscular dystrophies

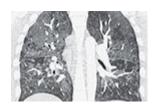


November 7, 2019

CASE CHALLENGE

A Man with Dyspnea, Odynophagia, and Abdominal Pain

A 34-year-old HIV-positive man presented with progressive dyspnea and abdominal pain. What is the most likely diagnosis?



Vote and comment. Find the answers in the full text of the case, to be published on November 21.

PERSPECTIVE

The U.S. Insulin Crisis — Rationing a Lifesaving Medication Discovered in the 1920s

M. Fralick and A.S. Kesselheim N Engl J Med 2019;381:1793-1795

Will Emergency Holds Reduce Opioid Overdose Deaths?

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N Engl J Med 2019;381:1843-1852

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N Engl J Med 2019;381:1863-1865 | Published Online October 31, 2019

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Nonalcoholic Fatty Liver Disease, Insulin Resistance, and Ceramides

V.T. Samuel and G.I. Shulman N Engl J Med 2019;381:1866-1869

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Health, Social Reform, and Medical Schools — The Training of American Physicians and the Dissenting Tradition

M. Chowkwanyun and B. Howell N Engl J Med 2019;381:1870-1875

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Total Penis, Scrotum, and Lower Abdominal Wall Transplantation

Deaths Associated with Emicizumab in Patients with Hemophilia A

Teplizumab in Relatives at Risk for Type 1 Diabetes

Warm Autoimmune Hemolytic Anemia

Pheochromocytoma and Paraganglioma



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Learning from the Dead

K.M. De Cock, E. Zielinski-Gutiérrez, and S.B. Lucas N Engl J Med 2019;381:1889-1891

Modernizing the FDA's 510(k) Pathway

V.K. Rathi and J.S. Ross

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Last Song — Sharing Humanity while Maintaining Boundaries

J. Wales

N Engl J Med 2019;381:1894-1895

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Phase 3 Efficacy Trial of Modified Vaccinia Ankara as a Vaccine against Smallpox

P.R. Pittman and Others

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Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation

M.V. Perez and Others

N Engl J Med 2019;381:1909-1917

Trial of Apremilast for Oral Ulcers in Behçet's Syndrome

G. Hatemi and Others

N Engl J Med 2019;381:1918-1928

Secondary Surgical Cytoreduction for Recurrent Ovarian Cancer

R.L. Coleman and Others

N Engl J Med 2019;381:1929-1939

A Phase 3 Trial of Difelikefalin in Hemodialysis Patients with Pruritus

S. Fishbane and Others

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Acute Upper Airway Obstruction

A. Eskander, J.R. de Almeida, and J.C. Irish N Engl J Med 2019;381:1940-1949

IMAGES IN CLINICAL MEDICINE

Iris Transillumination Defects in Pigment Dispersion Syndrome

L. Lyons and A. Amram N Engl J Med 2019;381:1950

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D. Miyashiro and J.A. Sanches N Engl J Med 2019;381:e35

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Case 35-2019: A 66-Year-Old Man with Pancytopenia and Rash

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On the "Take" as a Biomarker

L.R. Baden and I.K. Damon N Engl J Med 2019;381:1962-1963

Watched by Apple

E.W. Campion and J.A. Jarcho N Engl J Med 2019;381:1964-1965

SPECIAL REPORT

10-Year Update on Study Results Submitted to ClinicalTrials.gov

D.A. Zarin and Others N Engl J Med 2019;381:1966-1974

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Apremilast in Treatment-Refractory Recurrent Aphthous Stomatitis

Selinexor for Refractory Multiple Myeloma

Measles

Drug Effects on the Thyroid



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Who Pays in Medicare Part D? Giving Plans More Skin in the Game

E.E. Trish and Others

DOI: 10.1056/NEJMp1912357 | November 20, 2019

Case Studies in Social Medicine: Biological Citizenship — A 53-Year-Old Man with Schizoaffective Disorder and PTSD Applying for Supplemental Security Income

I. Kalofonos

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Eastern Equine Encephalitis Virus — Another Emergent Arbovirus in the United States

D.M. Morens, G.K. Folkers, and A.S. Fauci N Engl J Med 2019;381:1989-1992

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S. Jha

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Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

J.J.V. McMurray and Others

N Engl J Med 2019;381:1995-2008 | Published Online September 19, 2019

Efficacy of a Tetravalent Dengue Vaccine in Healthy Children and Adolescents

S. Biswal and Others

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Nivolumab plus Ipilimumab in Advanced Non-Small-Cell Lung Cancer

M.D. Hellmann and Others

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Ticagrelor with or without Aspirin in High-Risk Patients after PCI

R. Mehran and Others

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Brief Report: Drug-Resistant $E.\ coli$ Bacteremia Transmitted by Fecal Microbiota Transplant

Z. DeFilipp and Others

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Reduced Leaflet Motion after Transcatheter Aortic-Valve Replacement

O. De Backer and Others

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A Controlled Trial of Rivaroxaban after Transcatheter Aortic-Valve Replacement

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Early Surgery or Conservative Care for Asymptomatic Aortic Stenosis

D.-H. Kang and Others

DOI: 10.1056/NEJMoa1912846 | November 16, 2019

Additional Published Content



VIDEOS IN CLINICAL MEDICINE

Focused Cardiac Ultrasonography for Left Ventricular Systolic Function

G. Prada and Others

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IMAGES IN CLINICAL MEDICINE

Lateral Knee Dislocation

L. Ganti and A. Hanna

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Myxomatous Mitral-Valve Prolapse

F.A. Farooqui and S. Deepti

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Case 36-2019: A 34-Year-Old Man with Dyspnea, Odynophagia, and Abdominal Pain

M. Saag and Others

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Heart-Failure Therapy — New Drugs but Old Habits?

J.C. Fang

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Fecal Microbiota Transplantation for Dysbiosis — Predictable Risks

M.J. Blaser

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Timing of Intervention in Aortic Stenosis

P. Lancellotti and M.A. Vannan

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An Anti-Opioid System, Courtesy of a Worm Model

B.L. Kieffer N Engl J Med 2019;381:2067-2069

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Donor Screening for Fecal Microbiota Transplantation

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Ambient Air Pollution and Mortality in 652 Cities

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Pulmonary Illness Related to E-Cigarette Use

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More on the Pathology of Vaping-Associated Lung Injury

DOI: 10.1056/NEJMc1914980 | November 20, 2019



November 28, 2019

INTERACTIVE MEDICAL CASE

Facing Uncertainty

C. Thomas and Others | N Engl J Med 2019;381:e39

This interactive case features a 57-year-old woman who presents with a 1-year history of a facial rash and a 2-week history of productive cough and worsening shortness of breath.

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PERSPECTIVE

<u>PrEParing to End the HIV Epidemic — California's Route as a Road Map for the United States</u>

D.S. Kazi, I.T. Katz, and A.K. Jha

DOI: 10.1056/NEJMp1912293 | November 27, 2019

Advancing Legislation on Drug Pricing — Is There a Path Forward?

S.B. Dusetzina and J. Oberlander N Engl J Med 2019;381:2081-2084

Which Drug Prices Should Medicare Negotiate? A "Too Little" or "Too Late" Approach

P.B. Bach

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Roadside Assistance

H. Kovich

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Supplemental MRI Screening for Women with Extremely Dense Breast Tissue

M.F. Bakker and Others

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J. Kapur and Others

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Trial of Satralizumab in Neuromyelitis Optica Spectrum Disorder

T. Yamamura and Others

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Diagnosis of Pulmonary Embolism with d-Dimer Adjusted to Clinical Probability

C. Kearon and Others

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Overall Survival with Osimertinib in Untreated, EGFR-Mutated Advanced NSCLC

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A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics

S. Mulangu and Others

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Essential Thrombocythemia

A. Tefferi and A. Pardanani

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J. Nangalia and P.J. Campbell N Engl J Med 2019;381:2145-2156
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A.C. Arrieta and J. Singh N Engl J Med 2019;381:2157
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F. Guerra and D. Coletta N Engl J Med 2019;381:e38
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Case 37-2019: A 20-Month-Old Boy with Severe Anemia

B.M. Cummings and Others N Engl J Med 2019;381:2158-2167

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Detecting Breast Cancer in Women with Dense Breasts

D.L. Longo

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Management of Established Status Epilepticus

P.E. Smith

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Monoclonal Antibody Therapy for Ebola Virus Disease

M.M. Levine

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Transforming Culture in Health Care

M. Nurok and T.H. Lee N Engl J Med 2019;381:2173-2175

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Imbalance in T-Helper 17 Cells and Targeted Therapy in an Infant with SAM-like

Syndrome

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