Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Ca^{2+} channel, further impairing myocardial contractility. Membrane NOS1 is also linked to the plasmalemmal Ca^{2+} pump, although the consequences of this association remain unknown.[11] Finally, although not addressed by Damy and colleagues, if increased NOS1 also translocated to mitochondria, respiration could be excessively inhibited.[12] This constellation of phenotypic alterations due to decreased NOS in the sarcoplasmic reticulum and increased membrane and mitochondrial NOS match well with characteristic changes of the failing heart—decreased function of the sarcoplasmic reticulum and its Ca^{2+} stores, decreased β-adrenergic responsiveness, and mechano-energetic uncoupling. The disruption of NOS spatial localisation described by Damy could have a substantial role in the pathophysiology of the failing heart.

The idea that NOS signalling is spatially confined raises the question of consequences in downstream signalling. At least two mechanisms for nitric-oxide signalling are known: post-translational modification of proteins via S-nitrosothiol bond-formation and cGMP production.[13] Thus specificity in nitric-oxide signalling might arise from specific protein-protein interactions between NOS and signalling effectors as well as from use of different signalling mechanisms in specific organelles. This hypothesis needs further testing but, if correct, could have major implications for understanding nitric-oxide signalling in the cardiac myocyte and in other cells. In-vitro evidence that nitric oxide in the sarcoplasmic reticulum influences excitation-contraction coupling by nitrosylation of the ryanodine receptor is robust,[6,9] whereas signal transduction at the cell membrane clearly involves cGMP formation.[6] Enzymes that metabolise nitrosothiols (glutathione-dependent formaldehyde dehydrogenase[13]) and cGMP (phosphodiesterase 5) control signalling by both of these mechanisms.

Another issue worthy of consideration is the mechanism(s) regulating NOS trafficking within cells. Both NOS1 and NOS3 have caveolin-binding sites, but only NOS1 has a PDZ domain, a specific peptide sequence that allows it to recognise and bind to other proteins. Given the established role of PDZ domains in protein-protein interactions, this motif probably determines the selective subcellular localisation of NOS1. There is also an interesting difference between muscle forms of NOS1 compared with the better characterised version found in the central nervous system: a 34-aminoacid insert between exons 16 and 17, termed the μ domain. Knowledge of the role of this and other endogenous regulatory peptides might offer valuable clues to the mechanism of NOS1 activity within muscle cells.[6]

The findings of Damy and colleagues are important not only for primary diseases of heart muscle but may also offer new insight into additional diseases, including arrhythmias, sudden cardiac death, myocardial infarction, ageing, and sepsis. Focusing attention on subcellular localisation of NOS isoforms and their specific signalling effectors will continue to shed light on a field that has been confusing and controversial.

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1 de Belder AJ, Radomski MW, Why HJ, et al. Nitric oxide synthase activities in human myocardium. *Lancet* 1993; **341:** 84–85.
2 Barouch LA, Harrison RW, Skaf MW, et al. Nitric oxide regulates the heart by spatial confinement of nitric oxide synthase isoforms. *Nature* 2002; **416:** 337–39.
3 Khan SA, Skaf MW, Harrison RW, et al. Nitric oxide regulation of myocardial contractility and calcium cycling: independent impact of neuronal and endothelial nitric oxide synthases. *Circ Res* 2003; **92:** 1322–29.
4 Matsumoto A, Comatas KE, Liu LM, Stamler JS. Screening for nitric oxide-dependent protein-protein interactions. *Science* 2003; **301:** 657–61.
5 Rizzo MA, Piston DW. Regulation of beta cell glucokinase by S-nitrosylation and association with nitric oxide synthase. *J Cell Biol* 2003; **161:** 243–48.
6 Hare JM. Nitric oxide and excitation-contraction coupling. *J Mol Cell Cardiol* 2003; **35:** 719–29.
7 Kobzik L, Stringer B, Balligand JL, Reid MB, Stamler JS. Endothelial type nitric-oxide synthase in skeletal-muscle fibers: mitochondrial relationships. *Biochem Biophys Res Commun* 1995; **211:** 375–81.
8 Eu JP, Sun J, Xu L, Stamler JS, Meissner G. The skeletal muscle calcium release channel: coupled O2 sensor and NO signaling functions. *Cell* 2000; **102:** 499–509.
9 Xu L, Eu JP, Meissner G, Stamler JS. Activation of the cardiac calcium release channel (ryanodine receptor) by poly-S-nitrosylation. *Science* 1998; **279:** 234–37.
10 Sears C E, Zhang YH, Ashley EA, et al. Myocardial NOS1 controls the lusitropic response to β-adrenergic stimulation in vivo and in vitro. *Circulation* 2004; **108:** IV-249 (abstr).
11 Schuh K, Uldrijan S, Telkamp M, Rothlein N, Neyses L. The plasma membrane calmodulin-dependent calcium pump: a major regulator of nitric oxide synthase I. *J Cell Biol* 2001; **155:** 201–05.
12 Clementi E, Brown GC, Feelisch M, Moncada S. Persistent inhibition of cell respiration by nitric oxide: crucial role of S-nitrosylation of mitochondrial complex I and protective action of glutathione. *Proc Natl Acad Sci USA* 1998; **95:** 7631–36.
13 Liu L, Hausladen A, Zeng M, Que L, Heitman J, Stamler JS. A metabolic enzyme for S-nitrosothiol conserved from bacteria to humans. *Nature* 2001; **410:** 490–94.

Communicable disease surveillance and management in a globalised world

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> "Epidemics appear, and often disappear without trace, when a new culture has started . . . The history of epidemics is therefore the history of disturbances of human culture."

Rudolf Virchow's sage words 150 years ago have not lost any of their relevance in our 21st-century globalised world. Despite monumental advances in biomedicine and related sciences, our society remains vulnerable to the re-emergence of ancient communicable diseases, while the culture and mechanics of sociopolitical and economic globalisation foster the emergence of new threats, their establishment, and rapid spread.

The evolution of the European Union (EU) is a fascinating geopolitical chapter in human history, and the erudite paper by Richard Coker and colleagues in this issue of *The Lancet* is a timely reminder that such societal developments can have profound public-health consequences. They provide a pertinent review of the impact of these changes on the epidemiology of communicable diseases in eastern Europe, particularly tuberculosis and HIV, and the constraints facing frail health-systems to adequately respond. Threats that appeared distant are now near. Diseases of antiquity (tuberculosis) and those of exotic and far-flung destinations are now a neighbourhood reality. Thus the call for increased political commitment by member states of the EU to tackle the challenges of establishing effective surveillance for communicable disease across frontiers and bolstering the health systems of EU neighbours is sensible, whether prompted by self-preservation, chauvinism, or benevolence. However, this action alone will not suffice to

minimise the risk of importation of communicable diseases, particularly those with outbreak potential, into the EU, nor is it morally defensible. A global threat calls for an equitable global response.

Globalisation has resulted in the unparalleled passage of people, animals, and goods across national borders, which in turn has fuelled the international spread of infectious diseases.[1] The liberalisation of trade and movement, with attendant economic migration, political instability, diminished employment opportunities, and social unrest has further widened the chasm between wealthy and deprived communities, and catalysed inequalities in health.[2] Rapid global communication has penetrated the consciousness of privileged nations with stark images of cholera in southern Africa and Latin America, pneumonic plague in India, diphtheria in eastern Europe, and Ebola haemorrhagic fever in Uganda and the Democratic Republic of the Congo. The resulting concern prompted several key international and regional initiatives, most notably the Global Outbreak Alert and Response Network (GOARN). GOARN was established in 1997 and now has over 120 partners around the world that identify and assist in responses to more than 50 epidemics, predominantly in developing countries, each year.[3] The draft revision of the international health regulations places emphasis on effective sharing of epidemiological information on transboundary spread of communicable diseases and rapid assistance to member states to support responses.[2]

The epidemic of severe acute respiratory syndrome provided many lessons for our global village, but none more pertinent than that "inadequate surveillance and response capacity in a single country can endanger national populations and the public health security of the entire world".[4] Early detection requires functional subnational surveillance capacity, and it is time to invest in strengthening sub-national outbreak surveillance and response capacity in developing countries. The value of training key health-personnel at district level to actively monitor the occurrence of a limited number of clinical syndromes and appropriately respond, while sustaining the surveillance system through regular training, networking, and feedback to reporters, weekly zero-reporting, and defined action on all reports, has been convincingly shown in several developing settings.[5,6] Recently, encouraging evidence has been gathered in west Africa to confirm what appears obvious, that strengthening health services to effectively detect and control epidemics of measles, cholera, and meningococcal meningitis is cost effective.[7]

Investments in improving communicable disease surveillance and response capacity are certainly required beyond the leading eastern edge of the expanded EU, and must extend to all developing countries with poor subnational capacity.

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1 Walt G. Globalisation of international health. *Lancet* 1998; **351:** 434–37.
2 World Health Organization. Global crises, global solutions—managing public health emergencies of international concern through the revised International Health Regulations. WHO/CDS/CSR/GAR/2002.4. Geneva: World Health Organization, 2002: http://www.who.int/csr/ resources/publications/ihr/WHO_CDS_CSR_GAR_2002_4_EN/en/ (accessed March 30, 2004).
3 Heymann DL, Rodier GR, WHO Operational Support Team to the Global Outbreak Alert and Response Network. Hot spots in a wired world: WHO surveillance of emerging and re-emerging infectious diseases. *Lancet Infect Dis* 2001; **1:** 345–53.
4 Heymann DL, Rodier GR. Global surveillance, national surveillance, and SARS. *Emerg Infect Dis* 2004; **10:** 173–75.
5 Durrheim DN, Harris BN, Speare R, Billinghurst KG. The use of hospital-based nurses for the surveillance of potential disease outbreaks. *Bull World Health Organ* 2001; **78:** 22–27.
6 John TJ, Samuel R, Balraj V, John R. Disease surveillance at district level: a model for developing countries. *Lancet* 1998; **352:** 58–61.
7 Van Damme W, Van Lerberghe W. Strengthening health services to control epidemics: empirical evidence from Guinea on its cost-effectiveness. *Trop Med Int Health* 2004; **9:** 281–91.

Pilates to pit

England's Andrew Flintoff was named among the prestigious five cricketers of the year in the 141st edition of the *Wisden Cricketers' Almanac*, published earlier this month. His all-round success with the England cricket team greatly contributed to their recent test series victory against the West Indies in the Caribbean. How different it might have been for this particular cricketer, who had had a chronic back condition for most of his early career and more recently a series of groin injuries.

Flintoff seemed to be another of those talented cricketers lost to injury, who would never quite deliver his true potential. In fact, Flintoff could have been used as a metaphor for the state of English cricket—overweight, overbowled, and overworn. It seemed that every English bowler selected in recent years would almost immediately break down, and interviews would turn straight from the joy of selection to the despair of injury. It was not so much: "Has the player got the right stuff?" but "Is the stuff strained, fractured, or prolapsed?"

What has changed recently for Flintoff, and England, has arguably been the introduction of pilates and yoga into their training regimen. Pilates was the brainchild of Joseph Pilates, born in Germany in 1880. Often sick as a child, Pilates decided to train himself using gymnastics to improve his health. By targeting the body's core muscles, his method improves strength and posture, helping to prevent injury.

First used by dancers, pilates may have cricketers of an older generation choking on their pints of ale. But perhaps they have more in common with the training methods of today than they might think. Many of the great fast bowlers of yesteryear came from backgrounds of hard physical labour. For instance, Harold Larwood—the English bowler from the infamous "bodyline" series—spent his formative years down a coal mine, increasing his core strength.

Today's cricketers could be at greater risk of injury due to the tendency of modern generations to have a more sedentary early life. This begs the question that, although pilates and yoga might help prevent injury, perhaps young cricketers might consider working on the farm or down the pit.

As Peter Roebuck, the former Somerset captain and now an influential cricket writer, suggested: "Pick those young players who had shown genuine promise. Send them to the Australian outback where they might cut trees or shave sheep for a year and come back with the physical resources to play professional cricket without constant fear of breakdown."

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