

Inhalační plicní vasodilatancia: oxid dusnatý

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EDITORIAL

The Molecule of the Year

The Molecule of the Year is nitric oxide, NO, a molecule of versatility and importance that has burst onto the scene in many guises. In the atmosphere it is a noxious chemical, but in the body in small controlled doses it is extraordinarily beneficial. It helps maintain blood pressure by dilating blood vessels, helps kill foreign invaders in the immune response, is a major biochemical mediator of penile erections, and is probably a major biochemical component of long-term memory. These are just a few of its many roles, which are just beginning to be discovered, and so many roles is not surprising because the same biological second messengers usually are used in many diverse systems, but a gas was indeed a surprise for an endogenous role, and a labile and toxic gas even more so. As the first surprise of such an unlikely agent was overcome, the gas as a messenger seemed logical because it could pass through biological membranes readily and oxidize foreign substances.

NO's role in sexual dysfunction, that of impotence, supports further a new liberation from old mental straitjackets. The future is sure to bring more insights into the effect on complex processes such as IQ, bad behavior, and alcoholism by single genes or chemical reactions. Many people will be happy to learn that some forms of sexual dysfunction may not be caused by psychiatric disorders or the failure of a marriage but may instead reflect a deficiency in a chemical reaction that can be compensated for by medical treatment. New research on the role of NO may also lead to new insights into the loss of memory, which is so debilitating to so many.

This year's Molecule of the Year once again shows that scientific rewards can come from pursuing unconventional thinking. The recent presidential election focused on the persistent question of providing jobs and correcting ailing economies. Hopefully, the political and social scientists advising our leaders will pursue these problems with the same creativity that characterized the research on NO. The new, the unexpected, and the incongruous will be needed to address these social problems. In addition, our elected officials as well as the general public must face unpleasant realities, including the need for the United States to work hard to maintain its standard of living in a competitive world and the need to be open-minded enough to welcome unexpected solutions such as gaseous messengers.

Every year *Science* picks a Molecule of the Year along the lines described in our editorial of 22 December 1989. Molecule is a term we use to emphasize that we are honoring the discovery rather than the people who made the discovery, not because people are unimportant but because many other awards honor the discoverers, and most discoveries involve the contributions of many people. As in the case of "people prizes," there are many "runner-up" discoveries that are extremely important to humanity but, in our opinion, are not yet quite as developed as our winner. For example, one of our runners-up, the discovery of the structure of nitrogenase, has no immediate industrial application, but the way enzymes fix nitrogen is bound to be of great importance to agriculture. As more intense farming and cheaper fuel become the necessities of the future, better mechanisms for nitrogen fixation become more important. Enzymes certainly appear to have solved the problem better than man-made solutions so far. The hope is that the enzyme mechanism and the chemical knowledge can be combined to make a new solution that will benefit millions. The widespread use of supercomputers is not a sudden event, but the increased utility of this powerful tool in industry and science for applications such as aircraft design and oil exploration will solve many problems that were previously beyond approach.

All of the runners-up are discussed in the accompanying story. This year they are an impressive group ranging from discoveries that are already being applied, such as fetal diagnosis and treatment (in utero treatment of a fetus to correct its deficiencies and transplanting fetal tissue to adults with Parkinson's disease), to those that are now far enough along so that application seems inevitable, for example, antisense RNA. In addition, there are landmarks such as the mapping of chromosomes Y and 21, which will certainly lead to medical discoveries, and the use of magnetic resonance imaging to diagnose medical problems and to locate areas of the brain identified with specific thought processes. Those who sometimes question the advances of science should think for a moment about the incredible developments that have slipped into everyday life without headlines. The Molecule of the Year and the runners-up are a good place to start for the discoveries that will inevitably make the future better than the past.

Daniel E. Koshland, Jr.

Downloaded from <http://www.sciencemag.org> on September 11, 2025

Nitric oxide discovery Nobel Prize winners

Robert F. Furchgott, Louis J. Ignarro, and Ferid Murad shared the **Noble Prize** in **1998** for their discoveries concerning nitric oxide as a signalling molecule in the cardiovascular system





2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

Developed by the task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS).

Endorsed by the International Society for Heart and Lung Transplantation (ISHLT) and the European Reference Network on rare respiratory diseases (ERN-LUNG).

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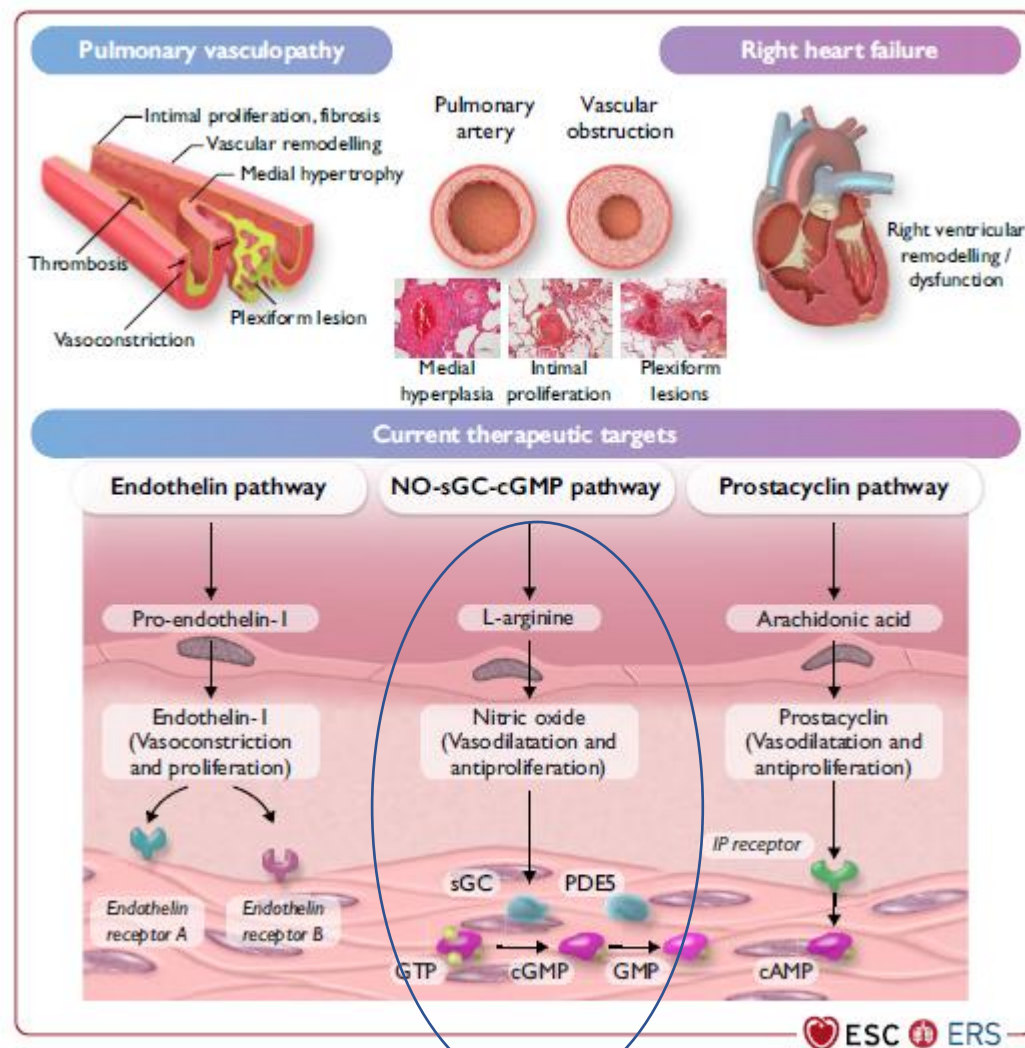


Figure 7 Pathophysiology and current therapeutic targets of pulmonary arterial hypertension (group 1). cAMP, cyclic adenosine monophosphate; (c) GMP, (cyclic) guanosine monophosphate; GTP, guanosine-5'-triphosphate; IP receptor, prostacyclin I2 receptor; NO, nitric oxide; PDE5, phosphodiesterase 5; sGC, soluble guanylate cyclase.



Plicní hypertenze

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

Developed by the task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS).

Table 1. New Hemodynamic Definitions for PH

Definition	Hemodynamic profile	Typical clinical group
PH	mPAP >20 mmHg	All
Precapillary PH	mPAP >20 mmHg PVR >2 WU PAWP ≤15 mmHg	Pulmonary arterial hypertension PH attributable to lung disease CTEPH
Combined precapillary+postcapillary PH	mPAP >20 mmHg PVR >2 WU PAWP >15 mmHg	Left heart disease Left heart+lung disease overlap
Isolated postcapillary PH	mPAP >20 mmHg PVR ≤2 WU	Left heart disease
Exercise PH	mPAP/CO slope between rest and exercise >3 mmHg/L per min	Exertional dyspnea with preserved LV ejection fraction with normal resting PAWP

PULMONARY HYPERTENSION WITH SPECIAL REFERENCE TO THE VASOCONSTRICTIVE FACTOR*

BY

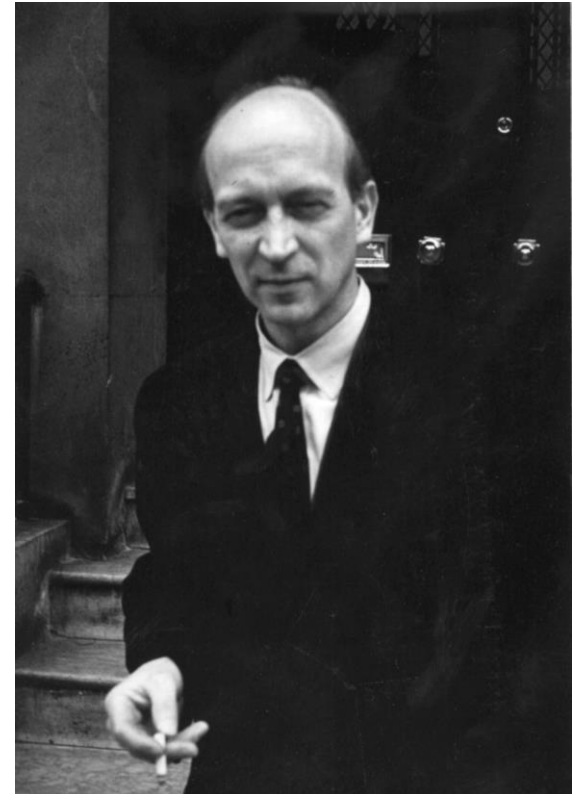
PAUL WOOD

From the Institute of Cardiology, National Heart Hospital, and the Brompton Hospital

Received July 2, 1958

Wood Unit = (mPAP-PAOP)/CO

$$PVR = 80 \times (mPAP - PAOP) / CO$$



Pulmonary Hypertension by the Method of Paul Wood

John H. Newman, MD

TABLE 4] Vasoconstrictors and Vasodilators in the Pulmonary Circulation

Vasoconstrictors	Vasodilators	Mixed Effects
Alveolar hypoxia	Oxygen	Histamine (1 vs 2)
Alpha-adrenergic agonists	Beta-adrenergic agonists	Serotonin (NO production)
Angiotensin II	Nitric oxide, Nitroprusside	Endothelin (A vs B receptor)
Thromboxanes	Prostacyclins, PGE _{1,2}	Acetylcholine (NO vs muscarinic)
Leukotrienes	Phosphodiesterase 5 inhibitors	Calcium channel blockers

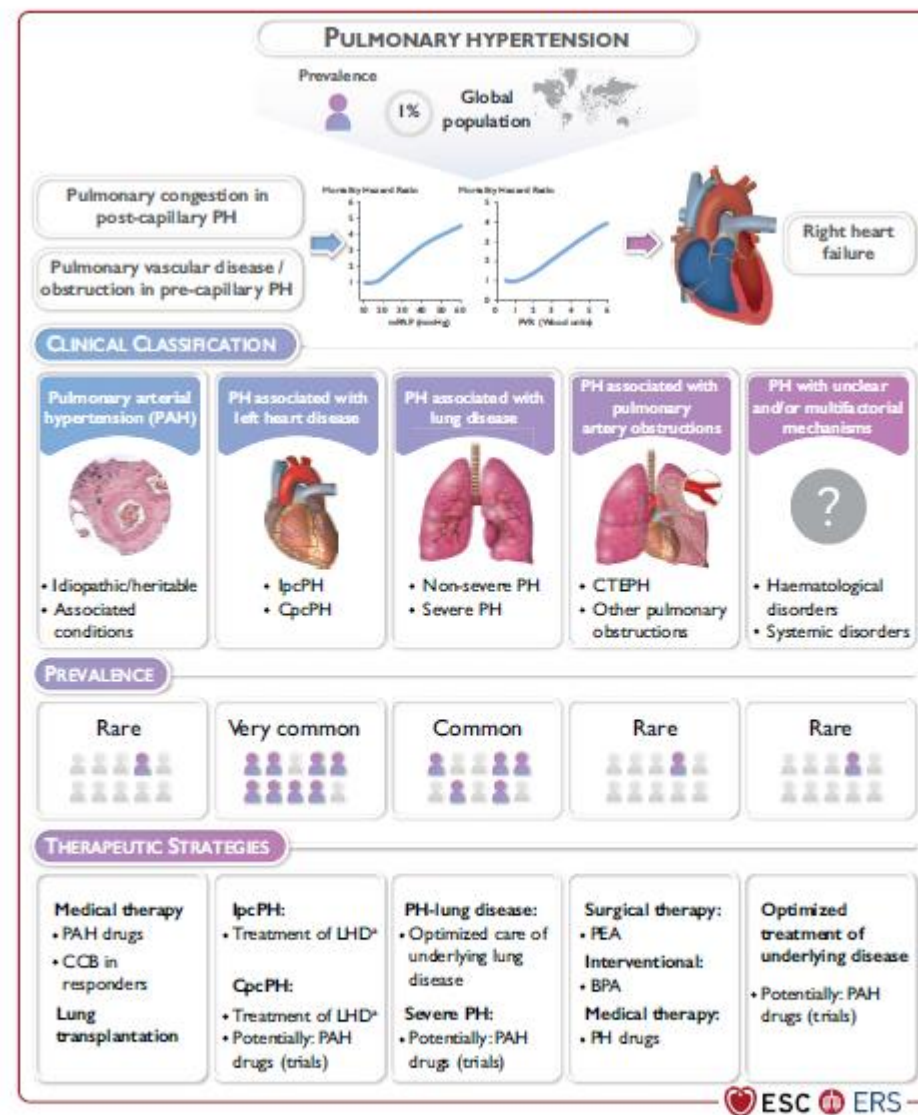
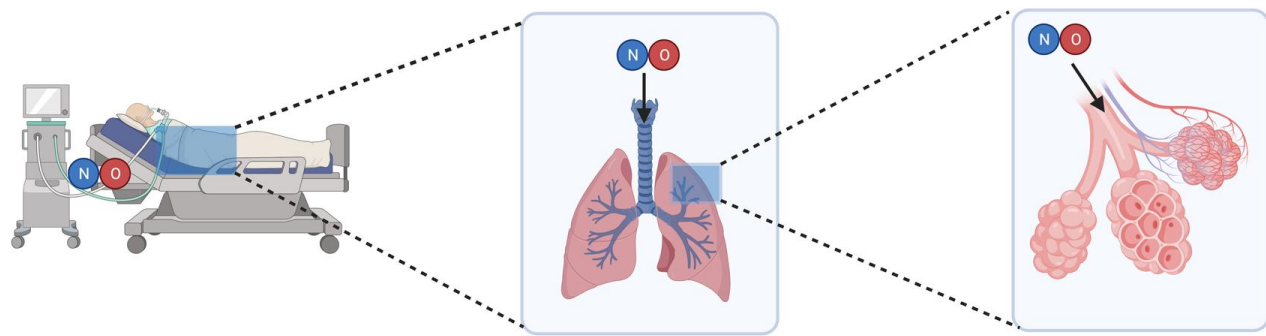
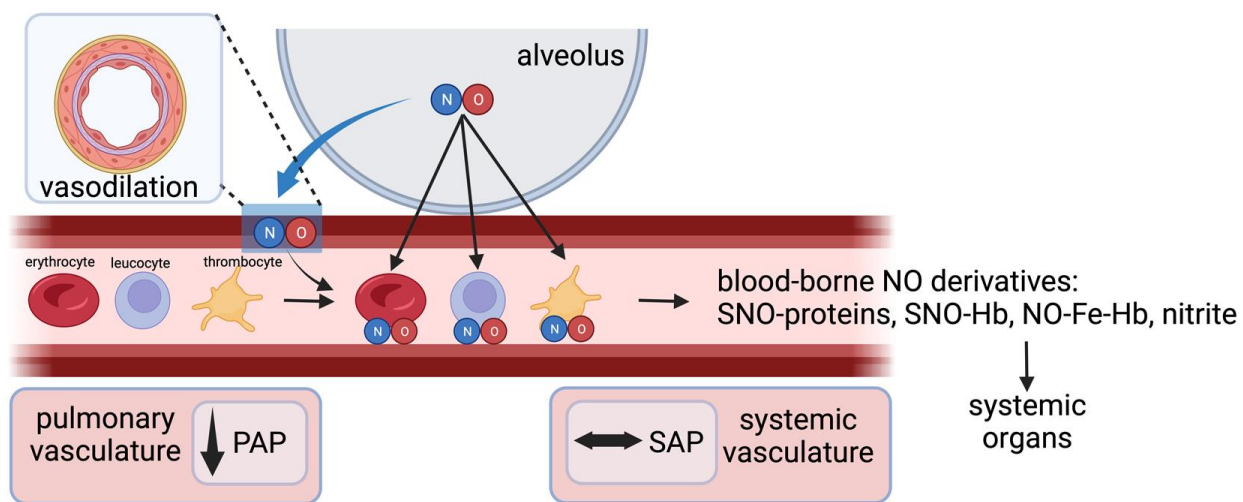


Figure 1 Central illustration. BPA, balloon pulmonary angioplasty; CCB, calcium channel blocker; CTEPH, chronic thrombo-embolic pulmonary hypertension; CpCPH, combined post- and pre-capillary pulmonary hypertension; lpcPH, isolated post-capillary pulmonary hypertension; LHD, left heart disease; PAH, pulmonary arterial hypertension; PEA, pulmonary endarterectomy; PH, pulmonary hypertension. *Treatment of heart failure according to the ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.²⁷ Treatment of left-sided valvular heart disease according to the 2021 ESC/EACTS Guidelines for the management of valvular heart disease.²⁸

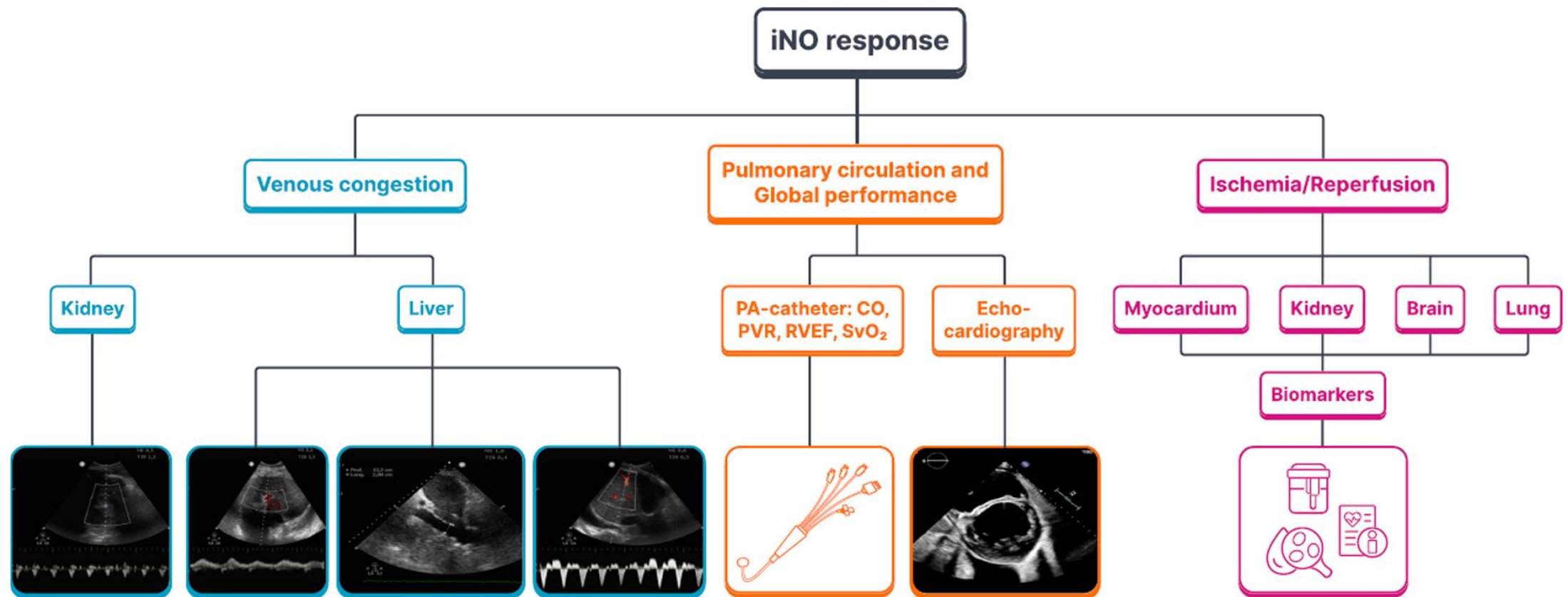


Inhaled NO at a crossroads in cardiac surgery: current need to improve mechanistic understanding, clinical trial design and scientific evidence

Stefan Muenster^{1*}, Iratxe Zarragoikoetxea^{2†}, Andrea Moscatelli³, Joan Balcells⁴, Philippe Gaudard⁵, Philippe Pouard⁶, Nandor Marcin^{7‡} and Stefan P. Janssens^{8‡}

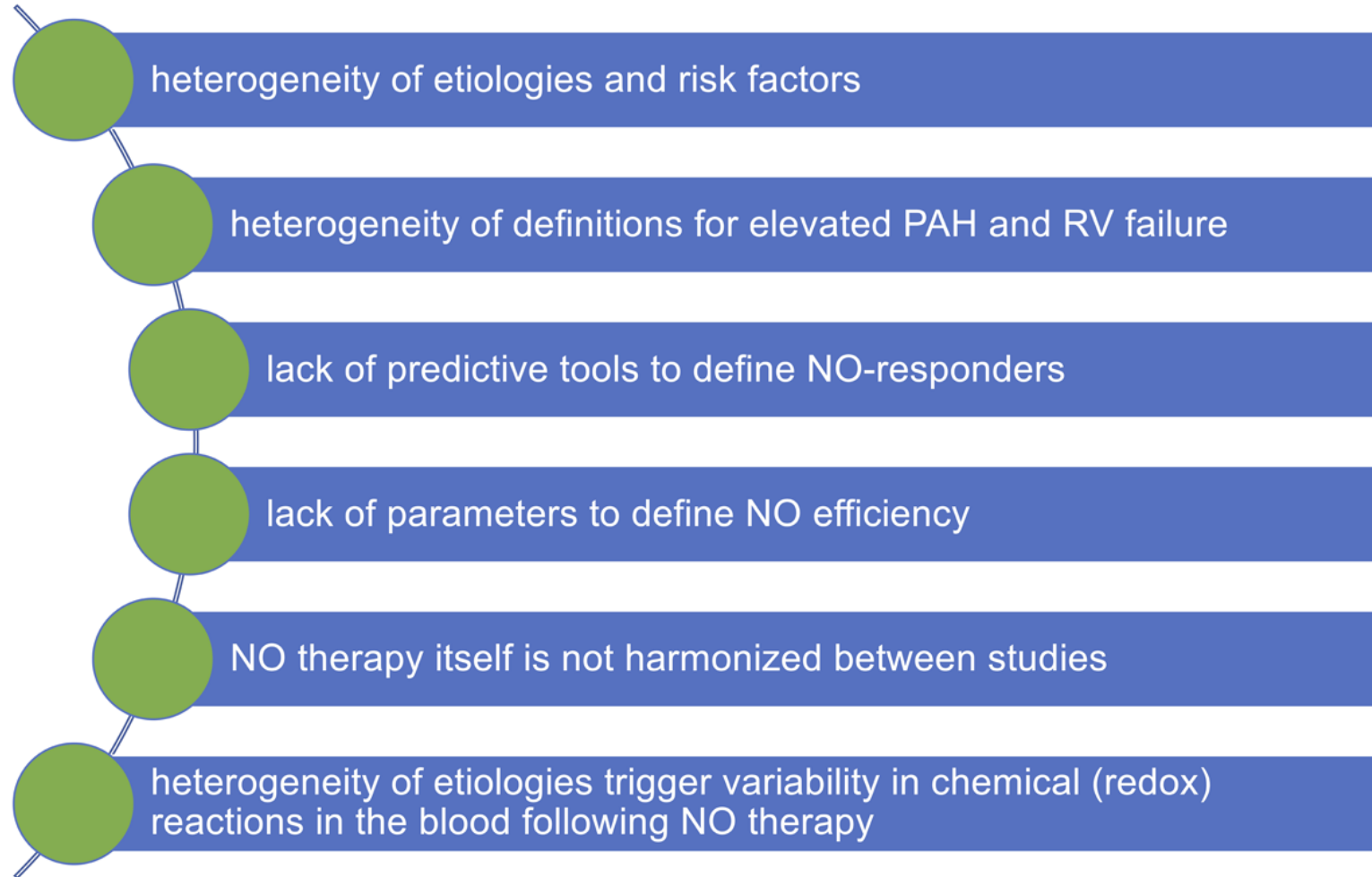


Inhaled NO as a selective pulmonary vasodilator and interactions with various blood components. NO, nitric oxide; PAP, pulmonary arterial pressure; SAP, systemic arterial pressure; SNO-Hb, S-nitrosohemoglobin; NO-Fe-Hb, ferrous nitrosyl-hemoglobin. Created with BioRender.com.



The mandate of inhaled NO for cardiac surgery: inhaled NO response to venous congestion, the pulmonary circulation and to the ischemia/reperfusion injury. iNO, inhaled nitric oxide; PA-catheter, pulmonary artery catheter; CO, cardiac output; PVR, pulmonary vascular resistance; RVEF, right ventricular ejection fraction; SvO₂, venous oxygen saturation.

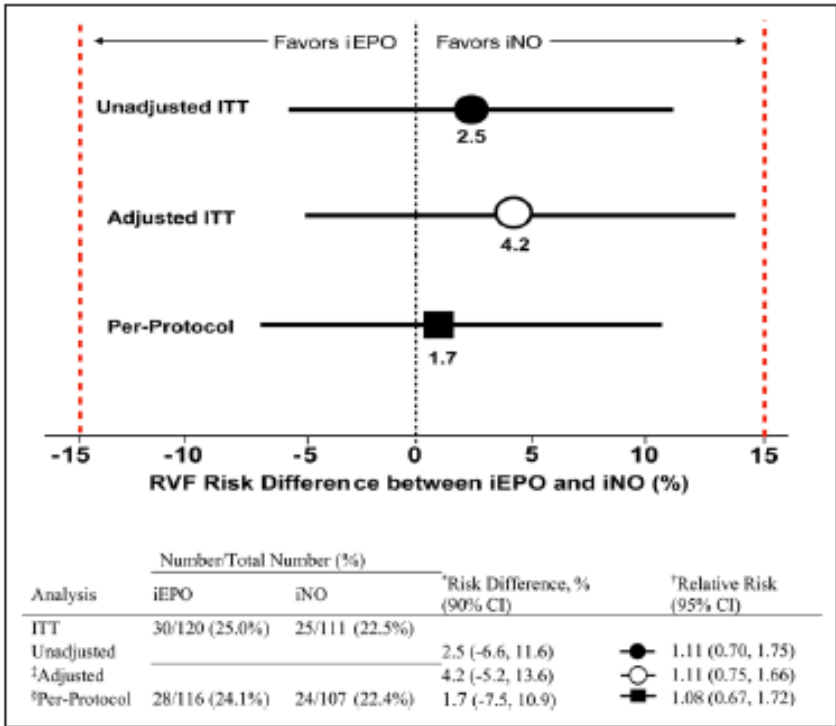
inhaled NO - reasons for the lack of evidence on outcome



ORIGINAL RESEARCH ARTICLE

Inhaled Epoprostenol Compared With Nitric Oxide for Right Ventricular Support After Major Cardiac Surgery

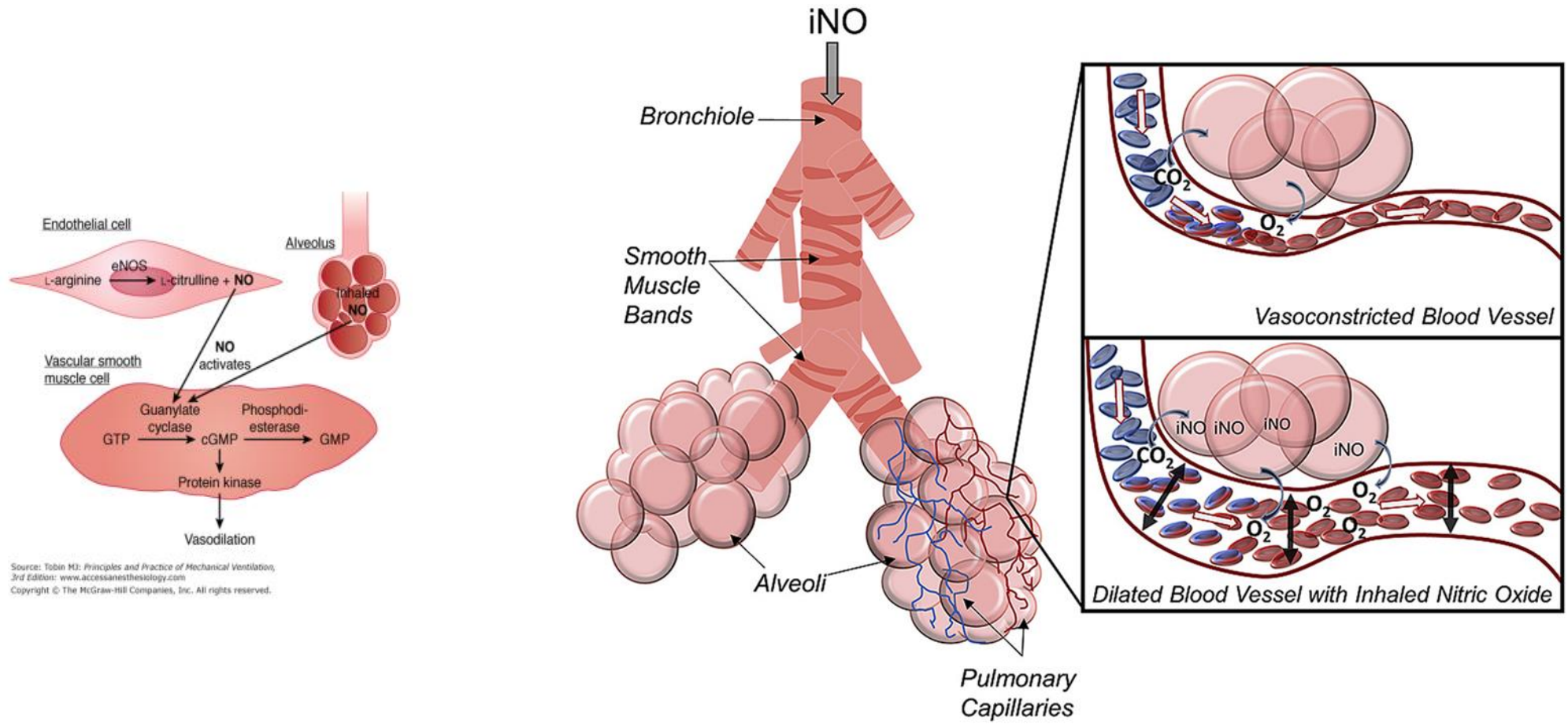
Kamrouz Ghadimi, MD, MHS; Jhaymie L. Cappiello, RRT; Mary Cooter Wright, MS; Jerrold H. Levy, MD; Benjamin S. Bryner, MD, MS; Adam D. DeVore, MD, MHS; Jacob N. Schroder, MD; Chetan B. Patel, MD; Sudarshan Rajagopal, MD, PhD; Svati H. Shah, MD, MS, MHS; Carmelo A. Milano, MD; for the INSPIRE-FLO Investigators



Risk difference in RVE development between iNO and iEPO treatment groups

- In a double-blind, parallel-design, randomized controlled trial of 231 adult patients undergoing major cardiac surgery, inhaled pulmonary-selective vasodilator treatment with either inhaled epoprostenol or nitric oxide was associated with similar risks for the development of acute postoperative right ventricular failure.
- No statistical differences were seen between groups for secondary outcomes after surgery, including mechanical ventilation duration, hospital and intensive care unit length of stay for the index hospitalization, acute kidney injury development, renal replacement therapy initiation, or death at 30 days, 90 days, and 1 year after treatment.

Efekt NO



V jakých klinických situacích?

Inhaled pulmonary vasodilators in pulmonary hypertension: Perioperative use and clinical considerations

Rebecca Klingbeil, DNP,^{a,*} Clara Hjalmarsson, MD, PhD,^{b,c}
Bailey Colvin, PharmD,^d Katherine Kozarek, MD,^e
and Anna Bovill Shapiro, MD^a

JHLT Open 2026;14:100627

Akutní selhání pravého srdce

ARDS

Transplantace srdce s plicní hypertenzí

Transplantace srdce a plic

Transplantace srdce a implantace LVAD

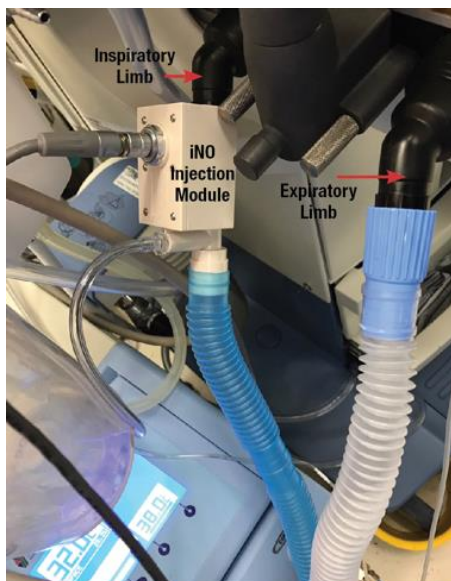
Kardiochirurgické výkony u pacientů s plicní hypertenzí

Náhrady mitrální chlopně u pacientů s plicní hypertenzí

Jak podávat ?



LungFit® PH - Nitric Oxide Delivery System



V jaké dávce?

Acute effects of inhaled nitric oxide in adult respiratory distress syndrome

G.A. Iotti*, M.C. Olivei*, A. Palo*, C. Galbusera*, R. Veronesi*, A. Braschi*

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G.A. IOTTI ET AL.

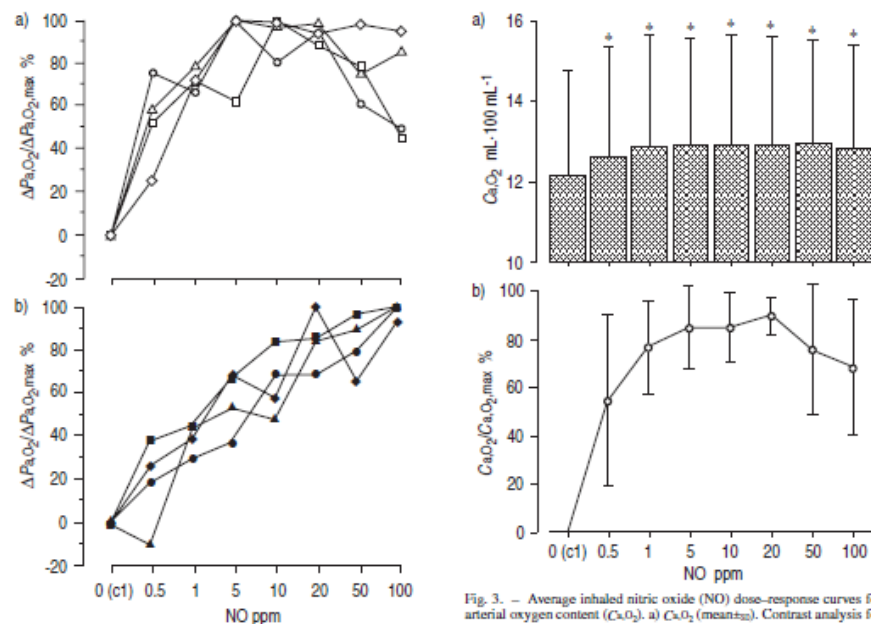


Fig. 2. — Individual inhaled nitric oxide (NO) dose-response curves for arterial oxygen tension (PaO_2). PaO_2 changes are expressed as a per cent of the individual maximal increase relative to initial control ($\Delta PaO_2 / \Delta PaO_{2,max} \%$). a) patients No. 2 (○), 3 (□), 4 (△) and 8 (◇); b) patients No. 1 (●), 5 (■), 6 (▲) and 7 (◆). c1: initial control; ppm: parts per million.

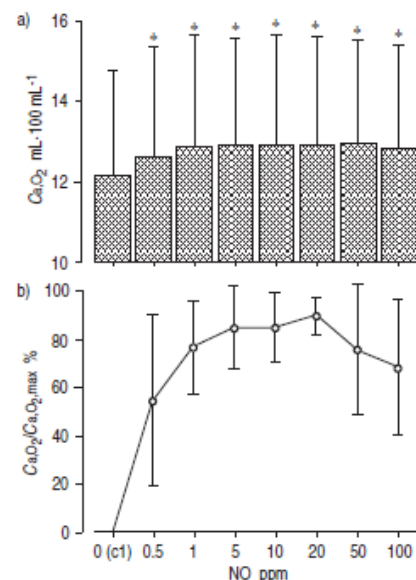
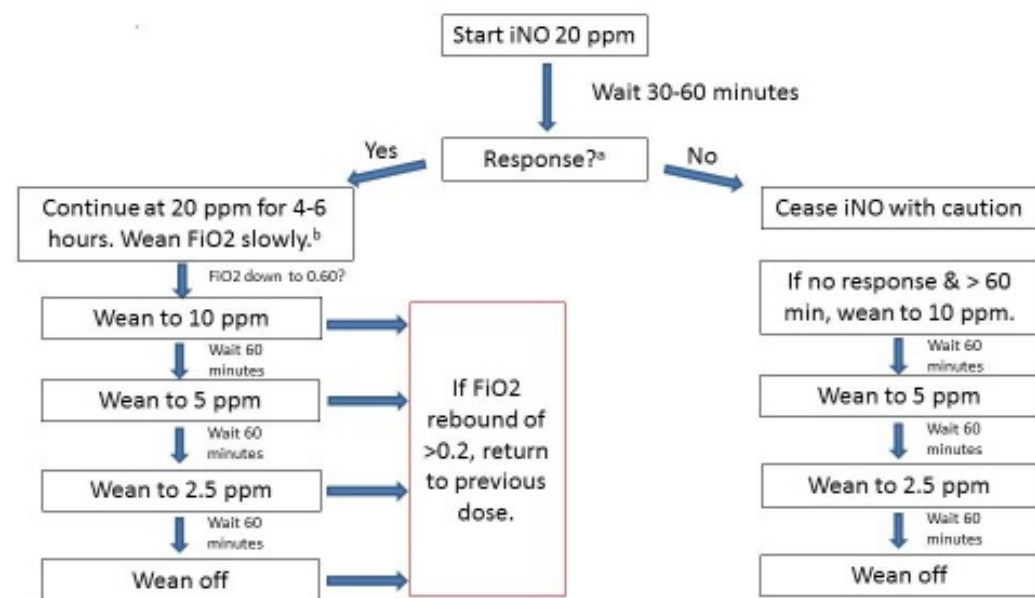


Fig. 3. — Average inhaled nitric oxide (NO) dose-response curves for arterial oxygen content (CaO_2). a) CaO_2 (mean±SD). Contrast analysis for effect of NO treatment: * $p < 0.0001$, compared with initial control (c1); analysis of variance for effect of NO dose: $p < 0.05$. b) CaO_2 changes (mean±SD), normalized as per cent of the individual maximal increase relative to c1 ($\Delta CaO_2 / \Delta CaO_{2,max} \%$); ppm: parts per million.



a. See definition of Response (or Partial Response) above.
b. Maintain $saO_2 \geq 95\%$.

NO

- Indikace :

Akutní selhání pravého srdce

ARDS ? VV, VA ECMO

Transplantace srdce u pacientů s plicní hypertenzí

Transplantace srdce a plic (weaning ECMO)

Transplantace srdce a implantace LVAD

Kardiochirurgické výkony u pacientů s plicní hypertenzí

- Pomocná metoda
- Jednoduché užití, snadno říditelný efekt
- Limity
- Relativně drahý provoz
- NO – VV/VA ECMO/RVAD – NO - sildenafil