

Pediatric and neonatal individualized Medicine: care and cure for each and everyone

Vassilios Fanos

Editor in Chief JPNIM

Neonatal Intensive Care Unit, Puericulture Institute and Neonatal Section, AOU and University of Cagliari, Italy

*One should immerse oneself into tradition
with the greatest skill to play in,
with the greatest courage to break out*
Li Keran (1907-1989)

Keywords

Individualized Medicine, Evidence Based Medicine, Medicine Based Evidence, Narrative Based Medicine, newborn, child, “omics”.

Corresponding author

Vassilios Fanos, Neonatal Intensive Care Unit, Puericulture Institute and Neonatal Section, AOU and University of Cagliari; email: vafanos@tin.it, vafanos@tiscali.it; tel.: +390706093403 (direct), +390706093438 (NICU).

How to cite

Fanos V. Pediatric and neonatal individualized Medicine: care and cure for each and everyone. J Pediatr Neonat Individual Med. 2012;1(1):7-10. doi: 10.7363/010115.

The dramatic improvements in basic biological research, as well as the impact of high technology, are associated with a rapid increase in life expectancy, social change and public health measures, all leading to important modifications in Medicine [1].

In the past few years, we have seen radical changes in Medicine: we have gone from paternalism to therapeutic alliance, from treating patients to taking care of them, from the concept of disease to the concept of illness, from compliance to adherence. All this has marked the change from a medical-centred system to a patient-centred one, where patients are less passive and play an increasingly active role in their treatments (empowerment). Moreover, communication (to communicate “with” the patient and not “to” the patient) has become more relevant [2]. In all cases, the background philosophy is “to look at things from the patient’s perspective”, who, in our case, is a child, necessarily linked to his/her parents.

In the next few years we will witness a profound change in Medicine and healthcare, due to progress in technology and the ability to analyse large amounts of data from single patients.

In **Tab. 1** the present and future scenarios of Medicine are presented. The complexity of biological systems (Systems Biology) is strongly emerging in the most recent literature. If we analyse what are considered the five great ideas in Biology and Medicine, the genome, the cell, biochemistry and evolution, we find Systems Biology (recently more specifically referred to as Systems Medicine) [3].

“Omics” (genomics, transcriptomics, proteomics and metabolomics) represent the complexity of biological systems [4]. They represent the future and are destined to replace traditional laboratory methodologies (not sensitive or specific enough to diagnose a disease) thanks to their capacity to distinguish a single subject in

normal conditions and, in the case of disease, with a simultaneous, and often noninvasive analysis of a large amount of data (the so-called “direct intelligence of data”) [5]. Scientific knowledge is so broad that researchers can miss important links, not because they are subtle or difficult to recognise, but because nobody has such a wide understanding of science as to notice them: in a huge haystack it is difficult even to find a fifteen-meter-long needle [5]!

In particular, it is important to study and consider not only the potential of genes but also their interactions with the environment, which bring the phenotype into being [6]. The role of epigenetics emerges strongly, unless it is considered “The current fashionable response to any question to which you do not know the answer” [7].

Genetics is printed in ink and cannot be deleted, while epigenetics is written in pencil and can be modified [8]. Genetics proposes while epigenetics provides. We cannot change our past, but we can try to influence or modify our future, for example by changing our eating habits and limiting or personalising the use of drugs, thus modulating our life styles.

Many years ago Thomas Edison predicted that doctors of the future would no longer treat the human frame with drugs, but rather would cure and prevent diseases with nutrition.

For all clinical issues, it is important to use an updated multidisciplinary approach and one that is tailor-made at the same time.

By reading scientific papers and attending the most important conferences in each discipline, one has the impression of being attracted by apparently opposing forces: on one side there are meta-analyses and on the other personalised Medicine [9].

If we wish to hypothesize a simple formula to summarise things that matter, we would have that in **Tab. 2**. Along with Evidence Based Medicine, in the table appear also Medicine Based Evidence (which is not a play on words, but is indeed the evidence based on Medicine, i.e. on what

Table 1. Differences between medicine of the past and of the future.

Medicine of the past	Medicine of the future
Epidemiologic	Individualized
Descriptive	Predictive
Reductionistic	Holystic
Reactive	Prospective
Genetics-based	Epigenetics-based

Table 2. Synthetic formula for contemporary medicine.

EBM + MBE + NBM

EBM: Evidence Based Medicine, MBE: Medicine Based Evidence, NBM: Narrative Based Medicine.

we know and we have learned by working day by day in the “front line”) and Narrative Based Medicine (which means paying attention and giving importance to communication and Medical Humanities).

These factors are the opposite of Error Based Medicine + Impressions Based Medicine + Arrogance Based Medicine, a Medicine that is perceived as strong and almost infallible but which is, in fact, coarse and inattentive.

Meta-analyses have been, and will be, very important for Medicine and have led to rapid progress in the evolution of science. However, we can say that meta-analyses are not everything and that, in meta-analyses, the absence of evidence is not evidence of absence.

Contemporary Medicine is strongly influenced, if not obsessed, by healthcare protocols. These are often necessary in countries with more developed healthcare systems, where reference points can be used in the defensive Medicine field. Actually, by definition, protocols do not take into account (or take into slight account) the individuality of each patient [10], a situation that requires a diagnostic and, more importantly, a personalised and tailor-made therapeutic approach.

Pharmacogenomics and pharmacometabolomics, for example, are ready or nearly so to allow a personalisation of therapy [11].

In pediatric or neonatal Medicine these observations are even more important as children have a dynamic and constantly growing organism. Of relevance, for example, is the height-ponderal growth in the first year of life, or the morpho-functional growth and maturation of the encephalon in the first 1,000 days of life (about 1 g of weight increase per day). In this period crucial events occur in connecting neurons (connectomics and selective synaptogenesis) [12]. They follow the scale free networks [13]. Moreover, a large amount of experimental, clinical and epidemiological data underlines the relevance of perinatal programming in determining the health or disease status of an adult subject [14]. It is all mostly decided in the first stages of life or even in the womb. The predisposition to many diseases starts in this period of life and their prevention can start during pregnancy itself [15] or in the perinatal period [16].

As concerns this, we believe that there are important challenges to be faced and overcome in Neonatology (**Tab. 3**).

The key question is if we can provide high-technology Medicine in a context of drastic

Table 3. New trends in Neonatology.

- Decreasing the neonatal mortality rate, especially in low-income countries
- Decreasing health care expenditure, maintaining a high quality of neonatal care
- Avoiding long term complications
- Gender Medicine in Neonatology
- Long term consequences of type of delivery
- Neuroprotection in perinatal Medicine
- Non invasive identification of phenome and diseaseome
- Nutrimetabolomics
- Pharmacometabolomics
- Immunohistochemistry of embryofetal tissues and regenerative Medicine
- Simulation in Neonatology
- Medical Humanities

containment of health care costs. Moreover, can we improve neonatal survival in low-income countries with limited health care resources worldwide? There is probably no single answer, but the need for a new strategic perspective in global health care organizations and research networks is mandatory [17].

Research should be addressed towards new ambitious goals (think more and think different), but it should also look differently at old results [18].

The winning intuition would be not just having new ideas, but finding better results in existing ones.

We believe for example that many experimental data obtained from animal experiments do not always have full correspondence in humans. However, some pathologies in animals can be helpful in understanding human diseases and healing processes [19].

We need more research and better research. Now it's time to individualize our approaches in Pediatrics and Neonatology: care and cure for each and everyone.

References

1. Mussap M, Fanos V. Reducing neonatal mortality and expenditure in the era of health care crisis: is it possible? *J Matern Fet Neonat Med* 2012; Early Online: 1-2.
2. Fanos V. [Communication in Pediatrics]. [Chapter in Italian]. In: Cadeddu A, D'Aloja E, Faa G, Fanos V, Granese A, Rutelli P. *Qualità e sanità: un dialogo per l'umanizzazione*. Franco Angeli, Milano, 2007.

3. Fanos V. Cells, the tree, medicines and the tailor. *Curr Pharm Des.* 2012;18(21):2995.
4. Atzori L, Griffin JL, Noto A, Fanos V. Metabolomics: A new approach to drug delivery in perinatology. *Curr Med Chem.* 2012, Aug 9. [Epub ahead of print].
5. Michael Nielsen. *Reinventing discovery: the new era of Networked Science.* Princeton, NJ: Princeton University Press, 2011.
6. Dunn WB, Broadhurst DI, Atherton HJ, Goodacre R, Griffin JL. Systems level studies of mammalian metabolomes: the roles of mass spectrometry and nuclear magnetic resonance spectroscopy. *Chem Soc Rev.* 2011;40(1):387-426.
7. Smith GD. Epidemiology, epigenetics and then Gloomy Prospect: embracing randomness in population health research and practice. *Int J Epidemiol.* 2011;40(3):537-62.
8. Miller P. A thing... or two about twins. *National Geographic.* 2012;1:38-65.
9. Fanos V, Yurdakök M. Personalized neonatal medicine. *J Matern Fetal Neonatal Med.* 2010;23(Suppl 3):4-6.
10. Faa G, Gerosa C, Fanni D, Nemolato S, Locci A, Cabras T, Marinelli V, Puddu M, Zaffanello M, Monga G, Fanos V. Marked interindividual variability in renal maturation of preterm infants: lessons from autopsy. *J Matern Fetal Neonatal Med.* 2010;23(Suppl 3):129-33.
11. Fanos V. New Frontiers in Perinatal Pharmacology. *Curr Med Chem.* 2012 Aug 9. [Epub ahead of print].
12. Gao W, Zhu H, Giovanello KS, Smith JK, Shen D, Gilmore JH, Lin W. Evidence on the emergence of the brain's default network from 2-week-old to 2-year-old healthy pediatric subjects. *Proc Natl Acad Sci U S A.* 2009;106(16):6790-5.
13. Perpiñá Tordera M. [Complexity in asthma: inflammation and scale-free networks]. [Article in Spanish]. *Arch Broncopneumol.* 2009;45(9):459-65.
14. Nicoletto SF, Rinaldi A. In the womb's shadow: The theory of prenatal programming as the fetal origin of various adult diseases is increasingly supported by a wealth of evidence. *EMBO Rep.* 2011;12(1):30-4.
15. Adamo KB, Ferraro ZM, Brett KE. Can We Modify the Intrauterine Environment to Halt the Intergenerational Cycle of Obesity? *Int J Environ Res Public Health.* 2012;9:1263-307.
16. Golubnitschaja O, Yeghiazaryan K, Cebioglu M, Morelli M, Herrera-Marschitz M. Birth asphyxia as the major complication in newborns: moving towards improved individual outcomes by prediction, targeted prevention and tailored medical care. *EPMA J.* 2011;2(2):197-210.
17. Porter ME. What is value in health care? *N Engl J Med.* 2010;363:2477-81.
18. Faa G, Gerosa C, Fanni D, Nemolato S, Monga G, Fanos V. Kidney embryogenesis: how to look at old things with new eyes. In: Fanos V, Chevalier RL, Faa G, Cataldi L. *Developmental Nephrology: from Embryology to Metabolomics.* Quartu S. Elena (CA): Hygeia Press, 2012.
19. Natterson-Horowitz B, Bowers K. *Zoobiquity: What Animals Can Teach Us About Health and the Science of Healing.* New York: Borzoi, Knopf, 2012.