• Imprinting in Early Life • ADHD in the Young Child
• Primary Ciliary Dyskinesia – a Case Report
Contents

In Focus
Imprinting in Early Life Predisposes to Diseases in Adulthood ........................................... 4

What Else Is New? .................................................. 12

From the Practice
Use of Bioregulation Therapies for a Severe Otorhinological Problem ............................. 14

Meet the Expert
Dr. David Riley ................................................. 16

Around the Globe
Scientific Symposia in Belgium and the Netherlands: The Extracellular Matrix .................. 17

Refresh Your Homotoxicology
Attention-Deficit/Hyperactivity Disorder in Infancy and in the Preschool-aged Child ............ 18

Marketing Your Practice
Making Your Practice a Team .................................. 22

Research Highlights
New Approaches in the Treatment of Respiratory Insufficiency in Neonates ................. 24

Making of ...
Production of Homeopathic Suppositories ................................................................. 26

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The Importance of Early Intervention

Dr. Alta A. Smit

In bioregulatory medicine, treatment of pediatric patients poses not only many opportunities but also specific difficulties. Practice has shown that children respond very well to bioregulatory therapy, especially since the juvenile organism is mostly still reactive and regulates fairly easily. However, due to increases in environmental stressors (such as toxins and psychological factors) and in the use of suppressive drugs, treating today’s children can sometimes pose a challenge even for integrative practitioners.

Postnatal development remains a sensitive time, as many organ systems and autoregulatory systems continue to mature after birth. Tissues that are still developing are especially vulnerable to environmental imprints. The developing brain and nervous tissue, in particular, are sensitive to the effects of environmental toxins, as is the immune system. Many diseases of adulthood result from imprinting during the developmental period, and chronic pain syndromes in particular can often be traced back to events in childhood (e.g., maternal separation). This topic is discussed at length in our focus article by Professor Marietta Kaszkin-Bettag, who also suggests some interventions to correct and strengthen the bioregulatory apparatus. The issue of imprinting deserves to be taken seriously from the scientific, health economics, and social perspectives, since early intervention may prevent illness in later life.

The use of bioregulatory medicine as adjuvant therapy in even moderate to severe illness is discussed in two articles, the case study on ciliary dyskinesia by neonatologist Dr. Sergio Vaisman and the summary of a study by Professor Lidiya Ivanovna Ilyenko et al. on respiratory distress syndrome in neonates.

Dr. Leon Strauss tackles the difficult subject of attention deficit/hyperactivity disorder in three articles, the first of which, dealing with the young child, appears in this issue. The other two will follow in subsequent journals.

We also present our regular features: Marc Deschler’s valuable marketing column shows how your practice staff will become an efficient team; Dr. Cornelia Witt presents the manufacturing of bioregulatory suppositories in the Making of... series; and Meet the Expert introduces Dr. David Riley, the current president of the International Society of Homotoxicology and Homeopathy. Last but not least, Pascale Vlietinck reports on a successful international symposium in Belgium and the Netherlands.

We are sorry to see the last of the Making of... series in this issue but pleased to announce that Dr. Robert van Haselen has agreed to write a column on research methodology and the use of research data. We are eagerly anticipating this new series of articles, which will begin with the next issue.

References:
Imprinting in Early Life Predisposes to Diseases in Adulthood

By Marietta Kaszkin-Bettag, PhD
Professor of pharmacology, toxicology, and phytotherapy

Introduction
Prenatal development and early childhood are influenced by endogenous and environmental factors that act in concert by causing structural and functional changes that may persist for the life span. This phenomenon is termed “early-life programming.”1 The concept of early-life physiological “programming” or “imprinting” tries to explain the associations among prenatal environmental events, altered fetal growth and development, and the occurrence of diseases in later life (as previously reviewed).1 Such programming factors include nutrients and endogenous hormones; they may also involve environmental exposure to biological materials, chemicals, drugs, medical devices, and physical factors.2 Early-life programming reflects the action of certain factors on a specific tissue during a sensitive developmental period or “window,” thereby affecting its development, organization, and function. Different cells and tissues are sensitive at different times; therefore, the effects of environmental challenges will have distinct consequences, depending not only on the challenge involved but also on its timing.

Developmental immunotoxicity and health risks for adulthood
Developmental immunotoxicity (DIT) is an increasing health concern because DIT outcomes predispose children to certain diseases; the diseases with increasing incidences in recent decades include childhood asthma, allergic diseases, autoimmune conditions, and childhood infections.3 The enhanced vulnerability of the developing immune system for environmental influences is based on unique immune maturation events that occur during critical windows in early life (e.g., negative selection against autoreactive T cells in the developing thymus).

Environmental influences on prenatal development and immunologic responses
The in utero environment is thought to play a major role in the risk of later life disease. The semiallogeneic pregnancy state is characterized by a suppression of graft rejection because during the course of maturation, the potential for maternal-fetal allogeneic reactions must be minimized. This situation is associated with an impairment of the fetal and neonatal immune system, which may influence the specific nature of DIT outcomes.4 The last-trimester fetus and the neonate normally have decreased T-helper cell (Th) 1–dependent functions, and postnatal acquisition of necessary Th1 capacity is a major concern with DIT.4 Evidence for the reduced Th1 capacity of newborns is reflected by the fact that the production of interferon γ (the hallmark Th1 cytokine) is severely reduced in the neonate.

In utero exposure to pesticides, such as polychlorinated biphenyls, or tobacco smoke is known to produce a range of immunotoxic outcomes (e.g., immunosuppression, autoimmunity, or misregulated tissue inflammation). Beyond T cells, dendritic cells and macrophages are sensitive targets to chemicals, resulting in macrophage dysregulation, changes in innate immunity, and inflammatory damage.

Immune response during early life
A cesarean delivery can affect neonatal immune responses and can increase the risk of atopy. Children born by cesarean section have a 2-fold higher odds of atopy than those born by vaginal delivery (odds ratio, 2.1; 95% confidence interval, 1.1–3.9). In multivariate analyses, birth by cesarean section was significantly associated with increased odds of allergic rhinitis (odds ratio, 1.8; 95% confidence interval, 1.0–3.1), but not of asthma.5 This study demonstrated that cesarean delivery may be associated with allergic rhinitis and atopy, particularly among children with a parental history of allergies. This could be explained by lack of contact with the
maternal vaginal/fecal flora during cesarean delivery. During the neonatal period, the mammalian host is exposed through mucosal surfaces to a broad spectrum of environmental macromolecules and microbial agents. The neonatal mucosa has all major elements of innate and adaptive immunologic repertoire. The early neonatal period is also characterized by a relative deficiency in antigen-presenting cell functions, altered cell-mediated immune responses, and a relative increase in apoptosis and eosinophilic responses. Recent investigations have shown that the nature of mucosal microflora acquired in early infancy determines the outcome of mucosal inflammation and the subsequent development of mucosal disease, autoimmunity, and allergic disorders later in life. It seems that altered mucosal microflora in early childhood affect signaling reactions that determine T-cell differentiation and/or the induction of tolerance. Reduced Th1 and increased Th2 cytokine expression in the respiratory tract, associated with increased allergic disease, has been correlated with reduced exposure to microbial agents associated with Th1 responses. These observations suggest that the interaction between the external environment and the mucosal tissues in the early neonatal period and infancy may be critical in directing and controlling the expression of diseasespecific responses in later life.

Thus, early-life toxicologic exposure to xenobiotic infectious agents or stress may be pivotal in producing the later-life onset of increased childhood infections; neurologic disorders; fatigue-related illnesses; autoimmune diseases; allergic diseases, including asthma; food allergies; and even cancers (e.g., childhood leukemia). Recent investigations have shown that the nature of mucosal microflora acquired in early infancy determines the outcome of mucosal inflammation and the subsequent development of mucosal disease, autoimmunity, and allergic disorders later in life. It seems that altered mucosal microflora in early childhood affect signaling reactions that determine T-cell differentiation and/or the induction of tolerance. Reduced Th1 and increased Th2 cytokine expression in the respiratory tract, associated with increased allergic disease, has been correlated with reduced exposure to microbial agents associated with Th1 responses. These observations suggest that the interaction between the external environment and the mucosal tissues in the early neonatal period and infancy may be critical in directing and controlling the expression of disease-specific responses in later life.

Childhood allergic diseases

The incidence of asthma in industrialized countries has increased dramatically in recent decades, with the consequences of significant public health cost. In 2002, there were already approximately 16 million adolescents with asthma. For childhood allergic asthma and rhinitis in particular, various toxins, infectious agents, airborne pollutants, and maternal smoking were identified as significant risk factors. In addition, the likelihood is discussed that fetal-expressed genes promoting Th2 may continue to be inappropriately expressed in some neonates, thereby increasing the risk of asthma. In an 8-year prospective study of 308 children, younger than 7 years, who had recurrent wheezing, a personal history of allergic disease, parental asthma, atopy, and late-onset symptoms were identified as prognostic risk factors for asthma symptoms. The origin of this disease may be traced to early childhood (i.e., the years before exposure to allergen).

In summary, it was proposed that managing the fetal and neonatal immune system to reduce the persistence of the fetal immune phenotype and to promote rapid and effective Th1 maturation has the potential to significantly reduce the risk of asthma in childhood (Figure 1).
thermore, an increased risk for several childhood allergic diseases was identified after maternal use of antibiotics during pregnancy.\textsuperscript{2}

**Childhood neurologic disorders**

Another example is chronic fatigue syndrome (CFS) in children, for which the causes are certainly early-life events.\textsuperscript{9} Immune dysfunction is recognized as part of the CFS phenotype but has received comparatively less attention than aberrant neurologic or endocrine function. However, recent research results suggest that early-life immune insults, including DIT, which is induced by xenobiotics, may offer an important clue to the origin of CFS. Pediatric fibromyalgia seems to be a variant of CFS, with a predominance of hypothalamic-pituitary-adrenal (HPA) dysfunction\textsuperscript{10} (Figure 2). Fibromyalgia is most common in midlife, but may be seen at any age. It is characterized by chronic widespread pain.\textsuperscript{11} The syndrome is associated with a constellation of symptoms, including fatigue, nonrefreshing sleep, and irritable bowel. Central nervous system sensitization is a major pathophysiologic aspect of fibromyalgia; in addition, various external stimuli, such as trauma and stress, may contribute to the development of the syndrome. Many early postnatal neurologic lesions associated with postnatal neurobehavioral diseases are recognized as being linked to a prenatal immune insult and inflammatory dysregulation (e.g., autism, autism spectrum disorders, and increased risk of schizophrenia). Also, neurologic diseases of later life may be connected to DIT because the gestational environment is thought to be important in both Parkinson and Alzheimer diseases.\textsuperscript{2,12}

**Cancer**

Dysfunctional immune responses may even lead to cancer, and childhood leukemia is thought to be directly linked with DIT.\textsuperscript{2,7} A key risk factor seems to be an early-life dysfunctional immune response to common childhood infections.

**Prenatal imprinting of the metabolic syndrome**

**Prenatal glucocorticoid stress**

Glucocorticoids are powerful mediators of early-life developmental processes. Their potent effects on tissue development (i.e., the accelerated maturation of organs, notably the lung) underline their widespread therapeutic use in obstetric and neonatal practice in threatened or actual preterm delivery. In contrast, glucocorticoids are rarely used in the antenatal treatment of fetuses at risk of congenital adrenal hyperplasia.\textsuperscript{1,13-14} However, glucocorticoid administration during pregnancy reduces offspring birth weight. It was hypothesized that prenatal stress derived from DIT, as previously described, or exposure to excess glucocorticoids might represent a mechanism linking fetal growth with adult pathophysiology.\textsuperscript{15} Epidemiological evidence suggests that particularly low birth weight is associated with an increased risk of cardiovascular, metabolic, and neuroendocrine disorders in adult life. Experimental studies in rats have shown that the birth weight is reduced after prenatal exposure to the synthetic steroid dexamethasone, which readily crosses the placenta; or to carbenoxolone, which inhibits 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2), the physiological fetal-placental “barrier” to mater-

![Figure 2. Treatment of Hypothalamic-Pituitary-Adrenal Axis Dysfunction in Stressed Individuals and Patients With Chronic Pain Syndromes: Tonsilla compositum, Thalamus compositum, and Spascupreel](image-url)
nal glucocorticoids. As adults, the offspring exhibit permanent hypertension, hyperglycemia, increased HPA axis activity, and behavior reminiscent of anxiety. Physiological variations in placental 11β-HSD2 activity correlate directly with fetal weight.

In humans, 11β-HSD2 gene mutations cause low birth weight. Moreover, low-birth-weight newborns have higher plasma levels of cortisol as a potential stress hormone throughout adult life.1,13 In human pregnancy, severe maternal stress affects the offspring’s HPA axis and is associated with neuropsychiatric disorders; moreover, maternal glucocorticoid therapy may alter offspring brain function.13

**Low birth weight and metabolic complications**

Numerous studies have revealed an association between lower birth weight and the subsequent development of the common cardiovascular and metabolic disorders of adult life (i.e., hypertension, insulin resistance, type 2 diabetes mellitus, and cardiovascular disease–related deaths).1 The early-life events described above that alter birth weight are important predictors of adult morbidity.

In a study16 of 22,000 US men, those who weighed less than 2.2 kg at birth had relative risks of adult hypertension of 1.26 and of type 2 diabetes of 1.75 compared with those with an average birth weight. Similar observations were made in women.17 Moreover, the association between birth weight and later cardiometabolic disease seems largely independent of classic lifestyle risk factors (e.g., smoking, adult weight, social class, excess alcohol intake, and sedentariness) that are additive to the effect of birth weight.18

**Prenatal origin of obesity, cardiovascular disease, and insulin resistance**

The fetal origins of obesity, cardiovascular disease, and insulin resistance have been investigated in a wide range of epidemiological and animal studies, which revealed an adaptation of the nutritionally manipulated fetus to maintain energy homeostasis for ensuring survival.19 One consequence of such developmental plasticity may be a long-term resetting of cellular energy homeostasis, most probably via epigenetic modification of genes involved in a number of key regulatory pathways.20 For example, reduced maternal-fetal nutrition during early to mid gestation affects adipose tissue development and adiposity of the fetus by setting an increased number of adipocyte precursor cells.21 More important, clinically relevant adaptations to nutritional challenges in utero may only manifest as primary components of the metabolic syndrome if followed by a period of accelerated growth early in the postnatal period and/or if offspring become obese. This suggests that obesity is not simply the result of lifestyle but has developmental determinants that are not of genetic origin. Thus, an understanding of the mechanisms that mediate the epigenetic changes is crucial to determine dietary and pharmaceutical approaches that can be applied in the postnatal period.

Fetal undernutrition and hypoxia are associated with an increased susceptibility to a number of adult-onset metabolic disorders. In addition to obesity, these include cardiovascular disease and insulin resistance. Interestingly, premature neonates also have an increased cardiovascular risk in adult life.18 It was observed that different feeding regimens, particularly in human premature neonates, have long-term metabolic consequences.19 Some developmental responses may persist through several generations. For example, the female reproductive tract develops in the first half of human fetal life. Girls who were growth retarded in utero have a reduced uterine size, and this reduction may lead to impaired uterine-placental function when these women become pregnant.

On the other hand, there is increasing evidence that maternal obesity is linked to numerous metabolic complications, including subfertility, gestational diabetes, hypertensive disorders of pregnancy, and throm-
boembolism, with potential long-term health consequences for both mother and child. Obesity and diabetes in women before pregnancy, gestational diabetes, and glycosuria (both diagnosed and ascertained during pregnancy) result in a higher mean birth weight and an increased offspring obesity risk. Thus, maternal lifestyle should be altered as possible to improve maternal and fetal outcomes.

Metabolic syndrome in childhood

Mechanisms for the development of metabolic syndrome in early life

The risks for obesity and insulin resistance may be programmed in utero as a result of decreased or increased birth weight because of the reasons previously described. The development of metabolic syndrome, however, is the result of a complex interaction of specific genes and environmental influences. A primary mechanism accounting for perinatal adaptation is the epigenetic modification, via DNA methylation, that affects gene expression permanently, with consequent endocrine and behavioral changes persisting into adulthood. In addition, genetic polymorphisms in a regulatory pathway may accompany environmental factors acting on fetal development and, thus, the origins of many human diseases. Polymorphisms in the insulin promoter gene and a parental background of metabolic syndrome predispose children to be overweight and to have insulin resistance (Figure 3).

In addition, an enhanced release of inflammatory cytokines (tumor necrosis factor α and interleukins 1 and 6) is correlated with the extent of adiposity in adolescents. These cytokines decrease insulin receptor signaling, thereby contributing to the insulin resistance state. Childhood weight gain and obesity have been shown to be linked to the overall mortality risk in adulthood, including the risk from cardiovascular disease. A recent update of the worldwide prevalence of metabolic syndrome in overweight children and adolescents between the ages of 2 and 19 years indicated a rate of up to 60%.

Nonalcoholic fatty liver disease in children

Further metabolic consequences of obesity include nonalcoholic fatty liver infiltration, which is rapidly emerging in the pediatric population. Nonalcoholic fatty liver disease is increasingly prevalent in pediatric individuals, in parallel with increasing obesity, and can lead to liver inflammation, fibrosis, and even cirrhosis. Nonalcoholic fatty liver disease is thought to occur as a consequence of an increase in free fatty acid release into the portal circulation by abundant visceral adipocytes. This results in higher triglyceride levels and subsequent excessive intrahepatic lipid storage. The prevalence of fatty infiltration of the liver was recently estimated at 9.6% of the US pediatric population. Fatty liver prevalence differs significantly by race and ethnicity (Asians, 10.2%; blacks, 1.5%; Hispanics, 11.8%; and whites, 8.6%). The highest rate of fatty liver was seen in obese children (38%).

Pediatric nonalcoholic fatty liver disease may improve with lifestyle therapy (maintaining weight and...
regular exercise) and agents that improve insulin sensitivity. Thus, identifying effective strategies for treating these obesity-related comorbidities in children and adolescents is crucial to the prevention of future cardiovascular disease and poor health outcomes.

**Metabolic risk factors for sexual development of female adolescents**

A risk factor for female sexual development of adolescents, connected with type 2 diabetes mellitus and cardiovascular disease, is polycystic ovary syndrome (PCOS). Polycystic ovary syndrome refers to hyperandrogenism, anovulatory menstrual cycles or oligomenorrhea, hirsutism, and the appearance of polycystic ovaries on ultrasonography.\(^2\) Insulin resistance and elevated serum luteinizing hormone levels are also common features of PCOS. Polycystic ovary syndrome is associated with an increased risk of type 2 diabetes and cardiovascular events. Insulin resistance, in conjunction with altered regulation of the HPA axis, promotes a hyperandrogenic state at the level of the ovary and adrenal gland.\(^2\) Obese adolescents with PCOS have an increased prevalence of impaired glucose tolerance, insulin resistance, and atherogenic lipid profiles compared with lean counterparts with PCOS.

**Precocious puberty**

Another factor of health and social importance is precocious puberty (i.e., early sexual maturation in female children). There is evidence that girls are maturing at an earlier age and that precocious puberty is increasing.\(^2\)

Precocious puberty affects 1 in 5,000 children and is 10 times more common in girls. Statistics indicate that girls in the United States are maturing at an earlier age than they did 30 years ago and that the number of girls with diagnosed precocious puberty (i.e., the appearance of secondary sex characteristics before the age of 8 years or the onset of menarche before the age of 9 years) is increasing. Early menarche has been linked to a greater risk of breast cancer as an adult. Therefore, a precocious onset would seem to increase that risk.

Responsible factors included genetic and ethnic background, pediatric obesity, and environmental variables that disrupt endocrine function (i.e., chemicals, toxins, plasticizers, infant feeding methods, skin and hair products, and assisted reproductive technologies), psychosocial stress, and early exposure to a sexualized society.\(^2\) The role of obesity is often cited in association with the earlier onset of puberty. The number of overweight children aged 6 to 11 years has more than doubled in the past 20 years (from 7.0% in 1980 to 18.8% in 2004), and the rate has more than tripled among adolescents aged 12 to 19 years (from 5.0% in 1980 to 17.1% in 2004).

**Conclusions**

There is increasing evidence that genetic and epigenetic factors (i.e., early-life environmental influences) can affect prenatal development and cause structural and functional changes that may be responsible for the onset of diseases in childhood and adulthood. This concept of early-life physiological programming or imprinting\(^2\) has been examined for prenatal and postnatal exposure to endogenous factors (e.g., sex hormones) and exogenous agents (including toxins and drugs). Certain windows of vulnerability are identified, in which different tissues, signaling pathways through the HPA axis, and more important, the immune system, are sensitive to these challenges. Many chronic diseases with an increasing incidence (e.g., childhood asthma, allergies, neurologic syndromes, and metabolic syndrome) are triggered through early-life environmental risk factors and immune dysfunction. Therefore, the identification of and protection against risk factors for the developing immune system and resulting immune dysfunction and tissue damage provide a major opportunity to reduce health risks for the most prominent chronic diseases of children and adults.
References:

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Sunburn from energy-saving bulbs

Saving energy is a good thing, but is it totally safe? Researchers at the British Health Protection Agency have discovered that under normal operating conditions, compact fluorescent lamps (CFLs) give off significant amounts of UV radiation. In close proximity to the bulb, UV radiation easily reaches levels comparable to sun exposure on a summer day. But don’t replace all your compact fluorescents with conventional incandescents out of fear of sunburn. At distances of as little as 30 centimeters (one foot), the intensity of the radiation is reduced to levels safe for people with normally sensitive skin. And UV radiation is an issue only with single-envelope CFLs. According to the study, double-walled bulbs are perfectly safe.


Pain relief from swearing?

Although swearing is a common response to pain, a recent British study was the first to investigate the effects of swearing on pain tolerance. The 64 participants were asked to immerse one hand in icy water until they could no longer stand the pain. The procedure was then repeated, with participants either swearing out loud or saying “neutral” words. Pain intensity was assessed, along with the length of time required for the pain to become unbearable. The findings indicate that swearing actually does increase pain tolerance and decrease perceived pain. The pain-reducing effect was more pronounced in women than in men.

NeuroReport. 2009;20(12):1056-1060. doi:10.1097/WNR.0b013e32832e64b1

Marriage prevents dementia

Being married or living with a partner at around age fifty is associated with reduced risk of dementia in comparison to those who live alone, according to a recent Swedish-Finnish study that analyzed Finnish WHO data from the 1970s and 80s. The study found that men and women living in stable partnerships around age 50 are significantly less likely to develop dementia at ages 65 to 79 than are single, separated, or widowed individuals. The greatest increased risk of Alzheimer’s was found in widowed or divorced carriers of the apolipoprotein E e4 allele who remained single during the follow-up period.

BMJ. 2009;339:b2462. doi:10.1136/bmj.b2462
What Else Is New?

Paradise for bacteria

Especially for frail elders, taking a nice, relaxing shower could be dangerous. Scientists at the University of Colorado, USA discovered that showering may entail a significant risk of infection. The researchers tested a total of 45 showerheads taken from various locations around the US for genetic traces of bacteria. The locations included major cities such as New York and Denver. Almost one-third of the samples contained significant quantities of mycobacteria, which can cause pulmonary infections in individuals with compromised immune systems. Plastic showerheads were more heavily contaminated than metal ones.

In addition to mycobacteria, the scientists discovered more than a dozen other opportunistic pathogens that accumulate in varying combinations in so-called biofilms in showerheads. The concentration of germs can be more than 100 times that of each city’s tap water and is especially high when the shower is first turned on, so the researchers advise not allowing the first flow of water to strike the face.


A few extra pounds increase life expectancy

“Being overweight is unhealthy.” Without further qualification, however, this bit of conventional wisdom appears to be only partially true. A Canadian study of the relationship between BMI and mortality has concluded that average life expectancy is actually greater for individuals with only a little extra fat on their ribs (BMI 25-30) than for people of normal weight. The study, which analyzed data on 11,000 Canadian men and women aged 25 years or older, noted that both underweight (BMI < 18.5) and class II obesity (BMI > 35) entailed a significantly increased risk of mortality (1.73 and 1.36, respectively) in comparison to normal weight, whereas the relative mortality rate among the slightly overweight (BMI 25-30) was significantly reduced at 0.83. Even for class I obesity (BMI 30-35), life expectancy was approximately the same as for normal weight.


Smart people live longer

Individuals of higher intelligence have a greater chance of living to a ripe old age than their less intelligent contemporaries. That’s the greatly simplified conclusion of a study of over 4,000 US veterans of the Vietnam War. As always, the reality is more complex.

David Batty of the University of Glasgow (UK) was lead author of the study, which analyzed data from two intelligence tests as well as socioeconomic data and cardiovascular risk factors. As expected, higher socioeconomic status was associated with reduced cardiovascular and overall mortality. Including the GIs’ IQs in the calculation, however, reduced the significance of social and economic differences, indicating the soldiers’ intelligence is an additional significant factor in statistical life expectancy. The question remains as to how to interpret these findings. One possible explanation is that individuals with higher IQs are more aware of the importance of healthy lifestyle choices.

A case of a patient with primary ciliary dyskinesia is presented. This condition resulted in difficult otorhinological management, including several surgical interventions, the use of multiple antibiotics, numerous radiological and immunological investigations, and prolonged conventional medical treatments, without satisfactory clinical results. The incorporation of bioregulatory therapies into her treatment regimen had a significant impact on her progress and quality of life.

**Introduction**
Primary ciliary dyskinesia is a congenital disorder affecting the structure of cilia and flagella. It is an autosomal recessive disease with a low incidence (1 in 15,000 live births). Clinically, it manifests with various signs and symptoms, such as recurrent obstructive bronchitis, repeated pneumonia, recurrent sinusitis, recurrent acute otitis media, and bronchiectasis. The ciliary ultrastructure defects include impairment of the dynein arms, absent or changed radial proteins, and a switch in the number of microtubules and/or their arrangement in the axoneme. Major defects can be an absence of or changes in the axoneme or plasma membrane of the cilia and flagella. A definitive diagnosis is made by using electron microscopy to determine ciliary ultrastructure changes in transverse sections of cilia.

**Clinical case**
The case is that of a female patient born at full term by spontaneous delivery, weighing 3450 g at birth. The neonate was not breastfed, and she had received replacement milk products since birth. The newborn also received the full program of vaccinations, including pneumococcal polysaccharide vaccine. Family medical history: The patient’s father experienced repeated otitis, and her mother experienced frequent pharyngotonsillitis. Her paternal aunt experienced repeated sinusitis.

Disease history: At the age of 1 month, the patient experienced viral disease of the upper respiratory tract. At the age of 4 months, she was diagnosed as having obstructive bronchial syndrome, which was treated with amoxicillin and puffs of a combination of salbutamol and beclomethasone. This disease recurred frequently, and at the age of 1 year 2 months, she was diagnosed as having infantile asthma. She received multiple treatments, including puffs of salbutamol, fluticasone, decongestants, antihistamines, mucolytics, and various antibiotics. Her subsequent course indicates rhinitis, rhinosinusitis, and otitis on repeated occasions. At the age of 4 years, cystic fibrosis was excluded by a normal sweat test result.

At the age of 4 years 7 months, in view of the succession of episodes of rhinosinusitis with simultaneous otitis media with effusion and numerous attacks of acute otitis media, an adenoidectomy was performed and tympanostomy tubes were inserted. The anatomical pathology report indicated adenoidal lymphoid tissue with moderate follicular hyperplasia and an erosive acute and chronic inflammatory process of the surface lining epithelium.

At the age of 4 years 8 months, she was examined by an immunologist. At this time, she was diagnosed with acute otitis media 8 times a year and acute sinusitis 5 times a year. She also experienced transient hypogammaglobulinemia; this condition improved. The clinical investigations included the following: IgE positive to foods and certain foodstuffs (i.e., peanuts, eggs, and milk) and coloring agents; IgG1-IgG2-IgG3-IgG4, normal result; response antibodies to pneumococcal 23-valent vaccine, normal result; and a minor change...
in chemotaxis. The treatment recommendation was as follows: desloratadine, puffs of intranasal mometasone, montelukast, and amoxicillin, 1 dose per day for 3 months. At the age of 5 years, in view of the persistent repeated rhinosinusitis, endoscopic surgery of the paranasal cavities was performed. The anatomical pathology report indicated that the right maxillary sinus mucosa was affected by a marked acute and chronic inflammatory process and extensive erosion of the lining epithelium, without specific effects. The left maxillary sinus mucosa was affected by a moderate acute and chronic inflammatory process. At the age of 5 years 4 months, a biopsy specimen of the nasal respiratory mucosa was obtained. The specimen showed preciliated cells, calciform cells, and ciliated cells with mature stalks; these stalks showed a 9×2 microtubular skeleton with no internal arm or with both arms of dynein in approximately 50% of the cilia examined. A number of preserved additional peripheral microtubules, basal bodies, and radial spokes were also seen in the specimen. These findings were compatible with ciliary dyskinesia. At the age of 7 years 8 months, the patient was referred to me by the otolaryngologist because of rhinosinusitis infections, and she has not experienced further rhinosinusitis. At the age of 8 years 10 months, she was hospitalized because of acute gastroenteritis due to a rotavirus. At the age of 9 years 1 month, she was hospitalized because of viral pharyngitis and was given Angin-Heel, Engystol, and Mucosa compositum. At the age of 9 years, the patient experienced viral tracheitis and was given Engystol and Husteel. At the age of 9 years 10 months, the patient had influenza due to an AH1N1 virus. She was treated with oseltamivir. The girl is now aged 10 years 1 month and is doing very well. She has not experienced further rhinosinusitis infections, and she no longer has to miss school, and she is starting to lead a normal life for her age. This is an important achievement given the previous restrictions on her, something that is not often considered. Clearly, treatment with bioregulatory medications produced a notable change in the course of this patient’s disease. Their contribution in the integrated management of patients with repeated rhinosinusitis and primary ciliary dyskinesia must be considered.

**Discussion**

This patient presented with primary ciliary dyskinesia that could not be satisfactorily managed with what conventional medicine has to offer. After numerous treatments, several surgical interventions, and continued and repeated rhinosinusitis, she was referred to me to try supportive treatment with antihomotoxic medications. The patient’s condition was approached using the three therapeutic pillars of homotoxicology: treatment was started with the administration of drainage products (Lymphomyosot), the modulation of the patient’s chronic inflammatory state (Traumeel), and the stimulation of the body’s support for the recovery of the diseased tissues (Mucosa compositum). In a second stage of treatment, Galium-Heel was prescribed to stimulate nonspecific defenses and as a detoxifying agent; and Coenzyme compositum and Ubichinon compositum were added to stimulate blocked enzymatic processes. The patient’s response has been very good: she is no longer using antibiotics, she no longer has to miss school, and she is starting to lead a normal life for her age. This is an important achievement given the previous restrictions on her, something that is not often considered.

**References:**

David Riley was born in the United States and moved to Frankfurt, Germany as a boy. He studied music and psychology at the University of North Carolina in Chapel Hill and graduated in 1976. Prior to attending medical school, he worked professionally as a musician and chef in Europe and the United States.

After graduating from the University of Utah medical school in 1983, he completed a residency in internal medicine. During his residency he became interested in research and conducted his first informal clinical trial by doing pulmonary function testing on advanced yoga teachers attending a yoga workshop in San Francisco in 1984. Since his residency, David Riley has studied many integrative medical therapies, including yoga, homotoxicology, cranial osteopathy, nutrition, homeopathy, and herbal medicine.

He currently practices integrative medicine with Dr. Tieraona Low Dog in Santa Fe, NM. Since 1992, Dr. Riley has conducted or managed more than 50 clinical trials ranging from international practice-based research networks to randomized controlled clinical trials. In 1998, Dr. Riley founded Southwest Health Options, an independent practice association managing the delivery of complementary and alternative medicine for insured patients. At Southwest Health Options, he developed credentialing standards, managed peer review, and coordinated service utilization. He has been a member of the CONSORT (CONsolidated Standards of Reporting Trials) group and worked on the development of coding solutions for integrative medicine.

Dr. Riley is a board member of the Homeopathic Pharmacopoeia Convention of the United States (a technical advisory body to the FDA) and has consulted with other federal agencies. Since 2008, he has been the president of the International Society of Homotoxicology and Homeopathy. He currently lectures and consults internationally on a range of healthcare issues including healthcare policy and regulation, education and research, and issues surrounding integrative medicine.

Dr. Riley enjoys traveling and has visited North, Central and South America, Europe, Africa, the Middle East, and Asia. He is married and lives in a country home just outside of Santa Fe, New Mexico where he likes to work in his garden and orchard.
On the 16th and 17th of October, the Belgian Society for Homotoxicology and Antihomotoxic Therapy (BVHAT) organized two sessions of the same symposium, one in Brussels, Belgium, and one in Utrecht, the Netherlands, on the importance of the extracellular matrix (ECM) in preventive and curative medicine.

The symposium’s moderator, Professor Eddie Wisse, professor emeritus of Cell Biology and Histology at the College of Medicine and Pharmacy of the Free University of Brussels, opened each session by welcoming participants and giving a brief summary of current histological knowledge about the ECM. He then presented the first speaker, James Oschman, PhD from the USA, the global leading expert in bioregulatory matrix research. Dr. Oschman gave a history of matrix research and highlighted important new discoveries, primarily in cell-to-cell communication and molecule receptor triggering.

The second speaker in both sessions was cell biology expert Professor Rolf Gebhardt, professor of biochemistry at the University of Leipzig, Germany. His report on recent research illustrated the cell-protective effects of bioregulatory medications such as Lymphomyosot and Hepeel. In his research, Professor Gebhardt introduced toxins into novel ECM through a transfilter well system and studied the ability of carefully selected Heel medications to inhibit cell intoxication.

Last but not least, Bruno Van Brandt, medical education manager of the International Academy for Homotoxicology, presented the therapeutic possibilities and advantages of bioregulatory medications. Starting from the integrity of the ECM as absolute precondition for long-lasting therapeutic effects in bioregulatory medicine, he then went on to highlight immunomodulation and cell and organ support as the two other elements rounding out the comprehensive bioregulatory treatment of chronic degenerative pathologies. He described this entire approach as the “three pillar” concept in antihomotoxic therapy.

In both locations, the members of the audience were medical doctors with considerable experience in bioregulatory medicine, which resulted in interesting questions and discussions. Overall feedback on both sessions was excellent, and attendees expressed appreciation for the scientific content of the symposium. With this symposium, the BVHAT has once again proven itself to be an active medical education institute capable of organizing advanced scientific events in bioregulatory medicine.
Attention-Deficit/Hyperactivity Disorder

in Infancy and in the Preschool-aged Child

By Leon Strauss, MTechHom (TWR)

The diagnosis and treatment of attention-deficit/hyperactivity disorder (ADHD) has been focused on school-aged children, with recent attention drawn to adults with ADHD. Chronic treatment programs from childhood through late adulthood have become part of modern ADHD management programs, identifying and treating key areas of need within each age group.

Attention deficits are generally thought to be mostly associated with children; however, it has been recognized that attention problems not only continue into adulthood but also reveal themselves in more adults as they get older. The onset of ADHD typically occurs before the age of 3 years, with parents of children with ADHD commonly reporting excessive motor activity in toddlers. Peak presentation to health care professionals occurs between the ages of 7 and 10 years.

This article will concentrate on the early identification and management of ADHD in infants and preschool-aged children. Early treatment of ADHD can prepare children for the academic years, as well as improve relationships within the family, which are often strained. Numerous family studies have suggested a familial pattern to ADHD. These studies suggest that there is a higher prevalence of mood and anxiety, learning, substance-related, and antisocial personality disorders in family members of individuals with ADHD.

The chemical messengers
Neurotransmitters include chemicals classified as peptides, nitric oxides, neurotrophic factors, and cytokines. More than 300 substances that control our internal neural world and directly influence our interaction with others have been identified. Catecholamines, such as dopamine, and amines, such as serotonin, play an important role in the evolution of ADHD; these imbalances can be identified in the preschool-aged child with ADHD.

Dopamine plays a critical role in motivation, reward-seeking behavior, and attentional processes. Imbalances of dopamine in limbic regions have been linked to ADHD, schizophrenia, and subcortical neuropsychiatric disorders, including Tourette syndrome and possibly autism. Dopamine levels are preferentially reduced in the frontal brain regions of adult patients with ADHD. Furthermore, genetic abnormalities related to dopamine transporter proteins have been reported in patients with ADHD, supporting the concept that ADHD has strong genetic ties and is a disorder that begins early in life and changes form through the teenage years and adulthood.

Serotonin is essential in neurobehavioral processes, including mood and anxiety. Serotonergic imbalances are related to mood disorders, anxiety syndromes (including obsessive-compulsive disorder, posttraumatic stress disorder, and panic disorder), autism, and insomnia. Low platelet serotonin concentrations were identified in children with ADHD more than 20 years ago; increasing serotonin levels to within the normal range repeatedly lessens ADHD symptoms in children with low serotonin levels.

Circulating serotonin and dopamine levels and receptor site activity can be adversely affected by genetic and environmental factors. Functional polymorphisms of the serotonin transporter genes have been associated with depression and autism. Environmental toxins, such as 1-methyl-4-phenyl-1,2,3,6-tetrahy-
Dropyridine (MPTP), can produce a permanent hypodopaminergic state indistinguishable from Parkinson disease by killing neurons in the substantia nigra of the brain.\textsuperscript{10} Toxins from the environment include gases (e.g., carbon monoxide), metals (e.g., mercury), liquids (e.g., ethanol), and numerous solids. Prenatal exposure to lead can result in mental retardation and cerebral palsy. As many as 1 in 10 women are at risk of bearing children with learning disabilities and other neurological problems because of mercury exposure. Mercury affects both prenatal and postnatal brain development; it specifically damages or kills neurons in utero. The consumption of fish is the most common source of exposure, although airborne mercury contamination is becoming more of a concern. Exposure to neurotoxins in pregnancy is associated with disordered cognitive development, lowered IQ scores, impairments of memory and attention, and coordination deficits.\textsuperscript{13}

\textbf{Identifying ADHD in the preschool-aged child}

In early childhood, it may be difficult to distinguish symptoms of ADHD from age-appropriate behavior in active children. Family histories and environmental factors may be more valuable in determining whether treatment should be recommended in children with potential ADHD. Common symptoms in infancy include the following:
- excessive dribbling
- excessive motor activity
- increased thirst
- head banging
- fits
- tantrums
- screaming
- restlessness
- needing little sleep
- being difficult to feed
- inability to be pacified
- spurning affection and cuddles

Common symptoms in young children include the following:
- clumsiness
- impulsiveness
- being accident prone
- erratic disruptive behaviors
- compulsive touching
- constant motion
- nonstop and repetitive talking
- concentration deficits
- loud talking
- restless sleep
- nightmares
- being oversensitive to odors, lights, sound, and cold

An early diagnosis of ADHD is difficult. Symptoms in infants and toddlers include restlessness, frequent crying and fits of anger during which the child cannot be pacified.
**Treatment**

Prenatal neurotoxin exposure sets the scene for neurochemical imbalances in the newborn and highlights the need for drainage and detoxification, even in young children. Inherent tendencies to the development of illness may be genetic or the result of environmental toxin exposure.

Young children will all benefit from a two- to three-month course of Lymphomyosot (2-5 drops of each given 3 times daily). In more toxic environments (because of environmental or medicinal exposure), deeper detoxification protocols may be necessary, with ampoule preparations such as Thyreoidea compositum and Pulsatilla compositum (1 dose biweekly). Prenatal or postnatal heavy metal exposure is an indication for the use of biocatalysts and the corresponding low-dose metal-containing product (i.e., bioregulatory products that contain mercurius, lead, and arsenic). Lead exposure is an indication for Placenta compositum and Cerebrum compositum. The use of Cerebrum compositum is essential in all cases of potential brain injury (traumatic or toxic) in the young child.

Omega-3 fatty acids exert direct and indirect influences on neurotransmission through modifications at the postsynaptic receptor. They influence signal transduction by inhibiting the hydrolysis of inositol trisphosphate (IP3), an effect that closely resembles the activity of lithium. Essential fatty acids also inhibit membrane phospholipase activity and reduce arachidonic acid release from neuronal cell membranes. A deficiency of omega-3 fatty acids has been linked to low dopamine receptors in rats; there is a direct correlation between a low plasma or membrane-bound essential fatty concentration and lower dopamine receptor density.

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Young Children With Low Serotonin Levels</th>
<th>Young Children With Low Dopamine Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sleep disturbances</td>
<td>Listless behavior and possible delays in reaching milestones</td>
</tr>
<tr>
<td></td>
<td>Erratic and changing moods (often crying with screaming and uncontrolled tantrums)</td>
<td>Low metabolic rates may be seen, with a tendency toward constipation</td>
</tr>
<tr>
<td></td>
<td>Compulsive repetitive behaviors</td>
<td>Children rock back and forth to music (because they love rhythmic sounds), with sensitivity to loud and unexpected sounds</td>
</tr>
<tr>
<td></td>
<td>A history of depression is often seen in 1 or both of the parents</td>
<td>There may be a family history of addictive disorders</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Young Children With Low Serotonin Levels</th>
<th>Young Children With Low Dopamine Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nervoheel tablets (half a tablet 3 times daily)</td>
<td>Neuro-Injeel ampoules (1 dose twice weekly)</td>
</tr>
<tr>
<td></td>
<td>Ignatia-Homaccord drops (2-5 drops 3 times daily)</td>
<td>Barijodeel tablets (half a tablet 3 times daily)</td>
</tr>
<tr>
<td></td>
<td>Viburcol suppositories (to be used as needed for tantrums and sleeplessness)</td>
<td>Lymphomyosot drops (2-5 drops 3 times daily)</td>
</tr>
<tr>
<td></td>
<td>Thalamus compositum ampoules (1 dose every evening at sunset for 1 week for sleep disturbances)</td>
<td>Calcoheel tablets (half a tablet 3 times daily)</td>
</tr>
</tbody>
</table>

† The dosage of certain medications may vary depending on the age of the child. Please refer to the respective package insert.
Young children with ADHD find it hard to focus on one thing at a time. Constantly in motion, they are somewhat clumsy and tend to have more accidents than their healthy age peers.

Children aged 2 to 4 years: 500 mg of DHA and 30 mg of eicosapentaenoic acid (EPA)

- Children aged 4 years and older: 1000 mg of omega-3, with a minimum of 250 mg of DHA and 60 mg EPA

As signs and symptoms progress and differentiation between low serotonin and low dopamine levels in infants and children become apparent, specific treatment protocols can be approached (Table).

More specific protocols for the classic ADHD symptoms in school-aged children and the difficulties they face in learning will be addressed in a future article.

References:
Patients have significantly more confidence in a medical practice when they know who they’re dealing with. That’s why, for example, when I consult with physicians, I recommend name tags for assistants in the practice. The idea gets rejected for the strangest reasons, such as “The pins mess up our nice T-shirts.” Many office assistants don’t even have the self-confidence to give their names when answering the phone, let alone wear a name tag. The real reason, however, is usually that identifying yourself by name means you’re no longer able to hide behind anonymity. You’re afraid of making a mistake the boss will find out about. This is an expression of inadequate self-confidence.

You as a practitioner, however, must make it your explicit goal to have a strong team whose members radiate competence through their self-confident, professional manner. That’s a good reason for patients to stay with your practice and recommend it to others. Self-confidence doesn’t always come naturally to employees, however, so you, as the ultimate “manager” of your own practice, may have to actively promote it.

Here are some rules to follow in order to build up your assistants’ self-confidence and reap the benefits:

1. Show your assistants that their work is important to you. Don’t accept their good work as a matter of course and register only their mistakes. Offer praise – even in front of patients.

2. Help your assistants learn from their mistakes. Individuals with low self-esteem tend to doubt their own ability after making mistakes. Help them come up with ways to avoid repeating the same mistake. If you must criticize, do it in private, and never in front of patients.

3. Praise or criticize only what your employees do, not the individuals themselves. Personal criticism of an employee is strictly taboo; it can make that person start to disengage inwardly.

4. Assign tasks in a way that showcases your associates’ abilities. If one assistant is especially good at taking blood samples, make that one of his or her permanent assignments. You will save time because the work gets done more efficiently and the working environment improves because employees are content.

5. Delegate increasingly demanding jobs. Letting go of some things can be difficult, but in most cases you’ll soon get used to it, and you’ll gain time that you can devote to managing your practice, for example. Giving your employees more individual responsibility enhances both their commitment and their productivity.

6. Communicate with your employees in ways they understand, and find out what they expect from you. Surveys have shown that most employees who do unsatisfactory work simply don’t know what the boss actually wants.

At the moment, many of your colleagues are complaining about cost pressure, shortage of time, etc. and are looking for new services to offer or sources of income. In my opinion, however, the competitiveness of a practice depends not only on implementing new methods or technology but also to a great extent on “human capital.” Personal commitment, competence, and the results of creativity and energy – not just yours, but also your employees’ – are important resources available to you at no extra cost, so to speak.
Improving employee skills and delegating more demanding tasks will increase your staff's self-esteem and make your practice more efficient.

What motivates assistants in your practice?
More money, a more secure job, and the opportunity to make a career for oneself are the old standard motivating factors in workplaces. These resources are very limited, however, and not just in healthcare practices. The result is decreasing interest in work, accompanied by more frequent mistakes. How can you counteract this problem before it's too late? Here are some simple, no-cost ways to motivate your team:

1. Wherever possible, give your employees free rein. Set a goal, but leave it up to them how to accomplish it.
2. Broaden your assistants’ perspective by including them in decision-making.
3. Explain why specific work needs to be done.
4. Sharing important information, including bad news, shows that you appreciate and value your associates.
5. Support your employees’ individual development. For example, cover part of the cost of a continuing education seminar. Or for a no-cost variation, look for opportunities to invite them to accompany you to industry-sponsored educational events. Ultimately, you will be the one to benefit.
6. In a team, everyone has to compromise sometime. Whenever possible, take your employees’ personal needs into account. Show your employees that you value them not only as workers but also as individuals. These motivating factors can ensure that working in your practice remains fun in the long run. And there’s no limit on the availability of any of these resources.

Continuing education for your team
“If you don’t keep up with the times, you get left behind” is the motto of one licensed healthcare practitioner in Munich, Germany, meaning that his practice wouldn’t function as well without constant further education. In our fast-paced modern lives, it’s not so easy to find time to keep your knowledge and skills up-to-date, but to remain successful you must have a well-conceived plan for continuing education in your practice. The daily flood of information you’re subjected to can make this difficult. Always ask these three questions:

1. What matters most for my practice?
2. What are the options?
3. Is it realistic for us to implement what we would learn?

To answer the first question,
- set goals for the practice, your employees, and yourself
- plan in enough time
- establish a budget for individual continuing education programs

With regard to the second question, consider all the opportunities and evaluate which ones to take advantage of:
- newspapers and professional journals
- reference books
- seminars and workshops
- trade fairs and exhibitions
- exchanging information with other practices
- electronic options (web sites, mailing lists, and newsletters)

The third question is especially important, because education – whether for yourself or for your associates – is not a good investment if you can’t apply it. Here’s what to consider:
- Have I processed the information?
- Have I effectively introduced the information into my practice?
- Have I informed all my employees about what I learned?
- Are my employees all enthusiastic about implementing it?
- Have I established regular times for sharing information and experiences within the practice?
- Have I set criteria for and monitored the positive impact of newly acquired knowledge and skills?

When thinking about continuing education, don’t limit yourself to professional content. Continuing education in organization and management is equally important.
New Approaches in the Treatment of Respiratory Insufficiency in Neonates

By Professor Lidiya Ivanovna Ilyenko, DrMedSci, and Nataliya Aleksandrovna Suvalskaya, CandMedSci*

Abstract
In this study, 67 newborns receiving artificial respiration, who were diagnosed as having respiratory distress syndrome, were divided into 2 groups, were examined, and were treated. The first group (n = 33) received standard treatment plus Mucosa compositum sublingually, and the second group (n = 34) received only standard therapy. With the therapy provided, there was a 1.3-fold decrease in the duration of artificial respiration in the neonates in the Mucosa compositum group.

Keywords: neonates, respiratory insufficiency, respiratory distress syndrome, artificial respiration

Introduction
The successes that have been achieved in delivering resuscitation aid to neonates who are in critical states have mainly been brought about by the introduction of protocols and standards and by a comprehensive approach to therapy. However, intensive therapy for respiratory disorders remains a difficult problem, especially for neonates with respiratory distress syndrome (RDS). One new approach for solving this problem is the use of bioregulatory combination medications. In this study, the antihomotoxic medication Mucosa compositum (Heel, Baden-Baden, Germany) was applied in the treatment of RDS. The literature describes the use of this medication in neonates with dysbiotic disorders; in infants and in older children, as an efficacious antitussive agent; and in combination therapy for bronchial asthma.† The interest in this bioregulatory combination medication arises from its composition, which is based on a porcine mucosa extract, catalysts, and substances of vegetable and mineral origin. All components of the formulation are represented at high levels of dilution and do not possess any potential toxic or allergic effect. In terms of its action, the product is postulated to have anti-inflammatory, spasmolytic, reparative, vascular, and immunomodulating effects. Mucosa compositum is thought to assist the passage of mucus and has a drainage effect, reduces dyspnea and cyanosis and normalizes the respiration rhythm, reduces the number of attacks of coughs and of coughing instances in a single attack, prevents the process of respiratory distress from becoming chronic, and acts on the entire respiratory tract (upper, middle, and lower). The objective of the present study was to evaluate the efficacy of Mucosa compositum in the combination treatment of respiratory disorders.

Patients and methods
This study included 67 neonates under observation. All patients were similar in terms of sex, age, and week of gestation; they received standard treatment for RDS (i.e., correction of hemodynamic parameters and administration of surfactant, antibiotics, and infusion therapy). Thirty-three were included in the treatment group (i.e., newborns who received standard treatment plus Mucosa compositum for respiratory disorders), and 34 were included in the control group (i.e., newborns who received only standard treatment for respiratory disorders).

The inclusion criteria included premature infants in the first 24 hours of life, a gestational age of 36 weeks or younger, a body mass of 900 g or greater, and a clinical and/or X-ray diagnosis of RDS. The exclusion criteria included congenital developmental defects, periventricular hemorrhaging at level 2 or greater, and clear symptoms of intrauterine infection.

In the antihomotoxic treatment group, Mucosa compositum was ta-
ken sublingually at a dose of 0.5 mL every 6 hours for 5 to 7 days. The evaluation criteria included clinical, functional, and laboratory variables. The clinical parameters were as follows: altered chest excursion, auscultation sounds in the lung, skin color, increase in feed volume, body mass, and diuresis dynamics. The functional variables included altered artificial respiration (AR) parameters (i.e., fraction of inspired oxygen, peak inspiratory pressure, and ventilation rate), respiration mechanics (aerodynamic resistance and distension), heart rate monitoring results, respiratory frequency, blood pressure, and arterial oxygen saturation. The laboratory parameters were as follows: general blood analysis, blood gas measurement, and acid-alkali status. To exclude congenital developmental defects and to evaluate cerebral blood flow, the neonates underwent neurosonography and echocardiography.

**Results**

Within several minutes of product administration, the results showed that there was an improvement in chest excursion (i.e., a diminution in contraction of yielding places in the chest, a “swing” symptom, and an improvement in respiration rhythm and amplitude), respiration conducted in the lungs, a diminution in the number of rales, and an improvement in skin color. In control group patients, a tendency for general edema syndrome (i.e., soft tissue swelling) was noted. By day 3, with the treatment being administered, the incidence of this set of symptoms was almost 3 times lower in the antihomotoxic treatment group versus the control group (6.1% versus 17.0%). The subsequent comparative analysis showed that in the Mucosa compositum treatment group, a quicker reduction in the oxygen concentration in the respiratory mixture with AR was achieved: a fraction of inspired oxygen of greater than 0.3 was recorded for a mean ± SD of 50.28 ± 9.34 hours (versus 77.65 ± 10.68 hours for the control group; P < 0.05). There was also an earlier transfer of the neonates to independent respiration (overall duration of AR in the control group versus the antihomotoxic group, 116.15 ± 10.38 versus 87.63 ± 9.34 hours; P < 0.05).

**Discussion and conclusion**

The data obtained reflect the efficacy of Mucosa compositum in combination treatment for respiratory insufficiency. The product slows the rate of development of bronchospasm by 5 times (P < 0.01), has an established broncholytic effect, and reduces lethality (as shown in this experiment). When this product is used, the course of the clinical picture of RDS in neonates is ameliorated and the incidence of development of general edema syndrome is lowered by 3 times versus the control group. The use of this product shortens the time for which AR is required by 1.3 times (P < 0.05) and the time spent by newborns in the intensive care unit.
Many bioregulatory medications are produced in the form of suppositories, the preferred method of administration for infants and children who have difficulty swallowing or patients who are vomiting due to their illness. Pharmaceutical manufacturers confront special challenges in the production of suppositories, which must maintain their shape at room temperature but melt at body temperature once administered.

In Viburcol, Spascupreel, or Vomitusheel suppositories, the base material is hard fat with a melting point of 35°C/95°F, i.e., slightly below body temperature. Hard fat is derived from vegetable oils and consists of a mixture of tri-, di-, and monoglycerides. As a natural emulsifier, it aids in uniform distribution of the liquid homeopathic active ingredients in the base.

Pharmaceutical production must pay special attention to ensuring both uniformly high product quality and good consumer safety. The production instruction document for each medication describes all manufacturing steps in detail. These instruction documents also serve as records of the production process, since all successfully completed production steps (such as initial weighing of ingredients or machinery settings) are confirmed and can be monitored by a second person. Thus each production batch has its own record in which all of the individual steps can be retraced.

The fluid suppository base is pumped out of the melting vessel into sealable forms in a continuous strip of foil. Uniform pumping pressure ensures that each mold is filled with the same amount of material.
Suppository production takes place in several different phases. First the liquid ingredients are prepared. The required mother tinctures are made from the appropriate plant parts and from mineral components. After the mother tinctures have been tested in the lab to ensure they meet all specifications, they are released to be processed into specific homeopathic potencies, which are then ready to be used in making the suppositories.

Meanwhile, the appropriate quantity of hard fat is weighed out, placed in a temperature-controlled vessel, and melted overnight. The active ingredients are added just before further processing begins. The suppository base is then poured into sealable forms in a continuous strip of foil. During pouring, the melting vessel is held at a temperature of 37°C and the base is stirred constantly so the entire batch maintains a constant temperature and the active ingredients remain homogeneously distributed. The fluid mass is then pumped out of the melting vessel through tubes into the molds. Uniform pumping pressure ensures that the same amount of material is placed in each mold. The pour rate must be rapid enough so the suppository base does not begin to solidify before the mold is completely filled.

Next, the filled foil molds (still open) are run through a cooling tunnel where they are gradually cooled to room temperature. Controlled cooling and hardening of the suppositories is important because overly rapid cooling results in a brittle, breakable final product. Conversely, if the hardening process takes too long, some of the incorporated mixture of liquid active ingredients may separate from the base.

After the strips of suppositories leave the cooling tunnel, they are sealed and simultaneously imprinted with their batch number and expiration date. These “batch data” ensure traceability of individual production batches as required by Good Manufacturing Practice standards. The continuous strip of individual suppositories is then cut into sheets of six suppositories each, and a production worker packs them into cartons for storage until further packaging.

In-process monitoring takes place at regular intervals throughout the entire production process, which continues uninterrupted as samples are taken and tested for a variety of parameters. First, the seals and batch data printing are checked. Then sample suppositories are removed from the foil and weighed, and another test confirms that the foil forms are completely filled. These tests are conducted on whole suppositories as well as some that are cut open. Additional samples taken at various times in the process are submitted to the Quality Control department, together with the production report, when the production run is completed. In Quality Control, the finished suppositories and their documentation are checked again. Earlier in-process monitoring is now supplemented by more time-consuming testing of parameters such as melting time and tensile strength. These procedures ensure that the very exacting pouring process actually produces uniformly high-quality suppositories.

After the sheets of suppositories are released by Quality Control, they are packed together with an instruction insert into a folded box that is again imprinted with the batch data. In one final test, all packages are weighed again and checked for completeness. Any packages that deviate from the predetermined target weight are sorted out and discarded. Individual boxes of the final product are then packed into shipping cartons.

In the final step, the completed production documentation and individual samples of finished suppositories are again tested by Quality Control before they are released for sale.
 CASE STUDY COMPETITION

Submit your case study on bioregulatory treatment for presentation at a scientific symposium in Baden-Baden, Germany!

Authors of the two best case studies received by the International Academy for Homotoxicology (IAH):

➤ will present their findings in person at the scientific symposium of the International Society of Homotoxicology and Homeopathy (ISOHH) during Medical Week in late October 2010 in Baden-Baden, Germany;

➤ will have their studies published in a subsequent issue of the well-known “Journal of Biomedical Therapy;”

➤ will receive free travel and accommodations courtesy of the IAH.

For criteria and conditions of entry, along with guidelines for writing up your research, visit the IAH website at www.iah-online.com and click on “Case study competition.”

Let the world know about your expertise in bioregulatory medicine!