



caffeine, theobromine and theophylline. All of them are stimulators of the central nervous system, increase the vital functions of tissues, increase overall metabolism. Theophylline and theobromine are used in medicine as a vasodilator, as well as diuretics. The twentieth century is sometimes called the century of the Great Medical Revolution. One of its bright symbols, of course, is considered to be b-lactam antibiotics - penicillin and cephalosporins, which have saved millions of lives. Both are also derivatives of heterocyclic compounds.

Of course, this is only a small part of what heterocycles are interesting for. It is also worth mentioning the outstanding role of heterocycles in the respiratory process and energy conservation, photosynthesis, production of pesticides, dyes, heat-resistant polymers, analytical reagents and many other practically important materials. In recent years, heterocycles have been closely linked to a rapidly advancing branch of science, supramolecular chemistry, which studies the patterns of self-organization of molecules and their recognition of each other.

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### **NEW PROGNOSTIC MARKERS OF HEARING IMPAIRMENT IN CHILDREN: GENE-GENE INTERACTION AND APPROXIMATION MODELS**

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Nowadays 466 million people are estimated to be living with hearing loss (6.1% of the world's population). More than 5% - 360 million people (328 million adults and 32 million children), suffer from severe hearing loss.

The aim of the study is to evaluate the gene-gene interaction, assess the risks and develop some approximation models of hearing loss / deafness occurrence in children, depending on the genes polymorphism gap junction B2 (*GJB2*, rs80338939), and interleukin-4 (*IL-4*, rs 2243250) and other risk factors.

Study included 102 children with hearing impairment: 68 with sensorineural (SNHL) and 34 with conductive hearing loss (CHL), among them 36 (35.29%) girls and 66 (64.71%) boys. The patients' age varies from 8 to 18 yo (on the average  $13.90 \pm 3.11$  yo). Diagnosis set by otorhinolaryngology (ENT) methods: ENT examination, computer audiometry, impedancemetry, tympanometry. The control group included 60 practically healthy children: 22 girls (36.67%), 38 boys (63.33%). Polymorphism of *GJB2* (rs80338939) and *IL-4* (rs 2243250) genes was studied by polymerase chain reaction method. Risk assessed by Relative Risk, Odds Ratio and 95% Confidential intervals.

The combination of 35delG / TT, as well as Non-Del / TT and 35delG/ TC genotypes in the genome is associated with a high risk of hearing loss in general children population (from 0.932 to 1.432; OR=19.5;  $p=0.003$ ), as well as the appearance SNHL (from 0.765 to 1.765), stronger than the combination of unfavorable homozygotes TT / 35DelG - 1.765. The combination of homozygotes for the wild allele of both genes (especially CC / Non-Del) is associated with a low risk of deafness: hearing loss in general -1,068, for SNHL -0,908, for CHL -0,750 ( $p<0,01$ ), for CC / 35delG combination, or TC / Non-Del: in general -0.068 -, and for SNHL -0.235 and -0.11 respectively, ( $p>0.05$ ).

Infectious diseases in anamnesis (meningitis, measles, mumps, or rubella) increases the likelihood of CHL by 9.41 times (OR=12.0;  $p=0.007$ ). Concomitant chronic non-obstructive and obstructive upper and lower respiratory tract diseases increase the risk of both SNHL and CHL in children regardless of age: for SNHL 3.75-7.81 times (OR=6.50-10.9;  $p \leq 0.028-0.01$ ), for CHL - 4.29-8.75 times (OR=6.19-12.9;  $p \leq 0.03-0.009$ ). The revealed dependence of the indicators is best described by the logit-regression approximating models with high multiple correlation coefficient ( $R^2=0.9761$ ); low standard error of the model estimation ( $\varepsilon=0.1114$ ); connection criterion  $F=124.2$ ; degrees of freedom  $df=7.43$  ( $p<0.001$ ).

Thus, genes polymorphism's *GJB2* (rs80338939) and *IL-4* (rs 2243250) and their interactions are new prognostic markers of hearing impairment in children. Approximating models describe the likelihood of SNHL and CHL in observed population.