

BI OLO[KA OSNOVA NA NEPRAVI LNI OT RAST I RAZVOJ NA ^OVEKOT

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Rezi me

Bi olo{ kata osnova na nastanuvaweto na ` i votot ni z neodvoi vi ot proces na rastewe i razvoj, ja so~inuuvaat dve osnovni determi nanti. Toa se: genot nasleden od rodi tel ite vo koj e programirana morf ogenesata (razvojot) i f aktori te na sredi nata koi go uslovuvaat i naso~uvaat.

Genetski ot materijal od dvata rodi tel a potencijalno go opredeluuvaat novi ot organizam vo slo`eno anatomsko f unkcionalno milje vo ramkite na genetski ot kontinuitet vo koi se realiziraaat bi ohemiskite procesi. Genetski te promeni, a i { tetni te agensi od sredi nata imaat bitno vlijanie vrz pojavata { irok registar anomalii. Spored toa, izmenetata bi olo{ ka osnova, bilo so genetski te ili sredi nski te promeni doveduva do raznovidni o{ tetuvawa i hendikep.

Voved

Normalni ot razvoj na edinkata go determiniraaat dva va`ni f enomeni:

1. genetski te instrukcii za morf ogenesata;
2. sposobnost na tkivoto da gi nadopolni op{tite metabolni procesi.

Zna~i, **bi olo{ kata osnova** za nastanok na ` i votot ni z nedel i vi te procesi na rastot i razvojot se del i na:

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BIOLOGICAL FOUNDATION OF HUMAN ABNORMAL GROWTH AND DEVELOPMENT

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Abstract

Biological basis of life appearance throughout the inseparable process of growth and development, is consisted of two basic determinants. They are: the gene inherited from parents in which morphogenesis (development) is programmed and the factors of the environment which condition and direct it.

The genetic material of both parents potentially determines the new organism in the complex anatomic functional pattern within the genetic continuity in which biochemical processes are carried out. The genetic changes as well as the harmful agents of the environment have essential influence on occurrence of a wide range of abnormalities.

According to this the changed biologic basis, caused by genetic or environmental changes, results with impairments and disabilities.

Introduction

Normal development of an individual is determined by two major phenomena:

1. genetic instructions for morphogenesis,
2. tissue capability to complete general metabolic processes.

Biological foundation of the **life genesis**, through inseparable processes of growth and development are genetic instructions:

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- genetski instrukcii, **genom** nasl eden od roditel i te vo koi e zapi { an programot za morfogeneza (razvojot);
- **faktori na sredinata** { to go usluvuvaat i usmeruvaat.

Genetsko-sredinska interakcija, vo ramkite na normalni te varijacii go determinira normalni ot rast i razvoj (6).

Zigot, oplodeni te jajcevi kletki so genetski ot materijal od dvata roditela, potencijalno pretstavuva nov organizam. Vo anatomsko-funkcionalnoto milje, kao multipotentna kletka, mitotski se razmno`uva, a vo ramkite na genetski ot kontinuitet, od genetski potencijal so diferencijalna aktivnost na genot se opredeluva morfofunkcionalnata karakteristika na site kletki vo organizmot.

Se ostvaruva biopotencijalot na idnata edinka (biotip: morfologiki, fiziokemijski, mentalni). Diferencijacijata e uslo`nuvawe na organizmot vo razvojot kade { to kletkite od razli`ni oblasti se menuvaat i se prilagoduvaat na funkcijata { to }e jamaat vo novi ot organizam, menuvaj}i muja i formata i goleminata i polobata. Biokemijski se menuvaat biosintetski te procesi i za kletkata se sintetiziraat specifi`ni proteini.

Morfofunkcionalni te karakteristiki zavisat od tipot na specifi`ni ot protein`ija sinteza e regulirana so funkcijata na genot (2,5). Realizirawena planot na razvojot, osven genetski te faktori go kontroli`raat i usluvuvaat i faktorot na sredinata.

Kontrolni te mehanizmi, prvenstveno na nivo na kletka, pototki vata, organite i plodot, ovozmouvaat vo tekot na razvojot da se realizira genetski zapis na oplodnoto jajce.

Vo dijapazonot na normalni te variacii se eksponiraat individualni te razliki pri zlezene od me`aweto na postojanosta i promenlivosta, so dovolno prostor za popravki, niz slo`enite procesi { to vodat kon sozdavawe na edinkata.

Sprotivno, naru`uvawata preku granicata na motnata reparacija davaat gre`ki na

- the **genome** inherited from parents where the programmed for morphogenesis (growth) is written down;
- the **environmental factors** which condition and direct them.

Genetic environmental interaction, in normal variation boundaries, determines normal growth and development (6).

Zygote, the fertilized egg cell – with the genetic material of both parents, potentially represents a new organism. In an anatomofunctional milieu, as a multipotent cell, it multiplies mitotically within a genetic continuity; from the genome potential by differential activity of the gene it determines the morphofunctional characteristics of all cells in the organism.

The biopotential of the future individual is realized (biotype: morphologic, physicochemical, mental). The differentiation is creating complexity of the organism in the course of development when cells of various parts change themselves and adapt to the function they are going to have in the new organism; they change their form, size and location. Biochemical – biosynthetic processes are changing, specific proteins characteristic to cells are synthesized.

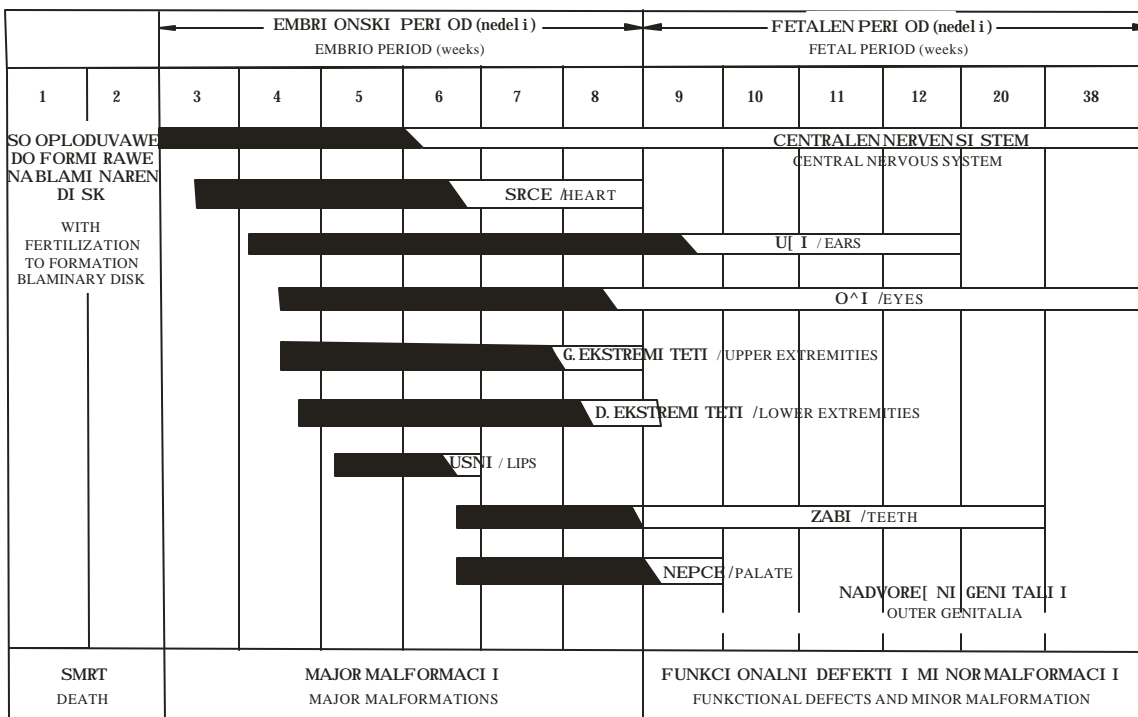
The morphofunctional characteristics depend on the type of specific protein's synthesis that is regulated by the gene function (2.5). Realization of development plan is controlled and caused not only by genetic factors but also by factors of the environment. Mechanisms of control, primarily at the level of cells, than that of tissue, organ and embryo enable that during development the genome note of the fertilized egg is realized.

Within the framework of normal variations individual differences occur as a consequence of intermingling of permanence and variability, with a lot of space for corrections throughout the complex process that leads to the creation of an individual.

As the opposite, disturbances beyond the limits of possible repair give errors of formation in case

oblikuvawe, dokolku ne dojde do gubitok ili resorpcija na plodot. Genetski te izmeni i/ili { tetnite agensi od sredinata (teratogeni) vo rani ot peri od na gestacija go prekinuvaat rastot i razvojot na embrionot (resorpcii, spontani abortusi), a vo kriti ~ni ot "senzi ti ven# peri od na organogenezata, predizvikuva pojava na kongenitalni anomalii. Pokraj toa: predvremeno poroduvawe, mrtvorodeno i rana neonatal na smrtnost (od 0 do 6 dena) - Slika 1.

it does not come to the loss or resorption of the embryo. Genetic changes and/or harmful agents of the environment (theratogenesis) in the early period of gestation interrupt the growth and development of the embryo (resorptions, spontane abortion). In the critical "sensitive" period of organogenesis they are the cause of congenital anomaly. Further on: premature delivery, stillborn and early neonatal mortality (from 0 to 6 days) - Figure 1.



Slika 1. ^uvst vit elnost na razni organski sist emi vo int ra ut erinarni ot rast i razvoj. Pol nat a linija gi ozna ~uva mnogu ~uvst vit el ~ni te peri odi.

Figure 1. Sensitiveness of different organ systems in int re ut era growth and development. The full line indicates highly sensitive periods

Kongenitalno (congenitalis=vroden, od ra|awe) ne ja defini ra pri ~inata, u{ te pomal ku go objasnuva etiopatogenetski ot mehani zam na nastanati te izmeni. Fenomenolo{ ki, ja pri ka` uva naslednata i/ili sredin skata osnova na o{ tetuvaweto.

Kongenitalni te o{ tetuvawa (sostojbi ili bol esti) baraat otkri vawe na pri ~inata i

The congenital (Congenitalis=inborn, from birth on) does not define the cause and it does not explain the etiopatogenetic mechanism of changes that occurred. Phenomenologically it shows the inherited and/or environmental foundation of the damage.

Congenital disorders (states or illnesses) require searching for the cause in fields of: **mutagenesis,**

toa vo oblasti te na: **mutageneza, teratogeneza, onkogeneza.**

Kon ova denes mu se pri dodavaat i sé popri - sutni te vo ~ovekata patologija, docne` no pojavuvawe na genetski te gre{ ki. Famili - jarnata, genetskata predi spozi cija i provo - ci ra~ki te f aktori na sredi nata usl ovuvaat pojavuvawe na multi f aktori jal ni bolesi (avtoimuni bolesi, razni psihozi, aler - gi i, tumori, bolesi na KVS i dr.).

I zmenetata biolo{ ka osnova, bilo so ge - netski i/i li so sredi nski izmeni -rezul ti ra so izol irani ili kombi ni rani o{ tetuvawa, hendi kepi.

Spored izvori te i poli wata na patolo{ ki - te zbidnuvawa se identi f ikuvaat i **pri~i - nite**. So observirawe i so etiopatogenet - ski mehанизmi se odreduva i vremeto na nastanuvawe na naru{ uvaweto.

Genetski te izmeni mo` no e da se utvrdat i pred zabremenuvaweto: vo genetski ot mate - rijal od roditelite, so generaciska trans - misija na mutirani geni, so hromozomski o{ tetuvawa, a i so mo` ni te sve` i (de novo) mutacii.

Po oploduvaweto, so razli~ni stepeni mo - ` at da se menuvaat dadenite genetski in - strukcii. Vo bremenosta, { tetni te agensi od sredi nata (f i zi ~ki, hemi ski, bi o{ ki) mo` at kako teratogeni patolo{ ki da go izmenat planot na razvojot.

Po ra|aweto, mo` no e podlo` uvawe na on - kogenetski pritisok, vo raniot i podocna vo i nvol uti vni ot ` i voten vek. I zstanuva - weto, od razli~ni pri~ini, egzatktni doka - zi vo etiologijata ja nametnuva kategorija - ta na pri~i nata: nepoznata.

Prif ateni ot tri jas na pri~ini: **genetski**, **sredi nski** (steknati) i **nepoznati**, kri teri - umski go standardizira podreduvaweto na dobi enite podatoci od istra` uvaweto na humanata patologija sa drugi i stranski literaturni podatoci. Na takov na~in se objektivizira sostojbata na zdravjeto na popul acijata i ovozmo` uva pretpostavki za pravewe program za prevencija.

theratogenesis and oncogenesis.

Late demonstration of genetic errors (that is be - coming more present in human pathology) is added to this today. Family, genetic predisposition and provoking factor of the environment bring to multifactorial diseases (autoimmune diseases, vari - ous psychoses, allergies, tumors, KVS diseases, etc).

A changed biological foundation – either by ge - netic and/or by environmental changes – results in isolated or combined damages, handicaps.

Causes are identified based on the resource and field of pathologic events. By observation and by etiopathogenetic mechanisms the time is deter - mined when it came to the disorder.

It is possible to determine genetic changes even before conception: in the genetic material of par - ents, through generation transmission of mutated genes, chromosome load and possible new (de novo) mutations.

Upon the conception the genetically given instruc - tions may be changed at different levels. During pregnancy harmful environmental agents (physi - cal, chemical, biological) as theratogenes may make pathologic changes in the development plan.

After birth it is possible to succumb to oncogene pressure in early and later in the involutive age. If there are no exact proofs in the etiology, the cause is marked as: unknown.

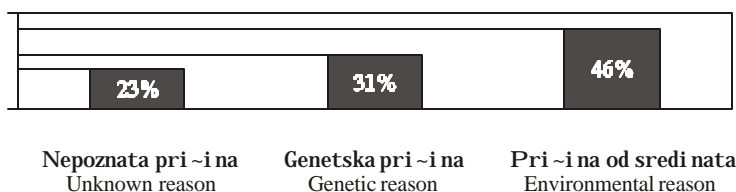
The accepted trias of causes: **genetic**, **environ - mental** (gained) and **unknown** standardize as cri - teria the comparison of the data got in the research of humane pathology from other and foreign data in literature. This makes the state of health of population objective and creates preconditions for developing programmes of prevention.

Ist ra` uvawa i diskusija

Na{ ite prvi ispituvawa spored biolo{ - kata osnova na nastanok na o{ tetuvawe, a komparativna so soodvetnite vo svetot, se objaveni vo Srbija vo periodot od 1983-1986 godi na zaradi utvrduvawe na pri~inata na slepilo kaj detskata populacija. Na statisti~ki reprezentativni ot primerok na slepi deca za toga{ na Jugoslavija e opredelena kako dominantna pri~ina: vlijanieto na {tetni faktori od sredinata (46%), genetski (31%), a za 23% od taa populacija pri~inata e prezentirana kako nepoznata (14) - Slika 2 i Slika 3.

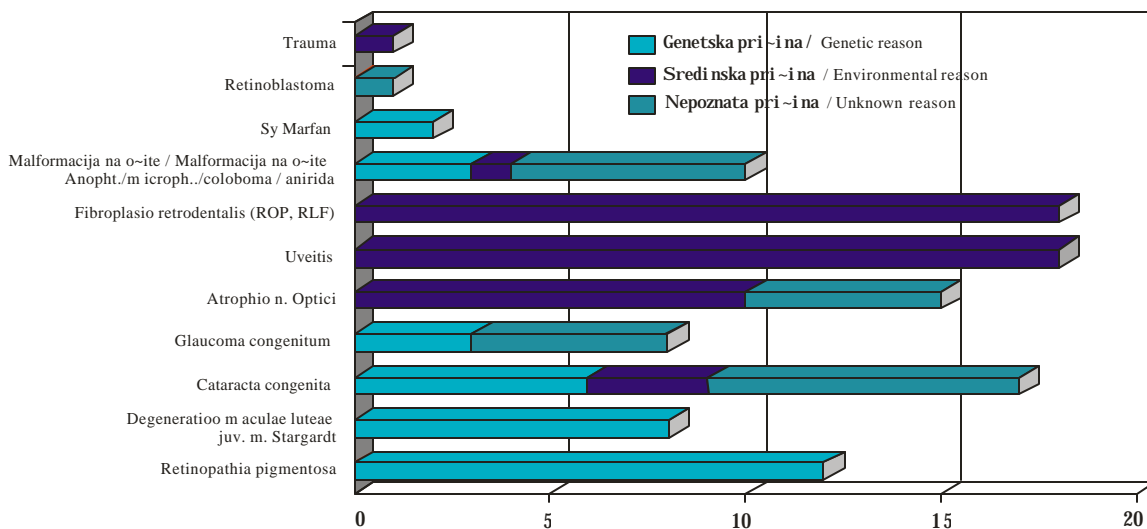
Research and discussion

Our first research made in this way – according to the biological foundation of the damage and comparative to relevant ones in the world, was made in Serbia in the period 1983 – 1986 in the aim to determine the cause of blindness with children. According to statistically representative sample of blind children in Yugoslavia of that time the following dominant causes were found: influence of harmful environmental factors (46%), genetic (31%), and for 23% of that population the cause was presented as unknown (14) – Figure 2 and Figure 3.



Slika 2. Ispitani ci od Zavodot - Zemun spored pri~inata za slepilo.

Figure 2. Cause of blindness – research in the Institute in Zemun.



Slika 3. Ispitani ci od Zavodot -Zemun spored klini~ki opt naod (pat olo{ ki izmeni na oko-t o) i pri~ina za slepilo (n = 110) 1986 god.

Figure 3. Research in the Institute Zemun according to clinical findings (pathologic changes of the eye) and cause of blindness (n = 110) 1986

Sostojbata korespondira{ e so sostojbata na zdravje to vo zemjite so poslabo organizirana zdravstvena za{ tita i so poniski ekonomsko-higienski uslovi za `iveewe. IAPB (International Association for Prevention of Blindness) 1983. (18).

Stranski avtor i, za Anglija, odnosno [kotska: Fraser R; Friedmann A; odnosno Phillip L. Istoboe S. prezenti raa genetskata pri~ina od 40 do 44% za detskoto slepilo vo navedeni te populacii (18).

Ednovremeno, Fischal i Falk za etiologijata na detskata gluvost utvrdile genetska pri~ina vo 30% od aficirana ta populacija, vo 35% ozna~ene sredinski ot faktor kako pri~ina, a 30% ostanale nepoznati.

Pred dvaeset godini, niz toga{ notonivo na dijagnostiki mo`nosti, nivo i organiziranost na zdravstveni te slu`bi, socio-ekonomski te uslovi na `ivotot vo razvieni te zemji, genetski te, sredinski te i nepoznatite pri~ini vo svetskata literatura aproksimativno se proporcionali ziraniso tretinska zastapenost (8).

The situations corresponded to the health situation of countries with less organized health protection and economically and hygienically lower life conditions, IAPB (International Association for Prevention of Blindness), 1983. (18).

At the same time, for England and Scotland, Fraser R; Friedmann A; Phillip L, Istoboe S. presented cause of blindness with children as genetic one in 40 – 44% (18).

Also at the same time, Fischal and Falk determined the cause of etiology of deafness with children as genetic in 30% of affected population, 35% were indicated as environmental factor and 30% as unknown.

Twenty years ago, at that level of diagnostic possibilities, level and organization of health service, socio-economic conditions in developed countries the genetic, environmental and unknown causes were identified approximately as one third per each in the world literature (8).



Slika 4 Anophthalmos cong. bill. Pri~inat a ostantana nepoznat a.

Figure 4 Anophthalmos cong. bill. Cause remained unknown.



Slika 5. Microphthalmos cong. bill. Pri~inat a ostantana nepoznat a.

Figure 5. Microphthalmos cong. bill. Cause remained unknown.



Slika 6 Retinopathia praematurorum (RLF) bliznaci od inkubator. Pri~inat a nepoznata.

Figure 6. Retinopathia praematurorum (RLF) of twins from incubator. Unknown cause.

Denes, zaradi zna~itelno povisoko nivo, kvalitete organizacija na za~titata na zdravje i ~ivotni ot standard, podobrenata higijena, zna~itelno se namali u~inokot na {tetni te predizvi kuva~i od sredinata. Kauzalitetot e nasoen kon genetski te bolesi. Pomalku e neutvrdeno zaradi primenata na novi metodi i tehnologii.

Duri, sovremeni te podatoci prezentiraat rezultati vo koi genetski te pri~ini se zastapeni so 50% od site detski slepila, 50% vo te{ ka gluvost, 50% vo site slu~aina mentalna retardacija (17).

Utvrduvaweto na pri~inite na etiopatogenetski ot mehani zam na bolesi i sostojbi vo humanata patologija, e osnova za pravewe program za prevencija: individualni, familijarni i nacionalni, pa i pri donesot na internacionalni te komiteti za prevencija na opredeleni bolesi i sosotojbi.

Vremenski, prevencijata mo`e da bi de pred zabremenuvaweto, po zabremenuvaweto, so prenatalen angaman, so neonatalen skrining i analiza na genetsko-sredinski otbalans za spre~uvawe na pojava na bolesi i sostojbi vo podocne`ni ot `ivoten period.

Vo multifaktorialnoto zaboluvawe se nametnuva analizata na naslednoto vlijanie i utvrduvawe na vlijanieto na faktorot od nadvorenata sredina (12).

Recently, due to considerably higher level, quality and organization of health protection and standard of living, improvement in hygiene, the contribution of environmental causes is lowered. Causality has moved toward genetic diseases. New methods and technologies decrease the share of unknown as well.

Moreover, contemporary data show results where genetic causes are represented as a cause for 50% of all cases of blindness with children, 50% of deafness with children and 50% of all cases of mental retardation (17).

To define the cause, etiopathogenetic mechanisms of the disease and conditions in human pathology are the basis for creating prevention programmes: individual, for families and national ones. It is also a contribution to international committees for prevention of certain diseases and conditions.

Prevention with a right timing can be before the conception, after the conception, by prenatal engagement, by neonatal screening and analysis of genetic-environmental balance for prevention of the disease and condition at a later age.

In multifactor cases an analysis of participation of heritage and identification of environmental causes must be carried out. (12).

Zaključok

- **Biološka osnova** za po~etok na ~ivotot ni z nerazdelni te procesi na rast i razvoj ja ~inat genetskata i nstrukcija, so gen nasleden od rodi tel i te vo koje zapi { an programot za morfogeneza (razvojot) i faktori te na sredinata { to go uslovuaat i usmeruaat.
- Genetsko-sredinskata interakcija vo ramki te na normalni te variacii, go determinira normalni ot rast i razvoj.
- Naru{ uvawa preku grani cata na mo` na reparacija, odnosno, prostorot na tolerirane te individualni razliki-se manifestiraat kako morfofunkcionalni gre{ki, rastrojstva na rastot i razvojot.
- Utvrduvawe na pri~inite vo humanata patologija e isto { to i kauzalnoto barawe vo oblasti te: **mutageneza, teratogeneza, onkogeneza** na postnatalnoto pojavuvawe na bolesi i sostojbi.
- Biolo{ kite procesi, nivelirani niz navedeni te oblasti na ~ove~kata patologija, vremenski gi determiniraat etiopatogenetski te zbidnuvawa.
- Pri~inite, etiopatogenetski ot mehанизam od pojdovnoto naru{ uvawe na rastot i razvojot se genetski, sredinski (akvirirani) i kade e neutvrden ili nesiguren-nepoznat. Kongenitalnoto ja podrazbira potrebната diferencijacija na naslednoto i nenaslednoto.
- Utvrdeni te pri~ini korespondiraat so nivoto, kvalitetot i organizacijata na zdravstvenata za{tita, socio-ekonomski te uslovi, standardot, sostojbata na higienata i mo`nosta na dijagnosti~ki ot instrumentarium.
- Utvrdeni te pri~ini i vreme za zapo~nuvawe na etiopatogenetski slu~uvawa se pretpostavka za programata na prevencija kon bolesa ili sostojbata: nacionalni, poedine~ni i semejni, a rezultati te se stavaat vo formirana banka na podatoci.

Conclusion

- **Biological foundation** of a living being, through inseparable processes of growth and development are genetic instructions, genome inherited from parents where morphogenesis (development) programme is written down including environmental factors, which condition and direct them.
- Genetic environmental interaction, in normal variation boundaries, determines normal growth and development.
- Disturbances over boundaries of possible reparations, including tolerated individual differences, are demonstrated as morphofunctional errors, disorders of growth and development.
- Determination of causes in human pathology is the same as a casual search in fields of: **mutagenesis, teratogenesis, oncogenesis** of postnatal manifestation of diseases and conditions.
- Biological processes, leveled through the mentioned areas of human pathology, determine the age of etiopathogenetic fulfillments.
- Causes, etiopathogenetic mechanism of disorder of growth and development are genetic, environmental (acquired). Where the cause is not defined or not reliable, it is marked as unknown. Congenital means necessary differentiation of inherited and not inherited.
- The determined causes correspond to the level, quality and organization of health protection, socio-economic conditions, standard, state of hygiene and possibilities of the diagnostic instruments.
- The determined causes and time of start of etiopathogenetic events are a precondition for programmes of prevention. According to the disease or condition these programmes are: national, individual or for families – results are kept in databases.

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