BIOLO[KA OSNOVA NA NEPRAVILNI OTRAST I RAZVOJ NA ^OVEKOT

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Rezime

Biolo{kata osnova na nastanuvaweto na `ivotot niz neodvoiviot proces na rastewe i razvoj, ja so~inuvaat dve osnovni determinanti. Toa se: genot nasleden od roditelite vo koj e programirana morfogenezata (razvojot) i faktorite na sredinata koi go uslovuvaat i naso~uvaat.

Genetskiot materijal od dvata roditela potencijalno go opredeluvaat noviot organizam vo slo`eno anatomsko funkcionalno milje vo ramkite na genetskiot kontinuitet vo koi se realiziraat biohemiskite procesi. Genetskite promeni, a i {tetnite agensi od sredinata imaat bitno vlijanie vrz pojavata {irok registar anomalii. Spored toa, izmenetata biolo{ka osnova, bilo so genetskite ili sredinskite promeni doveduva do raznovidni o{tetuvawa i hendikep.

Voved

Normalniot razvoj na edinkata go determiniraat dva va`ni fenomeni:

1. genetskite instrukcii za morfogenezata;
2. sposobnost na tkivoto da gi nadopolni op{tite metaboli~ki procesi.

Zna~i, **biolo{kata osnova** za nastanok na `ivotot niz nedelivite procesi na rastot i razvojot se deli na:

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 process 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** nasleden od roditelite vo koi e zapi{an programot za morfogenezata (razvojot);
- **faktori na sredinata** {to go uslovuvaat i usmeruvaat.

Genetsko-sredinskata interakcija, vo ramkite na normalnite varijacii go determinira normalniot rast i razvoj (6).

Zigot, oplodenite jajcevi kletki so genetskiot materijal od dvata roditela, potencijalno pretstavuva nov organizam. Vo anatomsko-funkcionalnoto milje, kao multipotentna kletka, mitotski se razmnoguva, a vo ramkite na genetiskiot kontinuitet, od genomski potencijal so diferencijalna aktivnost na genot se opredeluva morfofunkcionalnata karakteristika na site kletki vo organizmot.

Se ostvaruva biopotencijalot na idnata edinka (biotip: morfolo{ki, fizikohemiski, mentalen). Diferencijacijata e uslo`nuvawe na organizmot vo razvojot kade {to kletkite od razli~ni oblasti se menuvaat i se prilagoduvaat na funkcijata {to }e ja imaat vo noviot organizam, menuvaj}i mu ja i formata i goleminata i polo`bata. Biohemiski se menuvaat biosintetskite procesi i za kletkata se sintetiziraat specifi~ni proteini.

Morfofunkcionalnite karakteristiki zavisat od tipot na specifi~niot protein ~ija sinteza e regulirana so funkcijata na genot (2,5). Realizirawe na planot na razvojot, osven genetskite faktori go kontroliraat i uslovuvaat i faktorot na sredinata.

Kontrolnite mehanizmi, prvenstveno na nivo na kletka, potoa tkivata, organite i plodot, ovozmo`uvaat vo tekot na razvojot da se realizira genomski zapis na oplodenoto jajce.

Vo dijapazonot na normalnite variacii se eksponiraat individualnite razliki proizlezeni 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 mo`nata 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 mitotic 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.

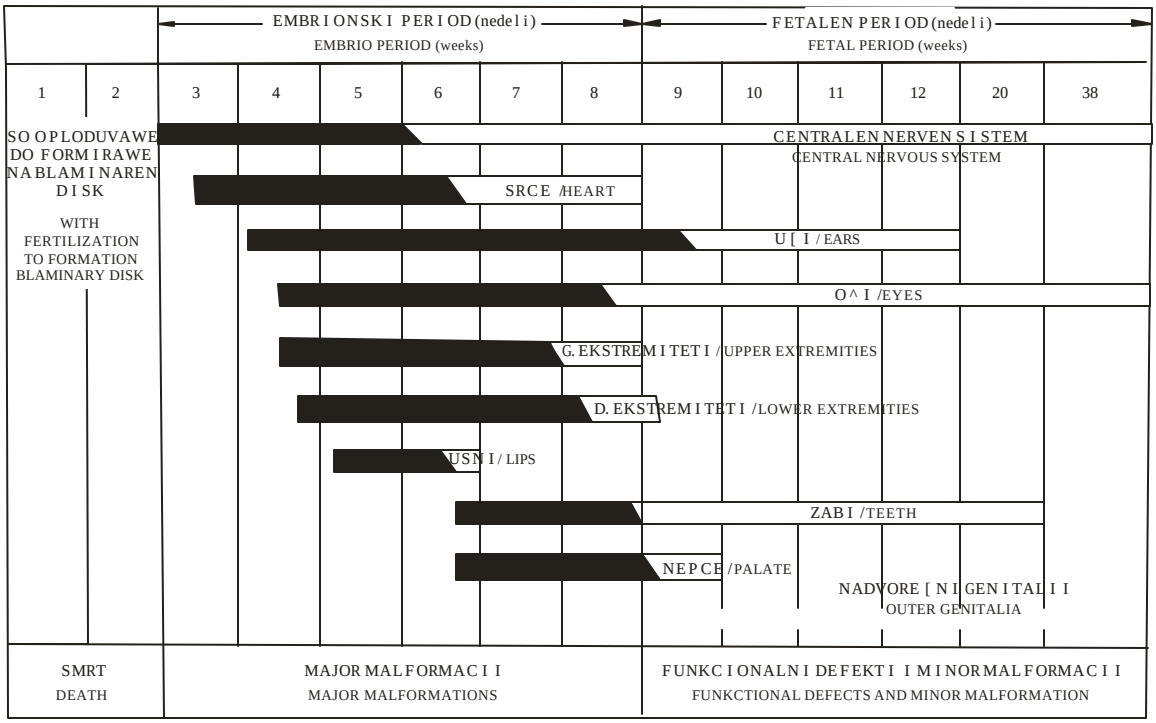
The morphofunctional characteristics depend on the type of specific protein's synthesis that is regulated by the gene function (2.5). Realization of development plan is controlled and caused not only by genetic factors but also by factors of the environment. Mechanisms of control, primarily at the level 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 reparation give errors of formation in case

oblikuvawe, dokolku ne dojde do gubitok ili resorpcija na plodot. Genetskite izmeni i/ili {tetnite agensi od sredinata (teratogeni) vo raniot period na gestacija go prekinuvaat rastot i razvojot na embrionot (resorpcii, spontani abortusi), a vo kriti~niot "senzitiven# period na organogenezata, predizvikuva pojava na kongenitalni anomalii. Pokraj toa: predvremeno poroduvawe, mrtvorodeno i rana neonatalna 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. *^uvstvitelnost na razni organski sistemi vo intrauterinarniot rast i razvoj. Polnata linija gi ozna~uva mnogu ~uvstvitelnite periodi.*

Figure 1. *Sensitiveness of different organ systems in intre utera growth and development. The full bar indicates highly sensitive periods*

Kongenitalno (congenitalis=vroden, od ra|awe) ne ja definira pri~inata, u{te pomalku go objasnuva etiopatogenetskiot mehanizam na nastanatite izmeni. Fenomenolo{ki, ja prika`uva naslednata i/ili sredinskata osnova na o{tetuvaweto.

Kongenitalnite o{tetuvawa (sostojbi ili bolesti) baraat otkrivawe 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 oblastite na: **mutageneza, teratogeneza, onkogeneza.**

Kon ova denes mu se pridodavaat i sé poprisutnite vo ~ovekata patologija, docne`no pojavuvawe na genetskite gre{ki. Familijarnata, genetskata predispozicija i provocira~kite faktori na sredinata uslovuvaat pojavuvawe na multifaktorijalni bolesti (avtoimmuni bolesti, razni psihozi, alergii, tumori, bolesti na KVS i dr.).

Izmenetata biolo{ka osnova, bilo so genetski i/ili so sredinski izmeni-rezultira so izolirani ili kombinirani o{tetuvawa, hendikepi.

Spored izvorite i poliwata na patolo{kite zbidnuvawa se identifikuvaat i **pri~inite**. So observirawe i so etiopatogenetski mehanizmi se odreduva i vremeto na nastanuvawe na naru{uvaweto.

Genetskite izmeni mo`no e da se utvrdat i pred zabremenuvaweto: vo genetskiot materijal od roditelite, so generaciska transmisija na mutirani geni, so hromozomski o{tetuvawa, a i so mo`nite sve`i (de novo) mutacii.

Po oploduvaweto, so razli~ni stepeni mo`at da se menuvaat dadenite genetski instrukcii. Vo bremenosta, {tetnite agensi od sredinata (fizi~ki, hemiski, biolo{ki) mo`at kako teratogeni patolo{ki da go izmenat planot na razvojot.

Po ra|aweto, mo`no e podlo`uvawe na onkogenetski pritisok, vo raniot i podocna vo involutivniot `ivoten vek. Izostanuvaweto, od razli~ni pri~ini, egzatktni dokazi vo etiologijata ja nametnuva kategorijata na pri~inata: nepoznata.

Prifateniot trijas na pri~ini: **genetski**, **sredinski** (steknati) i **nepoznati**, kriteriumski go standardizira podreduvaweto na dobienite podatoci od istra`uvaweto na humanata patologija sa drugi i stranski literaturni podatoci. Na takov na~in se objektivizira sostojbata na zdravjeto na populacijata i ovozmo`uva pretpostavki za pravewe program za prevencija.

theratogenesis and oncogenesis.

Late demonstration of genetic errors (that is becoming more present in human pathology) is added to this today. Family, genetic predisposition and provoking factor of the environment bring to multifactoral diseases (autoimmune diseases, various psychoses, allergies, tumors, KVS diseases, etc).

A changed biological foundation – either by genetic 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 determined when it came to the disorder.

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

Upon the conception the genetically given instructions may be changed at different levels. During pregnancy harmful environmental agents (physical, 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.

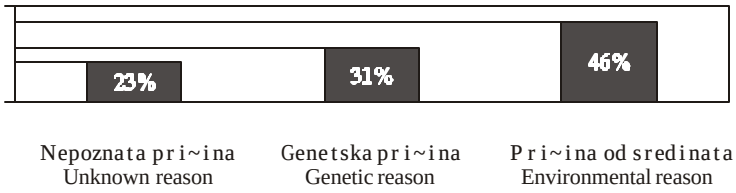
The accepted trias of causes: **genetic, environmental** (gained) and **unknown** standardize as criteria the comparison of the data got in the research of humane pathology from other and foreign data in literature. This makes the state of health of population objective and creates preconditions for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

Istra`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 godina zaradi utvrduvawe na pri~inata na slepilo kaj detskata populacija. Na statisti~ki reprezentativniot 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.

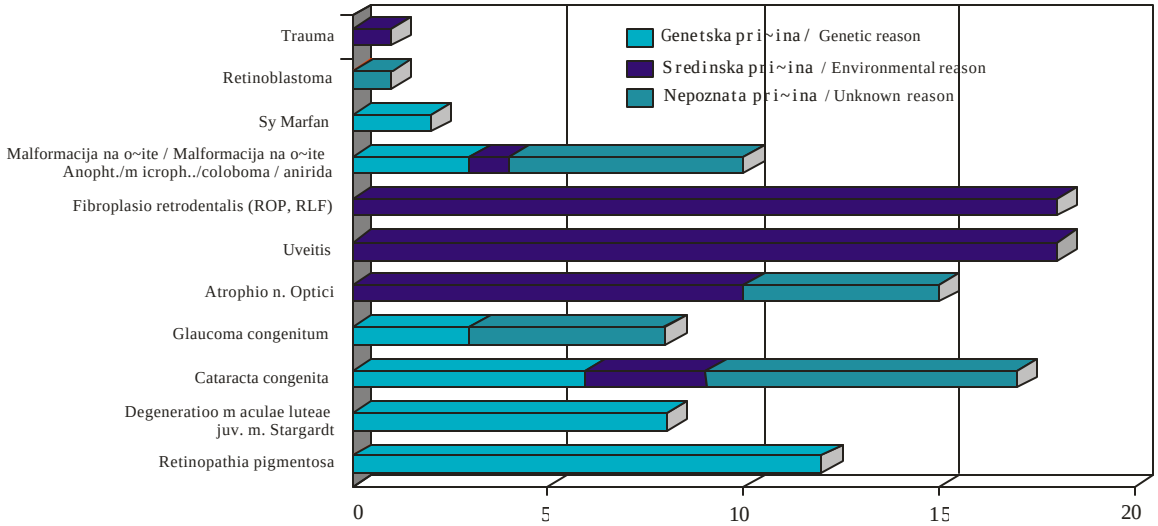
Research and discussion

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. *Ispitanici od Zavodot - Zemun spored pri~inata za slepilo.*

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



Slika 3. *Ispitanici od Zavodot-Zemun spored klini~kiopt naod (patolo{ki izmeni na oko-to) 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 zdravjeto 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 avtori, za Anglija, odnosno [kotska: Fraser R; Friedmann A; odnosno Phillip L. Istoboe S. prezentiraa genetskata pri~ina od 40 do 44% za detskoto slepilo vo navedenite populacii (18).

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

Pred dvaeset godini, niz toga{noto nivo na dijagnosti~ki mo`nosti, nivo i organiziranost na zdravstvenite slu`bi, socio-ekonomskite uslovi na `ivotot vo razvienite zemji, genetskite, sredinskite i nepoznatite pri~ini vo svetskata literatura aproksimativno se proporcionalizirani so 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).

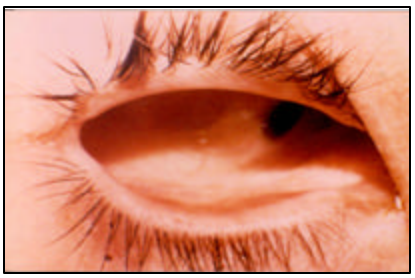
At the same time, for England and Scotland, Fraser R; Friedmann A; Phillip L, Istoboe S. presented cause of blindness with children as genetic one in 40 – 44% (18).

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~inata ostana nepoznata.*

Figure 4 *Anophthalmos cong. bill. Cause remained unknown.*



Slika 5. *Microphthalmos cong. bill. Pri~inata ostana nepoznata.*

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

Slika 6 *Retinopathia praematurorum (RLF) bliznaci od inkubator. Pri~ina nepoznata.*

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

Denes, zaradi zna~itelno povisoko nivo, kvalitet i organizacija na za{titata na zdravjeto i `ivotniot standard, podobrenata higiena, zna~itelno se namali u~inokot na {tetnite predizvikuva~i od sredinata. Kauzalitetot e naso~en kon genetskite bolesti. Pomalku e neutvrdeno zaradi primenata na novi metodi i tehnologii.

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

Utvrduvaweto na pri~inite na etiopatogenetskiot mehanizam na bolesti i sostojbi vo humanata patologija, e osnova za pravewe program za prevencija: individualni, familijarni i nacionalen, pa í pridonesot na internacionalnite komiteti za prevencija na opredeleni bolesti i sosotojbi.

Vremenski, prevencijata mo`e da bide pred zabremenuvaweto, po zabremenuvaweto, so prenatalen anga`man, so neonatalen skrining i analiza na genetsko-sredinskiot balans za spre~uvawe na pojava na bolesti i sostojbi vo podocne`niot `iveten period.

Vo multifaktorialnoto zaboluvawe se nametnuva analizata na naslednoto vlijanie i utvrduvawe na vlijanieto na faktorot od nadvore{nata 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).

Zaklu~ok

- **Biolo{kata osnova** za po~etok na `ivotot niz nerazdelnite procesi na rast i razvoj ja ~inat genetskata instrukcija, so gen nasleden od roditelite vo koj e zapi{an programot za morfogenezata (razvojot) i faktorite na sredinata {to go uslovuvaat i usmeruvaat.
- Genetsko-sredinskata interakcija vo ramkite na normalnite variacii, go determinira normalniot rast i razvoj.
- Naru{uvawa preku granicata na mo`na reparacija, odnosno, prostorot na tolerираните 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 oblastite: **mutageneza, teratogeneza, onkogeneza** na postnatalnoto pojavuvawe na bolesti i sostojbi.
- Biolo{kite procesi, nivelirani niz navedenite oblasti na ~ove~kata patologija, vremenski gi determiniraat etiopatogenetskite zbidnuvawa.
- Pri~inite, etiopatogenetskiot mehanizam od pojdovnoto naru{uvawe na rastot i razvojot se genetski, sredinski (akvirirani) i kade e neutvrden ili nesiguren-nepoznat. Kongenitalnoto ja podrazbira potrebnata diferencijacija na naslednoto i nenaslednoto.
- Utvrdenite pri~ini korespondiraat so nivoto, kvalitetot i organizacijata na zdravstvenata za{tita, socio-ekonomskite uslovi, standardot, sostojbata na higienata i mo`nosta na dijagnosti~kiot instrumentarium.
- Utvrdenite pri~ini i vreme za zapo~nuvawe na etiopatogenetski slu~uvawa se pretpostavka za programata na prevencija kon bolesta ili sostojbata: nacionalni, poedine~ni i semejni, a rezultatite se stavaat vo formiranata 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, threatogenesis, oncogenesis** of postnatal manifestation of diseases and conditions.
- Biological processes, leveled through the mentioned ares of human pathology, deternine 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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