Multifactorial disorders pdf

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Multifactorial disease such as work-related diseases, for example hypertension, coronary heart disease, chronic non-specific respiratory disease, low back syndrome, upper limb disorders, cancer, etc., are thought to be caused by complex interactions between genetic factors (polygenic basis) and various environmental factors. The term multifactorial means that there are many different influences acting together to cause the appearance of the disease. These include effects from a combination of genetic factors, none of which on its own would be likely to cause the disease, and environmental factors, which again would not cause the disease by themselves. It is believed that a particular combination of genetic and environmental factors act together in concert and trigger the development of multifactorial disease. Different environmental factors will influence the development of different multifactorial diseases. Besides environmental... Researchers are learning that nearly all conditions and diseases have a genetic component. Some disorders, such as sickle cell disease and cystic fibrosis, are caused by variants (also known as mutations) in single genes. The causes of many other disorders, however, are much more complex. Common health problems such as heart disease, type 2 diabetes, and obesity do not have a single genetic cause—they are influenced by multiple genes (polygenic) in combination with lifestyle and environmental factors, such as exercise, diet, or pollutant exposures. Conditions caused by many contributing factors are called complex or multifactorial disorders.Although complex disorders often cluster in families, they do not have a clear-cut pattern of inheritance. It may be difficult to identify the role of genetics in these disorders, particularly because families often also share environments and may have similar lifestyles. This makes it difficult to determine a person's risk of inheriting or passing on these disorders. Complex disorders are also difficult to study and treat because the specific factors that cause most of these disorders have not yet been identified. Researchers continue to look for major contributing genes for many common, complex disorders. Researchers are learning that nearly all conditions and diseases have a genetic component. Some disorders, such as sickle cell disease and cystic fibrosis, are caused by mutations in a single gene. The causes of many other disorders, however, are much more complex. Common medical problems such as heart disease, diabetes, and obesity do not have a single genetic cause—they are likely associated with the effects of multiple genes in combination with lifestyle and environmental factors. Conditions caused by many contributing factors are called complex or multifactorial disorders. Figure 1 The main symptoms of diabetes, a multifactorial disorder Although complex disorders often cluster in families, they do not have a clear- cut pattern of inheritance. This makes it difficult to determine a person's risk of inheriting or passing on these disorders. Complex disorders are also difficult to study and treat because the specific factors that cause most of these disorders have not yet been identified. Researchers continue to look for major contributing genes for many common complex disorders. Genetic Predispositions A genetic predisposition (sometimes also called genetic susceptibility) is an increased likelihood of developing a particular disease based on a person's genetic makeup. A genetic predisposition results from specific genetic variations that are often inherited from a parent. These genetic changes contribute to the development of a disease but do not directly cause it. Some people with a predisposing genetic variation will never get the disease while others will, even within the same family. Genetic variations can have large or small effects on the likelihood of developing a particular disease. For example, certain mutations in the BRCA1 or BRCA2 genes greatly increase a person's risk of developing breast cancer and ovarian cancer. Variations in other genes, such as BARD1 and BRIP1, also increase breast cancer risk, but the contribution of these genetic changes to a person's overall risk appears to be much smaller. Current research is focused on identifying genetic changes that have a small effect on disease risk but are common in the general population. Although each of these variations only slightly increases a person's risk, having changes in several different genes may combine to increase disease risk significantly. Changes in many genes, each with a small effect, may underlie susceptibility to many common diseases, including cancer, obesity, diabetes, heart disease, and mental illness. In people with a genetic predisposition, the risk of disease can depend on multiple factors in addition to an identified genetic change. These include other genetic factors (sometimes called modifiers) as well as lifestyle and environmental factors. Although a person's genetic makeup cannot be altered, some lifestyle and environmental modifications (such as having more frequent disease screenings and maintaining a healthy weight) may be able to reduce disease risk in people with a genetic predisposition. References "Mutations and Health" by U.S. National Library of Medicine is in the Public Domain Multifactorial diseases refer to diseases having a genesis known to be influenced both by the genome and the environment. Examples include cardiovascular diseases, asthma, autoimmune diseases and various neurological and psychiatric diseases. Technical development has made possible a considerably more accurate measurement of genetic variation, having already led to the identification of hundreds of predisposing genes. We do not, however, still understand enough about the mechanisms of action of genes. The increasing progress in DNA sequencing techniques is currently changing the prospects of research more quickly than ever before. Cleft lip; A multifactorial disorder Multifactorial diseases are not confined to any specific pattern of single gene inheritance and are likely to be associated with multiple genes effects together with the effects of environmental factors.[1] In fact, the terms 'multifactorial' and 'polygenic' are used as synonyms and these terms are commonly used to describe the architecture of disease causing genetic component.[2] Although multifactorial diseases are often found gathered in families yet, they do not show any distinct pattern of inheritance. It is difficult to study and treat multifactorial diseases because specific factors associated with these diseases have not yet been identified. Some common multifactorial disorders include schizophrenia, diabetes, asthma, depression, high blood pressure, Alzheimer's, obesity, epilepsy, heart diseases, Hypothyroidism, club foot and even dandruff. The Multifactorial threshold model[3] assumes that gene defects for multifactorial traits are usually distributed within populations. Firstly, different populations might have different thresholds. This is the case in which occurrences of a particular disease is different in males and females (e.g. Pyloric stenosis). The distribution of susceptibility is the same but threshold is different. Secondly, threshold may be same but the distributions of susceptibility may be different. It explains the underlying risks present in first degree relatives of affected individuals. Characteristics Multifactorial disorders exhibit a combination of distinct characteristics which are clearly differentiated from Mendelian inheritance. The risk of multifactorial diseases may get increased due to environmental influences. The disease is not sex-limited but it occurs more frequently in one gender than the other. The disease occurs more commonly in a distinct ethnic group (i.e., Africans, Asians, Caucasians etc.) The diseases may have more in common than generally recognized since similar risk factors are associated with multiple diseases The recurrence risk of such disorders is greater among relatives of an affected individual than in the common population. Additionally, the risk is higher in first degree relatives of an affected individual than distant relatives. Multifactorial disorders also reveal increased concordance for disease in monozygotic twins as compared to dizygotic twins or full siblings.[4] Risk Factors The risk for multifactorial disorders is mainly determined by universal risk factors. Risk factors are divided into three categories; genetic, environmental and complex factors (for example overweight). Genetic risk factors are associated with the permanent changes in the base pair sequence of human genome. In the last decade, many studies have been generated data regarding genetic basis of multifactorial diseases. Various polymorphism have been shown to be associated with more than one disease, examples include polymorphisms in TNF-a, TGF-b and ACE genes.[5][6][7] Environmental risk factors vary from events of life to medical interventions. The quick change in the patterns of morbidity, within one or two generations, clearly demonstrates the significance of environmental factors in the development and reduction of multifactorial disorders.[8] Environmental risk factors include change in life style (diet, physical activity, stress management) and medical interventions (surgery, drugs). Many risk factors originate from the interactions between genetic and environmental factors and referred as complex risk factors. Examples include epigenetic changes, body weight and plasma cortisol level.[9] Multifactorial Disorders; Continuous or Discontinuous Autosomal or sex-linked single gene conditions generally produce distinct phenotypes, said to be discontinuous: the individual either has the trait or does not. However, multifactorial traits may be discontinuous or continuous. Continuous traits exhibit normal distribution in population and display a gradient of phenotypes while discontinuous traits fall into discrete categories and are either present or absent in individuals. It is interesting to know that many disorders arising from discontinuous variation show complex phenotypes also resembling continuous variation [10] This occurs due to the basis of continuous variation responsible for the increased susceptibility to a disease. According to this theory, a disease develops after a distinct liability threshold is reached and severity in the disease phenotype increases with the increased liability threshold. On the contrary, disease will not develop in the individual who does not reach the liability threshold. Therefore, an individual either having disease or not, the disease shows discontinuous variation. An example of how the liability threshold works can be seen in individuals with cleft lip and palate. Cleft lip and palate is a birth defect in which an infant is born with unfused lip and palate tissues. An individual with cleft lip and palate can have unaffected parents who do not seem to have a family history of the disorder. History Francis Galton was the first scientist who studied multifactorial diseases and was the cousin of Charles Darwin. Major focus of Galton was on 'inheritance of traits' and he observed "blending" characters.[11] The average contribution of each several ancestor to the total heritage of the offspring [12] and is now known as continuous variation. When a trait (human height) exhibiting continuous variation is plotted against a graph, the majority of population distribution is centered around the mean. [13] Galton's work is contrary to work done by Gregor Mendel; as the latter studied "nonblending" traits and kept them in different categories.[14] The traits exhibiting discontinuous variation, occur in two or more distinct forms in a population as Mendel found in color of petals. See also Genetic disorders polygenes Quantitative trait locus References ^ Duarte, Christine W.; Vaughan, Laura K.; Beasley, T. Mark; Tiwari, Hemant K. 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