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Brain Tumors In Young Populations: Epidemiology, Risk Factors, And Prevention Strategies

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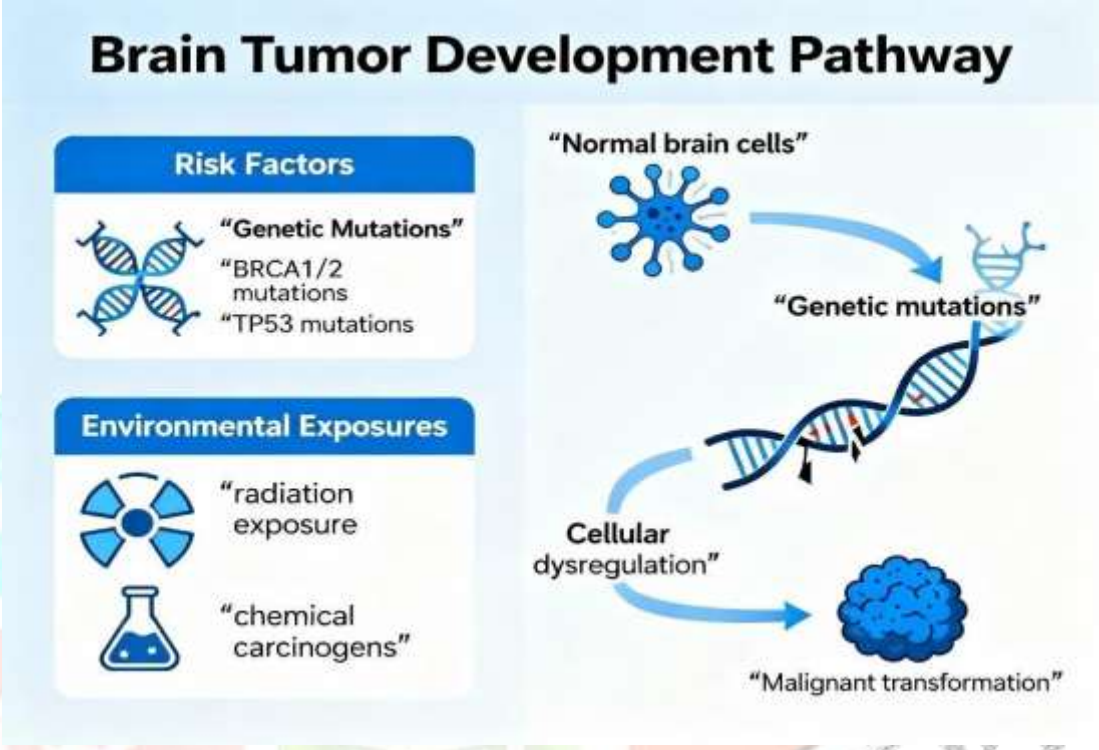
ABSTRACT

Central nervous system tumors represent a significant public health concern affecting adolescents and young adults (AYA) aged 15-39 years, with approximately 208,620 prevalent cases in the United States and over 57,645 new cases annually worldwide. This comprehensive review synthesizes current epidemiological evidence regarding disease burden, genetic predisposition factors, environmental and occupational exposures, lifestyle variables, and demographic disparities contributing to brain tumor risk in young populations. The age-standardized global incidence stands at 1.92 per 100,000 population annually, with distinct epidemiological patterns differing from older adult populations.[1] Ionizing radiation remains the only definitively established environmental risk factor with documented relative risks of 3-7 fold for glial tumors and tenfold for meningiomas.[2] Emerging evidence implicates pesticide exposure (effect size 1.44) and herbicide exposure (effect size 2.38) as modifiable risk factors.[3] Genetic susceptibility accounts for a minority of cases, with hereditary syndromes including Li-Fraumeni syndrome and neurofibromatosis type one conferring substantially elevated risks. Maternal dietary patterns significantly influence offspring risk, with cured meat consumption (relative risk 1.51) and elevated coffee intake (relative risk 1.45) during pregnancy associated with increased tumor development.[4] Conversely, maternal supplementation with vitamins and folic acid provides protective effects.[5] Significant disparities exist across racial, ethnic, and socioeconomic groups, with Black and Hispanic young adults demonstrating worse survival outcomes despite similar or lower incidence rates. Socioeconomic development indices correlate positively with reported incidence, likely reflecting diagnostic capability variations rather than true epidemiological differences. Projections through 2040 indicate rising absolute case numbers despite declining agestandardized rates. This review consolidates evidence-based findings to facilitate clinical risk stratification, guide prevention initiatives, and ensure equitable delivery of early detection and treatment services. Priority research directions include large prospective cohort studies integrating environmental exposure assessment with genomic analysis to clarify gene-environment interactions, advancement in biomarker-based surveillance, and implementation of health systems reforms addressing persistent disparities.

KEYWORDS: Brain tumors epidemiology; Adolescents and young adults; Risk factors; Central nervous system malignancies; Environmental exposures; Genetic predisposition; Prevention strategies; Health disparities

INTRODUCTION

Brain and central nervous system (CNS) tumors in young populations represent a unique and multifaceted challenge to contemporary healthcare systems and public health infrastructure.[1] The demographic group of adolescents and young adults aged 15-39 years experiences distinctive epidemiological patterns, diverse tumor histologies, and etiological determinants that differ substantially from brain tumors occurring in older adult populations.[2] Central nervous system malignancies encompass a heterogeneous group of neoplastic processes affecting the brain parenchyma, meninges, cerebrospinal fluid, spinal cord, and associated neural structures, each demonstrating distinct biological properties and clinical trajectories.[3]



Among AYA populations, CNS tumors hold the paradoxical distinction of being simultaneously the most common primary malignancy and among the rarest of all cancers in the general population, occurring at an age-standardized incidence of 1.92 per 100,000 individuals annually.[4] This apparent contradiction reflects the relative rarity of cancer in young populations combined with the predominant role of CNS malignancies within this age-specific disease landscape. The clinical significance extends far beyond epidemiological statistics, as brain tumors consistently rank as the leading cause of cancer-related death in young adults aged 15-24 years, surpassing lymphomas, leukemias, and all solid organ malignancies in this critical developmental age stratum.[5]

The epidemiological landscape of brain tumors in young populations has undergone substantial transformation over recent decades, driven by advancing diagnostic technologies, improved cancer surveillance systems, and refined classification schemes reflecting evolving understanding of tumor biology.[6] Magnetic resonance imaging with advanced sequences, positron emission tomography, and molecular techniques have revolutionized diagnostic capabilities, potentially contributing to observed increases in reported incidence rates.

The psychological and social ramifications of a brain tumor diagnosis during critical developmental periods of education, career formation, and relationship establishment amplify the public health significance of this disease cluster.[7] Understanding the epidemiology, risk factors, and prevention strategies applicable to brain tumors in young populations is essential for optimizing clinical management and public health policy.

EPIDEMIOLOGY AND GLOBAL BURDEN OF DISEASE

Current Disease Burden

The global epidemiological landscape of brain tumors in young populations reveals complex patterns with significant regional variations demanding urgent investigation.[1] Contemporary data from the Global Burden of Disease 2021 database demonstrates an age-standardized incidence rate of 1.92 per 100,000 individuals annually, with an estimated 57,645 new cases occurring worldwide each year.[1] In the United States, approximately 208,620 individuals aged 15-39 years currently live with primary brain or spinal cord tumors, representing a substantial and often underrecognized health burden within this demographic.[2] Central nervous system malignancies rank as the leading cause of cancer-related mortality in young adults aged 15-24 years, exceeding all other malignancy types in this age stratum, with profound implications for years of life lost and psychosocial morbidity.[2]

Histopathological Patterns

The heterogeneity of histopathological subtypes presents important epidemiological patterns requiring nuanced understanding. Non-malignant pituitary adenomas constitute the most frequently diagnosed CNS tumors overall, particularly in individuals under 30 years of age, accounting for a substantial proportion of all diagnoses despite their benign nature.[3] Among malignant neoplasms, lower-grade diffuse gliomas including astrocytomas and oligodendrogliomas predominantly occur in younger age groups, in striking contrast to high-grade glioblastomas more commonly observed in populations over 40 years of age, suggesting distinct molecular pathogenic mechanisms.[3]

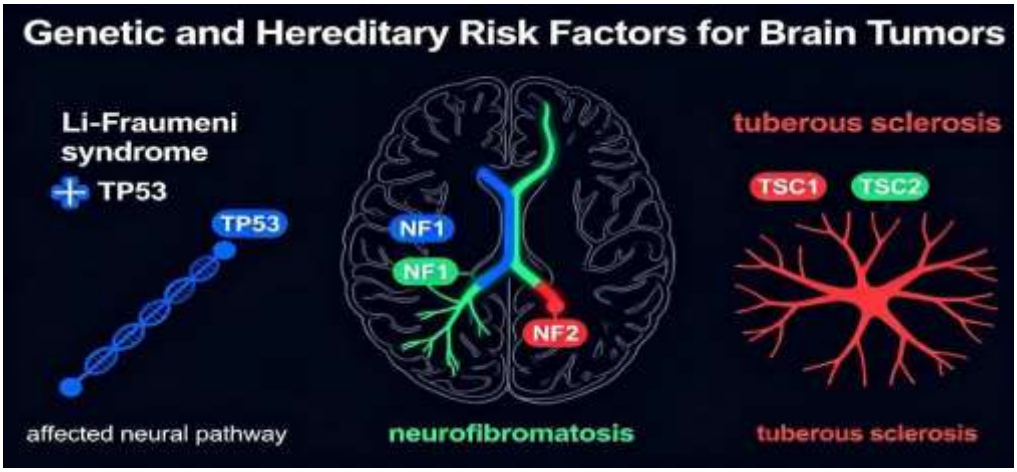
Sex distribution patterns vary considerably by histological subtype, with female adolescents and young adults demonstrating overall higher incidence due to greater prevalence of pituitary adenomas, yet males showing higher incidence of malignant tumor subtypes.[4] This apparent paradox reflects the predominance of benign tumors in females versus malignant tumors in males within the AYA population.

Temporal Trends and Projections

Temporal trends in brain tumor incidence over recent decades reveal modest increases in both children and adolescents, with complex etiological implications.[5] Data from 2008-2017 indicate a
0.7 yearly increase in incidence rates of cancerous brain tumors among children and a 0.5 yearly increase among adolescents.[5] These modest increases could reflect either true increases in disease occurrence or improvements in diagnostic capabilities and surveillance precision, with the latter explanation currently favored by epidemiologists.

However, projections through 2040 indicate that while absolute case numbers will increase due to population growth and demographic shifts, age-standardized incidence rates are expected to decline in many regions, reflecting anticipated improvements in therapeutic approaches and earlier detection capabilities.[1]

GENETIC AND HEREDITARY RISK FACTORS



Inherited Cancer Syndromes

Inherited genetic syndromes contribute to a minority of brain tumors in young populations but confer substantially elevated individual risks warranting dedicated clinical attention and specialized surveillance protocols.[6] Li-Fraumeni syndrome, caused by germline TP53 mutations, represents one of the most significant hereditary cancer predisposition syndromes, with affected individuals demonstrating dramatically elevated lifetime risk of multiple malignancies including brain tumors, often occurring at unusually young ages.[6] Affected individuals face cumulative lifetime cancer risks exceeding 70%, with brain tumors representing one component of this extraordinarily elevated risk profile.

Neurofibromatosis type one, resulting from NF1 gene mutations, confers increased susceptibility to optic nerve gliomas and other central nervous system neoplasms, with manifestations often appearing during childhood and adolescence requiring intensive monitoring and periodic neuroimaging surveillance.[6] Tuberous sclerosis complex, caused by mutations in TSC1 or TSC2 genes, predisposes to development of subependymal giant cell astrocytomas, particularly in the pediatric population, demanding close clinical surveillance and careful treatment consideration.

Familial Clustering and Polygenic Inheritance

Beyond single-gene syndromic conditions, familial clustering patterns suggest polygenic inheritance contributing substantially to brain tumor susceptibility in young populations.[7]

Population-based Nordic family study analyses documented a 1.7-fold increased risk for brain cancer diagnosed before age 20 when a parent carried a diagnosis of brain cancer, indicating that genetic contributions to early-onset tumors extend well beyond recognized syndromic conditions.[7] This familial aggregation observed in the absence of formally recognized hereditary syndromes suggests involvement of multiple genes of modest individual effect.

Genome-wide association studies have identified multiple common genetic variants associated with modest increases in brain tumor risk, though such variants individually explain only small proportions of population attributable risk.[7] The contribution of rare genetic variants with larger effect sizes remains incompletely characterized due to the relative rarity of brain tumors and methodological limitations in variant discovery and functional validation.[8]

ENVIRONMENTAL AND OCCUPATIONAL EXPOSURES

Ionizing Radiation

Ionizing radiation exposure represents the only unequivocally established environmental risk factor for brain tumors in young populations, with documented associations restricted primarily to therapeutic radiation contexts and specific occupational exposures.[9] Medical radiation exposures, including cranial radiotherapy for primary brain tumors, leukemia, or lymphoma, and therapeutic radiation to the head and neck region, demonstrate clear dose-dependent relationships with subsequent brain tumor development, with relative risks ranging from 3-7 fold for glial tumors and approximately tenfold for meningiomas.[9]

Latency periods for radiation-induced tumors typically exceed 10-20 years post-exposure, and risk persists well into adulthood for individuals exposed during childhood, requiring long-term surveillance protocols and careful clinical monitoring.[10] Diagnostic radiation including head computed tomography scans, though exposing recipients to substantially lower doses than therapeutic radiation, has not been conclusively demonstrated to increase brain tumor risk in epidemiological studies to date.[10]

Pesticide and Herbicide Exposures

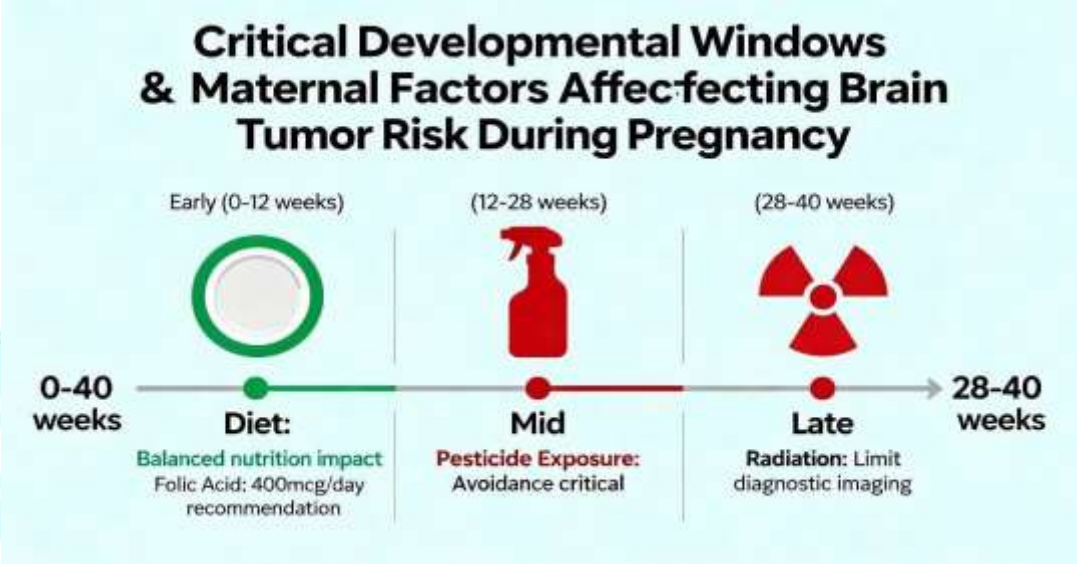
Pesticide and herbicide exposures during childhood have emerged as significant modifiable environmental risk factors through comprehensive systematic review and meta-analysis of epidemiological investigations across multiple countries.[11] Meta-analytic synthesis of 180 studies examining childhood pesticide exposures yielded effect sizes of 1.44 for pesticide exposure and
2.38 for herbicide exposure, suggesting that environmental chemical exposures warrant greater public health attention and preventive intervention strategies.[11]

Exposure pathways include direct occupational or recreational contact in agricultural settings as well as parental occupational exposure with subsequent household contamination affecting children through secondary exposure mechanisms.[11] The biological plausibility of these associations relates to the neurotoxic properties of many pesticides and herbicides and their potential to disrupt critical developmental neural processes during windows of brain maturation.[12] Understanding timing and dose-response relationships remains an important area for continued investigation.

Parental Occupational Exposures

Parental occupational exposures to various chemical agents represent important indirect pathways through which young individuals may acquire exposure to environmental hazards.[12] Paternal occupational exposures to chemical agents and maternal household contact with occupational hazards have been documented to substantially increase offspring cancer risk through mechanisms of prenatal contamination and developmental disruption. These findings underscore the importance of occupational health protection for workers during reproductive years.

MATERNAL FACTORS AND EARLY LIFE EXPOSURES



Dietary Patterns During Pregnancy

Maternal dietary patterns during pregnancy represent important modifiable risk factors influencing offspring brain tumor susceptibility and requiring evidence-based counseling for pregnant women.[13] Investigation of pregnancy and parental characteristics identified that maternal consumption of cured meats during pregnancy was associated with a relative risk of 1.51 for subsequent offspring brain tumor development, a finding with significant nutritional intervention implications.[13]

Additionally, elevated maternal coffee intake defined as two or more cups daily during pregnancy demonstrated a relative risk of 1.45 for pediatric brain tumors, suggesting that maternal dietary modifications might reduce offspring risk through mechanistically plausible pathways.[13] The mechanisms underlying these associations remain uncertain but may relate to mutagenic compounds generated during meat curing processes (including nitrosamines) or bioactive compounds in coffee that could influence fetal neural development during critical developmental windows.[14]

Protective Nutritional Factors

Conversely, maternal nutritional supplementation with vitamins and folic acid during pregnancy appears to confer protective effects against offspring brain tumor development and represents a modifiable prevention strategy with minimal adverse effects.[15] Systematic review and metaanalysis of prospective maternal dietary investigations demonstrated significant protective associations between maternal intake of vitamins, minerals, and antioxidants during pregnancy and reduced early childhood brain tumor risk.[15]

Folic acid supplementation, in particular, may reduce brain tumor risk through its critical role in DNA

methylation and cellular differentiation processes essential for normal neural development.[15] These findings suggest that dietary intervention programs emphasizing improved maternal nutrition during pregnancy could represent feasible, cost-effective prevention strategies applicable to high-risk populations with considerable potential for substantial population-level impact.[16]

DEMOGRAPHIC DISPARITIES AND HEALTH INEQUITIES

Racial and Ethnic Disparities

Substantial demographic disparities in both incidence and outcomes of brain tumors exist across racial, ethnic, and socioeconomic groups, reflecting profound inequities in healthcare access and quality that demand urgent policy intervention.[17] Incidence patterns vary significantly by race and ethnicity, with non-Hispanic white populations demonstrating the highest incidence of malignant central nervous system tumors compared to other demographic groups.[17]

However, survival outcomes follow paradoxical patterns, with Black and Hispanic young adults experiencing substantially worse five-year survival rates despite similar or lower incidence rates compared to white populations, a disparity that reflects systemic inequities in healthcare delivery, treatment access, and therapeutic quality.[18] These disparities likely reflect systemic healthcare inequities including delayed diagnosis due to limited imaging infrastructure in underserved communities, reduced access to experienced neurosurgeons and neuro-oncologists, insurance coverage barriers limiting access to advanced therapies, and reduced enrollment in clinical trials offering novel treatment approaches.[18]

Socioeconomic Factors

Socioeconomic status represents a critical social determinant of brain tumor outcomes in young populations with profound implications for health equity and clinical outcomes.[19] Low-income and lower middle-income regions demonstrate reduced incidence rates compared to high-income developed nations, a pattern that likely reflects diagnostic capability limitations and surveillance system deficiencies rather than true epidemiological differences in disease occurrence.[19]

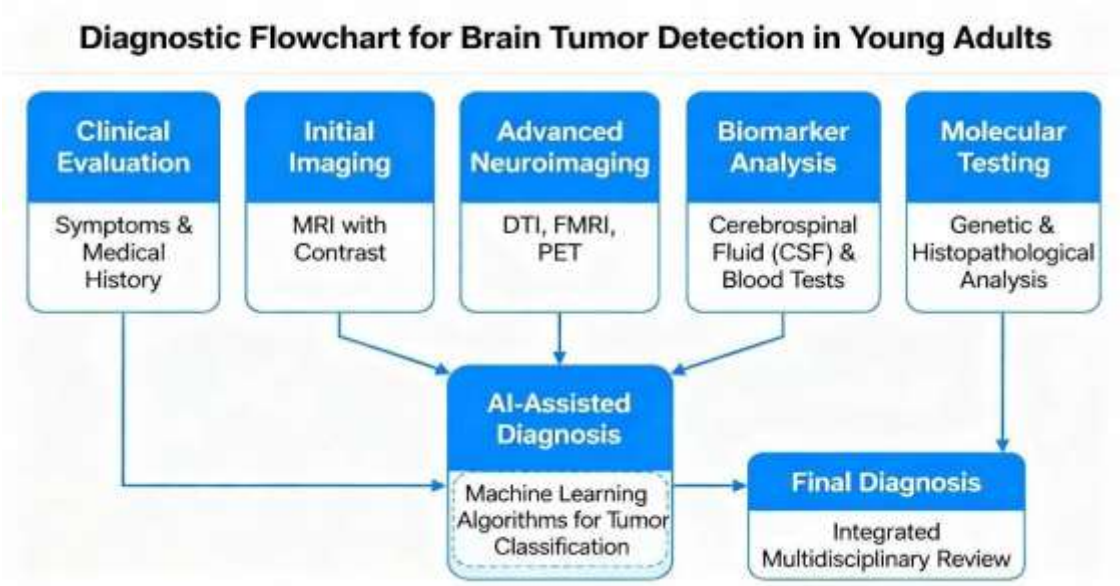
In resource-limited settings, substantial underdiagnosis of brain tumors occurs due to limited magnetic resonance imaging and computed tomography infrastructure, inadequate pathological expertise for tumor classification, and delayed healthcare-seeking due to poverty-related barriers affecting patient behavior.[20] Conversely, in high socioeconomic development index nations, superior diagnostic infrastructure including widespread advanced neuroimaging, trained neuroradiologists, and pathologists specializing in neuropathology contribute substantially to higher reported incidence rates.[20]

MOLECULAR PATHOGENESIS AND PATHOPHYSIOLOGICAL MECHANISMS

The pathophysiological mechanisms underlying brain tumor development in young populations involve remarkably complex interactions between genetic alterations, environmental exposures, developmental factors, and immune surveillance mechanisms.[21] Recent molecular studies have identified recurrent mutations and chromosomal abnormalities characteristic of specific tumor subtypes in adolescents and young adults, including BRAF mutations in pilocytic astrocytomas and IDH mutations in diffuse low-grade gliomas.[21]

The developmental windows of exposure appear critical to understanding brain tumor etiology, with evidence suggesting that exposures occurring in utero or during early childhood may have disproportionate effects on malignant transformation through effects on critical periods of neural progenitor proliferation and differentiation.[22] Gene-environment interactions represent a crucial but incompletely characterized aspect of brain tumor etiology, with preliminary evidence suggesting that genetic predisposition combined with specific environmental exposures may confer substantially elevated risk exceeding the sum of individual exposures.[23]

DIAGNOSTIC ADVANCES AND BIOMARKER DISCOVERY



Emerging diagnostic modalities and biomarker discovery represent promising avenues for earlier detection and improved risk stratification in young populations with considerable potential for substantially improved clinical outcomes.[24] Advanced neuroimaging techniques including highresolution magnetic resonance imaging with advanced sequences, positron emission tomography imaging, and spectroscopy have dramatically enhanced the sensitivity and specificity of brain tumor detection compared to conventional imaging approaches.[24]

Molecular biomarkers including circulating tumor DNA, exosome-derived biomarkers, and tumor microenvironment assessments offer considerable potential for noninvasive monitoring and early recurrence detection in brain tumor survivors through real-time biological sampling.[25] Implementation of artificial intelligence-assisted image analysis in routine clinical care may improve diagnostic sensitivity and specificity while reducing interobserver variability and enabling more precise characterization of tumor heterogeneity and prognosis.[25]

PROTECTIVE FACTORS AND PREVENTION STRATEGIES

Nutritional and Lifestyle Interventions

Modifiable protective factors and lifestyle interventions represent promising approaches for brain tumor prevention in young populations through evidence-based strategies grounded in epidemiological evidence.[26] Maternal supplementation with vitamins and folic acid during pregnancy represents a low-risk, potentially high-benefit intervention that warrants recommendation to women of childbearing age, particularly those with family history of brain tumors or genetic predisposition.[26]

Consumption of fruits and vegetables rich in antioxidants and phytonutrients, consistent with established cancer prevention guidelines, may offer protective effects against brain tumor development through mechanisms involving oxidative stress reduction and enhanced immune surveillance.[27] Physical activity and healthy body weight maintenance, established protective factors against many malignancies, represent reasonable recommendations for young populations seeking to reduce cancer risk through modifiable lifestyle factors with additional well-documented cardiovascular and metabolic benefits.[27]

Immunological Mechanisms

Atopic conditions and allergic diseases paradoxically associated with protective effects against glioma development have prompted investigation into immunological mechanisms potentially exploitable for preventive interventions and drug development.[28] These associations suggest that enhanced immune surveillance related to atopic responses may provide protection against malignant transformation, though mechanistic understanding remains incomplete.

Reduction of pesticide exposures through consumption of organic produce where feasible and avoidance of unnecessary household pesticide applications represent practical approaches to minimizing exposure to identified environmental risk factors with minimal lifestyle disruption.[29] Limiting maternal coffee consumption and consumption of processed cured meats during pregnancy, based on identified epidemiological risk associations, represent potentially beneficial dietary modifications with minimal adverse effects and other established health benefits.[29]

FUTURE PERSPECTIVES AND EMERGING DIRECTIONS

Genomic and Precision Medicine Approaches

The future of brain tumor risk assessment and prevention in young populations will likely be shaped by converging advances in genomic technologies, environmental epidemiology, and precision medicine approaches enabling increasingly nuanced characterization of individual and population-level risk.[1] Integration of high-throughput genomic sequencing with comprehensive environmental exposure assessment in prospective birth cohort studies represents a paradigm shift that could illuminate gene-environment interactions currently undetectable through traditional case-control designs.[1]

Emerging evidence suggesting the importance of critical developmental windows of exposure—particularly in utero and early childhood periods—suggests that longitudinal biomarker assessment in pregnancy cohorts and newborn screening programs may facilitate identification of high-risk individuals amenable to early intervention strategies.[30] Advancement in neuroimaging technology and biomarker development offers considerable promise for earlier detection of pre-malignant lesions and incipient tumors in young populations, potentially shifting the therapeutic landscape from treatment of symptomatic disease toward identification and management of precursor lesions.[31]

Liquid Biopsy and Monitoring Strategies

Molecular subtyping of brain tumors using liquid biopsy approaches, including circulating tumor DNA and exosome-derived biomarkers, could revolutionize non-invasive monitoring strategies and enable assessment of therapeutic response with unprecedented temporal resolution and specificity.[31] The identification of modifiable environmental risk factors, particularly pesticide and herbicide exposures, creates opportunities for primary prevention interventions through policy reform and behavioral modification strategies targeting high-risk populations.[32]

Health Systems and Equity Reform

Addressing persistent healthcare disparities through health systems reform, insurance policy modifications ensuring equitable access to advanced diagnostic imaging and neurosurgical expertise, and culturally tailored educational programs will be essential to achieving equitable outcomes across diverse populations.[33] Development of community-based participatory research approaches that genuinely engage young populations and their families in research design and implementation may enhance recruitment into prospective studies and improve the generalizability of findings to populations historically underrepresented in neuro-oncology

research.[33]

Precision prevention frameworks that integrate genetic predisposition testing, environmental exposure assessment, and biomarker surveillance offer promise for developing individualized risk profiles and tailored prevention strategies applicable to identified high-risk populations.[34]

CONCLUSION

Brain tumors in young populations remain a critical public health concern marked by complex epidemiology, limited understanding of causation, and persistent disparities in outcomes. While ionizing radiation is the only firmly established environmental risk factor, emerging evidence suggests that exposures such as childhood or parental pesticide contact, maternal diet, and certain occupational environments may influence susceptibility. Protective factors—including maternal vitamin use, healthy dietary patterns, and atopic conditions—highlight the significant potential for prevention through targeted behavioral and environmental interventions. At the same time, global and demographic variations in incidence and survival, especially among Black and Hispanic young adults, emphasize deep inequities rooted in limited access to advanced diagnostics, specialized care, and timely treatment.

Looking ahead, rising absolute case numbers driven by population growth make it essential to strengthen healthcare systems and research capacity worldwide. Improving diagnostic infrastructure, particularly in resource-limited regions, could reduce delays and reveal more accurate epidemiological patterns. Future priorities include large, integrated studies examining gene–environment interactions, as well as innovations in biomarker-based surveillance and AIenhanced imaging for earlier detection. Ultimately, reducing the burden of brain tumors in young populations will require coordinated action across research, clinical practice, public health policy, and community engagement to ensure equitable access to prevention, early diagnosis, and effective treatment.

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