PREVALENCIA DEL LABIO Y PALADAR HENDIDO POR EFECTOS DE LA RADIACIÓN EN HIROSHIMA, NAGASAKI, CHERNOBYL

Revisión Narrativa

Gisell Daniela Anaya Herrera
Silvia Fernanda Ariza Acuña

Universidad el Bosque
Programa de Odontología- Facultad de odontología
Bogotá DC. Diciembre 2021

Hoja de identificación

Universidad	El Bosque
Facultad	Odontología
Programa	Odontología
Título:	Prevalencia del labio y paladar hendido por efectos de la radiación en Hiroshima, Nagasaki, Chernobyl
Grupo de Investigación:	Unidad de Manejo Integral de Malformaciones Craneofaciales UMIMC
Línea de investigación:	Revisión Narrativa/revisión tematica
Tipo de investigación:	Pregrado
Estudiantes:	Gisell Daniela Anaya Herrera Silvia Fernanda Ariza Acuña
Director	Dra. Carolina Tellez
Codirector y/o Asesor metodológico	Dra. Marta Rojas

DIRECTIVOS UNIVERSIDAD EL BOSQUE

OTTO BAUTISTA GAMBOA	Presidente del Claustro
JUAN CARLOS LÓPEZ TRUJILLO	Presidente Consejo Directivo
MARIA CLARA RANGEL GALVIS	Rector(a)
RITA CECILIA PLATA DE SILVA	Vicerrector(a) Académico
FRANCISCO JOSÉ FALLA CARRASCO	Vicerrector Administrativo
MIGUEL OTERO CADENA	Vicerrectoría de Investigaciones.
CRISTINA MATIZ MEJÍA	Secretaria General
JUAN CARLOS SANCHEZ PARIS	División Postgrados
MARIA ROSA BUENAHORA TOVAR	Decana Facultad de Odontología
MARTHA LILILIANA GOMEZ RANGEL	Secretaria Académica
DIANA MARIA ESCOBAR JIMENEZ	Director Área Bioclínica
ALEJANDRO PERDOMO RUBIO	Director Área Comunitaria
JUAN GUILLERMO ÁVILA ALCALÁ	Coordinador Área Psicosocial
INGRID ISABEL MORA DIAZ	Coordinador de Investigaciones Facultad de Odontología
IVAN ARMANDO SANTACRUZ CHAVES	Coordinador Postgrados Facultad de Odontología

"La Universidad El Bosque, no se hace responsable de los conceptos emitidos por los investigadores en su trabajo, solo velará por el rigor científico, metodológico y ético del mismo en aras de la búsqueda de la verdad y la justicia"

GUÍA DE CONTENIDO

Resumen

PREVALENCIA DEL LABIO Y PALADAR HENDIDO POR EFECTOS DE LA RADIACIÓN EN HIROSHIMA, NAGASAKI, CHERNOBYL

Antecedentes: Las fisuras orofaciales de tipo labio paladar hendido representan una entidad multifactorial que afecta ampliamente a la población en general, entre 1 a 4 de 1000 nacidos vivos alrededor del mundo, rango que oscila dada la variabilidad de las características personales. La radiación ionizante ha sido ampliamente implicada en la teratogenia de diferentes patologías, entre las cuales destaca las malformaciones craneofaciales, dada su capacidad de alterar los enlaces moleculares y el ADN en especial, en la vida intrauterina donde la fragilidad de la formación tisular, celular y molecular se encuentran en proceso de fusión y crecimiento. La formación de estas patologías depende del nivel de irradiación y la etapa del desarrollo embrionario en el que se produce la exposición. En esta revisión bibliográfica se estudiaron los efectos producidos por tres grandes eventos radioactivos en la historia, las bombas atómicas en Hiroshima y Nagasaki y el accidente de la planta nuclear de Chernóbil, dos eventos en los cuales las poblaciones afectadas presentaron niveles significativamente altos de radiación ionizante con respecto a la población en general no afectada. **Objetivo:** Recopilar e integrar la información sobre la radiación como factor etiológico de las malformaciones craneofaciales y más específicamente de tipo labio paladar fisurado en poblaciones afectadas por tres eventos históricos asociados a radiación, como fueron las bombas atómicas en Hiroshima y Nagasaki y el accidente nuclear en Chernobyl, y sus efectos en la población, por medio de una revisión narrativa. **Materiales y métodos**: a partir de las variables establecidas se realiza la búsqueda en las bases de datos EMBASE Y PUBMED arrojando resultados de 31 y 97 artículos respectivamente de los cuales finalmente son escogidos 16 artículos. **Conclusiones:** La posibilidad de identificar cambios teratogénicos, que correspondan con labio paladar hendido en las poblaciones expuestas es casi nula, dado a que los análisis epidemiológicos realizados no permiten una asociación concreta que controle la amplia gama de variables que se asocia a dicha disrupción. Sin embargo, la prevalencia observada en cuanto a las poblaciones más afectadas por la ola radioactiva no reporta un aumento significativo en el número de casos esperados de esta malformación.

Palabras clave: Labio hendido con o sin paladar hendido, accidente de Chernobil, bombas atómicas, Hiroshima y Nagasaki

Abstract

PREVALENCE OF CLEFT LIP AND PALATE DUE TO RADIATION IN HIROSHIMA, NAGASAKI AND CHERNOBYL

Background: Cleft lip and palate represent a condition affecting general population between on and four of every 1000 newborns around the world varying depending on personal characteristics. Ionising radiation has been implicated in different pathologies due to its capacity to alter molecular bonds and DNA, especially in the womb where tissue, cellular and molecular formation fragility are in a process of fusion and growth. The formation ofsaid pathologies depends on the radiation level and development stage that receives the exposure. In the present review the effects produced by three major radioactive events: Hiroshima and Nagasaki atomic bombs and the leak of the nuclear plant in Chernobyl are studied. In two of these, the affected population presented significantly high levels of ionising radiation compared to the rest unaffected population. **Objective:** To collect and integrate information by means of a narrative review regarding radiation as an aetiological factor of craniofacial malformations, mainly cleft lip and palate, in populations affected in the three mentioned events. **Materials and methods:** A search was performed in EMBASE and PUBMED yielding 31 and 97 articles respectively from which 16 were selected. **Conclusions:** The possibility of identifying teratogenic changes corresponding to cleft lip and palate in the exposed populations is almost null because the epidemiological analyses do not allow a concrete association which controls the wide spectrum of related variables. However, the prevalence observed in the most affected by the radiation did not report a significant increase in the number of cases intended with this malformation.

Key words: cleft lip and palate, Chernobyl accident, atomic bombs, Hiroshima and Nagasaki

Introducción

Las malformaciones craneofaciales son algunas de las patologías más prevalentes entre las alteraciones congénitas. Se pueden distinguir dos grandes grupos: las producidas por un cierre precoz de las suturas del esqueleto craneofacial, las craneosinostosis y faciocraneosinostosis, y las neurocrestopatías, como los síndromes de primer y segundo arcos branquiales y las fisuras orofaciales, entre las cuales se encuentra la fisura labiopalatina (1).

Las hendiduras orofaciales hacen referencia a una macro disrupción de la configuración facial normal, que involucra un cambio indeseado en la estructura, forma y funcionalidad durante la ontogénesis, en el periodo embrionario. Estas anomalías del desarrollo tienen una base multifactorial en la región del esbozo cefálico, los arcos viscerales y las fisuras o surcos que los limitan a causa de una ausencia de tejido (2).

Estas malformaciones, particularmente el labio paladar hendido, son un problema importante de salud pública, que afecta a 1 de cada 500 a 1000 nacimientos en todo el mundo, cifra que varía ampliamente según el origen geográfico, grupos raciales y étnicos y el nivel socioeconómico, representando una situación de gran trascendencia para la sociedad, la vida del individuo y la de sus familias (3).

Del total de las hendiduras faciales, las hendiduras de labios representan del 20 al 30%; las hendiduras labio palatinas, del 30 al 50% y las hendiduras de labio y/o paladar se presenta en 1 de cada 1,000 nacimientos. La incidencia y la distribución geográfica de las hendiduras orofaciales, varían en todo el mundo debido a las diferencias en la prevalencia de nacimientos, así como a las deficiencias en el registro de nacimientos y sistemas de vigilancia de defectos congénitos, particularmente en muchas partes del mundo en desarrollo. Los nativos americanos muestran las mayores incidencias con 3.74 por 1000 nacidos vivos, mientras que entre los europeos la incidencia es de 1: 600 a 1: 700 nacidos vivos. La incidencia es alta entre los asiáticos (0.82-4.04 por 1000 nacidos vivos), intermedia en caucásicos (0.9-2.69 por 1000 nacidos vivos) y baja en africanos (0.18-1.67 por 1000 nacidos vivos) (4).

En cuanto a la etiología, es de origen multifactorial, ya que tanto los genes como los factores ambientales o los hábitos de la madre pueden contribuir a su presencia, así como también la interacción de los mismos, pues en algunos casos se interrelacionan, dando origen a una alteración en el proceso de formación intrauterina del feto. Aunque diversos estudios muestran diferentes factores que puedan asociarse como causantes, en general, ninguno se confirma asociado a la causalidad del labio paladar hendido. Circunstancias, tales como el factor socioeconómico, el estrés, la ocupación, la edad de los padres y la exposición a radiación, químicos, drogas o medicamentos como posibles teratógenos, se han estudiado, sin resultados contundentes de los diferentes autores (5).

La exposición a teratógenos, puntualmente a radiación ionizante, ha sido señalada como causa de este tipo de malformaciones. Esta se constituye como un flujo de energía en forma de partículas atómicas y subatómicas u ondas electromagnéticas que son capaces de liberar electrones de un átomo, haciendo que el átomo se cargue o ionice. A través del

desplazamiento de electrones u ionización, la radiación ionizante altera efectivamente los enlaces moleculares. En los organismos vivos, dicha interrupción puede causar daños extensos a las células y del material genético (6).
Se ha informado una asociación espacio temporal con las diferentes contaminaciones de materiales radioactivos como el uranio, carburo de boro, óxido de europio, erbio, aleaciones de circonio y grafito con el desarrollo de hendiduras faciales (7).
La exposición a radiaciones y/o fertilizantes durante el período de organogénesis incrementa el riesgo de presentar hendiduras faciales. La radiación ionizante actúa como un daño directo al embrión por la fragilidad de las células y tejidos en procesos de formación y crecimiento. Aunque los mecanismos celulares de la teratogénesis inducida por radiación no se comprenden completamente, se cree que varían desde lesiones subletales que afectan la diferenciación y las interacciones celulares, hasta efectos sobre las tasas de proliferación y muerte celular. Se ha demostrado que la radiación produce una permeabilidad alterada de las estructuras intracelulares y la liberación de enzimas, es decir, la ruptura de las membranas lisosómicas, y sugiere que esto se debe a la formación de peróxido de lípidos (8).
La frecuencia de anomalías físicas que pueden estar relacionadas con la radiación se identifica en mayor relación con la exposición intrauterina del feto, debido a que los radionucleidos liberados pueden causar mutaciones del ADN genómico y puede generar un efecto teratogénico en los tejidos durante el desarrollo embriológico (7). Se cree que muchos de los efectos de la radiación en los embriones en desarrollo tienen una dosis umbral segura del orden de 10 o 50 mSv (milisievert), o incluso más alta y sobre esta base, las malformaciones deben ser raras, incluso en áreas muy contaminadas (9).

Las personas están expuestas a diario tanto a la radiación de origen natural o producida por el hombre. La radiación natural proviene de muchas fuentes, como de los más de 60 materiales radiactivos naturales presentes en el suelo, el agua y el aire. La exposición humana a la radiación proviene también de fuentes artificiales que van desde el uso médico de la radiación para fines diagnósticos o terapéuticos, hasta la generación de energía nuclear (10). Las bombas atómicas en Hiroshima y Nagasaki en 1945 (Japón), el accidente de la planta nuclear en Chernóbil en 1986 (Unión Soviética) y las pruebas nucleares en el desierto de Nevada, Alaska, Colorado, Misissipi y Nuevo México, Estados Unidos, así como Francia haciendo pruebas nucleares en Argelia (Africa), zona de pruebas en Semipalatinsk (Kazajistan), son ejemplos de exposición a actividad radioactiva en diferentes partes del mundo que posiblemente afectan a los seres vivos, provocando contaminación por radiación. Producto de esto se observan dosis efectivas, niveles que reciben los órganos y tejidos en relación con el daño potencial que pueden causar en ellos, que superan los rangos de la seguridad, en un rango de más o menos 0.005 Gy(gray), equivalentes a 5 MSV, a 2 GY (2000 MSV), dependiendo de la cercanía a la zona de exposición (11). Y aunque transcurrido el tiempo, de ellos solo quedan lugares altamente contaminados e irradiados, también quedan grandes incertidumbres de las consecuencias en la salud de las personas que fueron afectadas directamente y aquellas poblaciones afectadas por la lluvia radiactiva. Aunque aún sea muy

debatido, se ha relacionado diversas secuelas en la salud humana como lo es el aumento de la prevalencia de cáncer, muerte infantil, defectos congénitos como microcefalia, anencefalia, labio y paladar hendido, entre otras (12).

Conocer la exposición, permite determinar los posibles efectos ante la contaminación radiactiva, saber qué consecuencias, si es que las tiene, en la reproductividad, en el desarrollo y crecimiento embriológico del feto, determinando si hay o no una relación causal entre la radiación y las hendiduras faciales, o el labio paladar hendido (13).

Según los reportes de la literatura hay una marcada incongruencia entre si hay o no una verdadera relación causal entre la radiación y el desarrollo de labio paladar hendido. Según Weigelt, E. y Scherb, H en sus estudios describen un aumento en la prevalencia de las hendiduras faciales, labio y paladar hendido, después del accidente de Chernobyl al igual que Zieglowski U. Hemprich, mientras que Nakamura, N. en su revisión, no encuentra tal relación causal, ni aumento de casos de hendiduras faciales en las explosiones atómicas de Hiroshima y Nagasaki.

El propósito de la presente revisión narrativa es recuperar la información más relevante y actualizada sobre la epidemiología de malformaciones craneofaciales de tipo labio y paladar fisurado no sindrómico y su asociación con la radiación como factor etiológico, en zonas de gran exposición a dicho agente como pueden ser Hiroshima, Nagasaki, Chernobyl y las áreas de pruebas nucleares en el mundo

Marco teórico

Estrategias de búsqueda

Se definen las siguientes variables de búsqueda

Variables dependientes:

- **Labio y paladar hendido:** malformación craneofacial que se describe como una macro disrupción de la configuración facial normal que involucra un cambio en la estructura y funcionalidad del esbozo cefálico durante la ontogénesis en el periodo embrionario (1).
- **Malformaciones craneofaciales:** anomalías congénitas en la forma y configuración de las estructuras anatómicas del área de la cabeza, cara y cuello (15).

Variables independientes:

- **Radiación ionizante:** flujo de energía en forma de partículas atómicas y subatómicas u ondas electromagnéticas que es capaz de liberar electrones de un átomo, haciendo que el átomo se cargue o ionice (6).

Se consultaron las siguientes bases de datos: EMBASE Y PUBMED

Se utilizaron las siguientes palabras clave: Abnormalities craniofacial, Abnormality Craniofacial, Craniofacial Abnormality, Cleft lip with or without cleft palate, Cleft lip palate, ionizing radiation, Chernobyl accident, Hiroshima, Nagasaki, atomic bomb, risk factor, radiation, ionizing, radiation effects, Chernobyl nuclear accident, epidemiology, Congenital malformations, Abnormalities Radiation Induced, Radiation-Induced Abnormalities, Abnormality Radiation-Induced.

Se buscaron los siguientes tipos de estudio: Metaanálisis, estudios de casos y controles, estudios de cohorte, estudios de prevalencia.

Se utilizaron las siguientes estrategias de búsqueda:

1: Congenital malformations

#2: (Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR (Radiation-Induced Abnormality)

#3: Hiroshima

#4: Nagasaki

#5:Accident radiation

EPIDEMIOLOGY

#6: #1 AND #2

#7:#6 AND #3 AND #4

#8:#6 AND #5

Entorno clínico del labio paladar hendido

Las malformaciones craneofaciales integran un grupo diverso de anomalías congénitas de amplia variedad y heterogeneidad, entre ellas, se destacan como las de mayor frecuencia el labio y paladar hendido, en relación a la región de cabeza y cuello. Estas anomalías hacen referencia a una macro disrupción de la configuración facial normal que involucra un cambio indeseado en la estructura y funcionalidad durante la ontogénesis en el período embrionario, son anomalías del desarrollo de base multifactorial en la región del esbozo cefálico, sus arcos viscerales y las fisuras o surcos que los limitan a causa de una falta de formación de células y tejidos (2,15).

El labio paladar hendido afecta a aproximadamente 1 de 500 a 1000 nacidos vivos en el mundo, esta cifra presenta alta variación según el origen geográfico, los grupos raciales y étnicos, así como a la exposición ambiental y el nivel socioeconómico, demostrando la influencia multifactorial de dicha patología. La incidencia y la distribución varía debido a las diferencias en la prevalencia de nacimientos, así como a las deficiencias en el registro de nacimientos y sistemas de vigilancia de defectos congénitos, particularmente en muchas partes del mundo en desarrollo. Los nativos americanos muestran las mayores incidencias con 3.74 por 1000 nacidos vivos, mientras que entre los europeos la incidencia es de 1: 600 a 1: 700 nacidos vivos. La incidencia es alta entre los asiáticos (0.82-4.04 por 1000 nacidos vivos), intermedia en caucásicos (0.9-2.69 por 1000 nacidos vivos) y baja en africanos (0.18-1.67 por 1000 nacidos vivos) (4).

Las revisiones de literatura informan que en cuanto a la aparición clínica del labio paladar hendido se refleja una tendencia a ser unilateral y a ocurrir con mayor frecuencia en el lado izquierdo. Los resultados de un estudio publicado en la base de datos internacional de las fisuras perinatales orales típicas mostraron que el 30.2% del grupo con labio paladar hendido tienen hendidura bilateral y el 69.8% a hendidura unilateral. Así mismo los defectos se presentaron en un 41,1% en el lado derecho y 58.9% en el lado izquierdo. Hendidura labial con o sin hendidura palatina se observó con mayor frecuencia en hombres; sin embargo, la hendidura palatina se observó con mayor frecuencia en mujeres. Van den Akker (25) y Stoll (26) descubrieron que los niños parecen estar más afectados en casos bilaterales. Por otra parte, Meskin y Henriksson informaron que las niñas tenían mayor incidencia bilateral de labio fisurado que niños (15,16).

La formación embriológica y morfogenética del labio y el paladar involucra el proceso frontonasal y el proceso maxilar, se inicia por la fusión de las prominencias nasales con las maxilares, de forma tal, que este proceso comienza con las apófisis nasales mediales y laterales, que en un principio están delimitadas por surcos, pero que posteriormente crecerán en altura alrededor de la placoda olfatoria formando una depresión llamada saco nasal. Junto a este crecimiento los epitelios de las apófisis nasales laterales y medial se fusionan, con lo

cual forman un puente entre ellas, que posteriormente se disolverá para ser reemplazado por la producción de células mesenquimatosas que se encargan de construir una unión homogénea este proceso inicia en el suelo de los sacos nasales y progresa a modo de cremallera sellando dicho surco; simultáneamente se fusionan de la misma forma los procesos nasales mediales, dando origen al proceso intermaxilar que se habrá unido al igual que los primeros descritos por el crecimiento medial de los procesos maxilares que promueven el empuje de las apófisis nasales mediales y laterales, que por medio de la migración mesodérmica y la transformación epitelial, producen una unión fuerte entre las estructuras que formarán la cara. De esta forma y hasta este momento se evidencia la formación del filtrum nasal, del tubérculo labial y el paladar primario por parte del proceso intermaxilar y adicionalmente las alas de la nariz por la fusión de los procesos nasales. La morfodiferenciación del paladar y de las porciones laterales de los labios continúa de forma simultánea a estas, pues al mismo tiempo los procesos maxilares, específicamente los segmentos inferiores o apófisis palatinas que inicialmente se ubican lateralmente a la lengua, la cual, con su desarrollo empieza a descender hasta tomar una posición caudal, induciendo un cambio de crecimiento en las apófisis palatinas que venían con un crecimiento vertical lateral a la lengua a una proliferación de forma horizontal, hasta la fusión de la izquierda con la derecha, resultando en la formación del paladar secundario. Este paladar secundario se unirá al paladar primario por medio del agujero nasopalatino, que, además, de los segmentos laterales de los labios producto de la fusión, darán como resultado los procesos maxilares superiores. En las hendiduras labio palatinas estos momentos de fusión o unión de las estructuras embriológicas mencionadas anteriormente no se logra, ya sea por ausencia de la formación del mesénquima, del epitelio, de la perpetuación del epitelio, migración insuficiente del mesodermo y/o separaciones del tejido en los surcos. El lugar de la falla, determinará la fenotipización de la anomalía craneofacial que presentará el niño (18).

Estas irrupciones en los procesos normales embriológicos poseen diferentes factores causales, pero, debido a su heterogeneidad genética, salida de los patrones de herencia mendeliana, la falta de herramientas genómicas y la necesidad de grandes bases de datos, impide los progresos en el avance de la comprensión de la etiología genética no sindrómica del labio-paladar hendido. El reciente desarrollo de enfoques innovadores para la fenotipificación y potentes herramientas genómicas son diversos y heterogéneos, a lo largo de los años podemos decir que el factor más estudiado es aquel que involucra el genoma, los genes, proteínas y moléculas están asociados al fallo de la proliferación y diferenciación de los tejidos, entre los cuales según Michael J, Dixon y colaboradores (17) están el gen IRF6 (Factor regulador de interferón) Investigaciones recientes han demostrado que los ratones con mutaciones de IRF6 exhiben una epidermis hiperproliferativa que no puede experimentar diferenciación terminal, lo que conduce a múltiples adherencias epiteliales que pueden ocluir la cavidad oral y provocar paladar hendido. Estos resultados demostraron que IRF6 es una clave determinante en la proliferación y diferenciación de queratinocitos. Las investigaciones posteriores indicaron que IRF6 también juega un papel clave en la formación del periderma

oral, cuya regulación espacio-temporal es esencial para garantizar la adhesión palatal adecuada (17).

Otro gen que mencionan es el MAFB. Se demostró que la expresión de MAFB es fuerte en el epitelio de los procesos palatinos y en el epitelio del borde medial durante la fusión palatina, adicionalmente codifica la transcripción de la cremallera de leucin. En estudios realizados genómicos se identifican unas variaciones en dicho gen en personas con labio- paladar hendido. El gen VAX1 también presenta una fuerte asociación pues estaba sobre expresado en casos de labio paladar hendido. VAX1 codifica un regulador de transcripción con un dominio homeobox de unión al ADN. Al igual que en los humanos, las mutaciones de pérdida de función en el gen homeobox Msx1 provocan paladar hendido en ratones. Msx1 es un objetivo posterior de la señalización de BMP en varios sitios embrionarios. Msx1 es necesario para la expresión de Bmp4 y / o Bmp2. En ratones, la pérdida de la función del receptor Bmp tipo I (Bmpr1a) en los primordios craneofaciales resultó en hendidura labial con o sin hendidura palatina, mientras que la deficiencia de Bmp4 resultó en labio hendido solo. Esto muestra que la señalización Bmp tiene funciones distintas en el desarrollo del labio frente al paladar secundario. En el contexto de la deficiencia de Bmp4, todos los embriones mutantes de Bmp4 exhibieron labio hendido bilateral en E12, pero solo el 22% todavía mostró labio hendido en E14 lo que sugiere algún mecanismo de reparación en el útero (17).

Dichos factores genéticos van de la mano, con la interacción que se realiza con los factores medio ambientales y los hábitos de la madre en este caso. Segun Michael J, Dixon y colaboradores(17) el tabaquismo materno se ha asociado con un mayor riesgo de labio paladar hendido y diferentes metanálisis apoya firmemente una odds ratio global (OR) para tener labio-paladar hendido de 1.3 en los hijos de madres fumadoras. La exposición al tabaquismo materno durante el período peri-concepcional plantea un aumento de la posibilidad de que los genes en ciertas vías metabólicas pueden desempeñar un papel en el desarrollo de esta patología. Específicamente, los marcadores en el GSTT1 (Glutatión theta S-transferasa) o NOS3 (óxido nítrico sintasa 3), genes que parecen factores de riesgo para el desarrollo de hendiduras en presencia de tabaquismo materno. Estos resultados proporcionan evidencia de que las interacciones genético-ambientales son importantes para el desarrollo de labio-paladar hendido. Además, algunos específicos teratógenos potenciales que se han informado incluyen ácido retinoico, fenitoína y ácido valproico. Otros factores de riesgo propuestos incluyen diversas exposiciones laborales y químicas, hipertermia, estrés, obesidad materna, suplementos de hormonas orales, radiación ionizante e infección materna (17).

Los factores nutricionales, como la deficiencia de ácido fólico, sugiere un mayor riesgo de incidencia de fisura labio-palatina, basado tanto en estudios observacionales y ensayos de intervención utilizando un suplemento de folato para prevenir recurrencias en las familias. Sin embargo, los estudios de la suplementación con vitamina con ácido fólico siguen siendo controvertidos y estudios recientes de los niveles de anticuerpos contra el receptor de folato

no encontraron una asociación. Además, los programas de fortificación de alimentos utilizando ácido fólico han mostrado disminuciones detectables en las tasas de hendiduras en algunos, pero no en todos los estudios (17).

En cuanto a los diferentes cuadros clínicos en los cuales se puede presentar las hendiduras faciales encontramos las hendiduras labiales, estas aparecen en la zona del borde del filtrum nasal, pueden presentarse como unilaterales y bilaterales y a su vez cada una de estas pueden ser parciales o totales. Las fisuras labiales unilaterales parciales se identifican como muescas en el borde del bermellón labial y la piel del labio. La fisura unilateral total labial, se presenta como una fisura que abarca hasta la entrada nasal, la cual se encuentra desviada lateralmente, en esta presentación el ala de la nariz no presenta inserción con el tabique nasal. Las fisuras labiales bilaterales poseen las mismas características de las anteriormente mencionadas en cuanto a si son parciales o totales, pero se diferencian en la apariencia del labio superior dividido en tres partes por la doble hendidura a ambos lados (2,15).

Otro de los cuadros clínicos que se puede presentar son las hendiduras labio alveolares, en estas, la apófisis alveolar está fisurada hasta el conducto nasopalatino, de modo que falta toda la porción del suelo nasal de un paladar intacto, en las que se presentan unilateralmente la fisionomía nasal se encuentra desfigurada, así como también se presenta una desviación del septum nasal hacia el lado sano. En la presentación bilateral la premaxila está aislada y solo se encuentra fijada al tabique nasal por el vómer (15).

En las hendiduras labio alveolo palatinas, se encuentra fisurado el labio, el maxilar superior y el paladar, de forma tal que no existe suelo nasal óseo en el lado fisurado. El tabique nasal y el vómer se encuentran desplazados al lado sano, por lo cual se observa una asimetría del tercio medio de la cara. En cuanto a las fisuras labio alveolo palatinas bilaterales totales se describen como la presentación más grave de este tipo de malformación craneofaciales pues hay una ausencia bilateral del suelo nasal óseo, la premaxila se encuentra aislada y unida por el vómer con el tabique nasal y puede presentar movimiento, además de encontrarse protruida o alineada con la arcada alveolar, la columnela es poco pronunciada lo que lleva a una forma aplanada de la nariz (2).

Las fisuras palatinas aisladas se presentan en su totalidad de forma bilateral pues embriológicamente involucra una ausencia de selle de la línea media, por lo que su alteración resulta involucrando a ambos lados y no existe unión con el vómer. Este tipo se puede presentar como total o parcial; la primera iniciará desde el final de la premaxila hasta la úvula, que puede verse comprometida en la fisura, y en las parciales entre la salida del orificio nasopalatino hasta el borde del paladar duro. Las fisuras velares son otra forma de presentación en la cual el defecto embrionario se limita al velo del paladar blando, incidiendo desde el borde posterior del paladar duro hasta la úvula (15).

Otra variación de las hendiduras como anomalía craneofacial son las fisuras submucosas en las que clínicamente a primera vista no se evidencia una separación, ni una macrodisrupcion

de la forma normal facial, pero se puede identificar una línea como vestigio de la unión de los tejidos cutáneos, sin embargo, debajo de esta capa en la fase subcutánea se encuentra la ausencia de unión ósea y/o muscular (2).

En cuanto a lo que podemos decir de los posibles trastornos del desarrollo maxilofacial asociados a las hendiduras labio-palatinas, se ha identificado un potencial de crecimiento normal, adicionalmente, se puede observar la presencia de disgnatias limitadas a la zona fisurada, mordida cruzada uni o bilateral, espacio intermolar aumentado y malposiciones dentarias en la zona inmediata la hendidura. En las fisuras unilaterales, el maxilar superior suele ubicarse retrognático en relación con la base de cráneo, en las fisuras bilaterales suele estar por el contrario prognático después del nacimiento. En cuanto a la mandíbula puede que en la mayoría de los casos incide en una dimensión normal, pero también puede ocurrir una dimensión más corta y retrognatica, ángulo mandibular engrosado y un aumento de la altura facial inferoanterior (2,15).

Otros trastornos asociados a las hendiduras cranefoaciales involucran el ámbito psicológico, la afectación de sus medios de comunicación y expresión como lo son la cara y el habla; se presentan características sociales reservadas, personalidad introvertida, dificultades para relacionarse, sentimientos de culpa y autoagresión. También se pueden identificar trastornos del habla, donde al interrumpir la funcionalidad del paladar en la fonación, impide la formación de una pared que interrumpa el paso del aire a la cavidad nasal desde la bucal originando una rinoglosia, que se distingue por una voz gangosa, rinolalia y una hiperrinolalia desencadenando un retraso del desarrollo del habla (2).

Los trastornos auditivos así como la enfermedades inflamatorias son frecuentemente asociados a las hendiduras craneofaciales entre los cuales están, las infecciones víricas nasales y faríngeas, bronquitis y neumonía, así como inflamaciones agudas y crónicas del oído medio debido a la anomalía que se asocia con la trompa de Eustaquio y el oído medio, sordera de conducción, como se muestra en una lesión del oído interno, tímpano seroso o mucoso además de ser respiradores orales por desviación del tabique y la fisura labial favoreciendo las infecciones de las vías aéreas superiores, unido a posibles alteraciones del calentamiento del aire, la difícil nutrición pues en esta patología el lactante se encuentra disminuido la capacidad de succión, la discapacidad de lectura y por consiguiente la disminución del coeficiente intelectual (2).

En cuanto a la rehabilitación del paciente con fisuras labio-palatinas se deben destacar dos factores importantes que van a reflejar el éxito del tratamiento integral del paciente, los cuales involucran en primer lugar un abordaje individualizado en el momento adecuado, es decir, una adecuada planeación, eligiendo el tratamiento que más se adapte a las características que presenta el paciente y en la edad adecuada para una recuperación exitosa a futuro, que debe tener en cuenta, las etapas de crecimiento por las cuales atravesará el niño. La segunda, es un abordaje interdisciplinario de la patología, donde se reintegre la estética del

paciente y la funcionalidad, además del control de las patologías a las cuales el paciente se encuentre más susceptible; así como el enfoque del trasfondo psicológico y psicosocial del paciente (2).

El tratamiento de dichas malformaciones congénitas se da a través de diferentes fases y de un acompañamiento constante a través de los años. El tratamiento primario incluye una primera fase de reconocimiento, que se debe realizar lo más pronto posible tras el nacimiento, específicamente a las dos semanas de vida, en esta fase entre el equipo interdisciplinario diseñarán el plan de tratamiento, con base en las necesidades quirúrgicas, fonoaudiológicas, pediátricas, odontológicas y psicológicas que pueda requerir el niño, fijaran la primera fecha de intervención quirúrgica en base la capacidad en la que se encuentra el niño de afrontar la anestesia y el tratamiento quirúrgico (2).

La fase quirúrgica inicial se centra en el selle de las hendiduras que presente el paciente, de forma que se obtenga unas condiciones funcionales y estéticas lo más parecidas a lo normal. La simetría y movimiento labial y nasal, un vestíbulo profundo con ausencia de perforaciones residuales, un reborde alveolar redondeado, bóveda palatina adecuada y un paladar blando con buena movilidad y suficientemente largo que permita el habla normal. Se recomienda que dicho tratamiento se realice entre los 3 y 6 meses de vida para las fisuras labiales y alveolares y a la edad de 12 a 18 años aquellas que involucran paladar blando y/o duro. (1) Hay dos tipos de procedimientos para realizar el selle de las hendiduras, Las plastias labiales o palatinas dependiendo del caso y las osteoplastias. Las primeras mencionadas se basan en una serie de técnicas que varían en cuanto al método quirúrgico pero que tienen como objetivo la remodelación del tejido que necesita ser confrontado, el levantamiento de colgajos y las sutura de los mismos, logrando un selle adecuado de las estructuras; entre estas podemos destacar las técnicas de colgajo de bipedículado de von Langenbeck, de empuje de Veau-Wardill-Kilner , doble Z plastia opuesta de Furlow, reparación palatina en dos etapas, palatoplastia libre de área cruda, palatoplastia de extensión alveolar (AEP), veloplastia intravelar, plastia de colgajos de Vomer y el colgajo miomucosal bucal entre otras. Las osteoplastias por otro lado hacen referencia a un trasplante óseo para conseguir una estabilización de los maxilares, el transplante se da injertando el tejido óseo donador en el lugar receptor y formando un sándwich de colgajo mucoperiostido interno, injerto óseo y colgajo mucoso (19).

Seguidamente se debe realizar controles con otorrinolaringología a partir de los 5 y 6 meses de edad, teniendo muy en cuenta los exámenes auditivos periódicos pues las inflamaciones e infecciones auditivas se presentan de manera habitual y deben ser tratadas, tomado medidas como la paracentesis y en caso de necesitarlo un drenaje linfático; la exploración de las adenoides y de la amígdalas también es de vital importancia pues son susceptibles a presentar engrosamientos patológicos característicos de los pacientes con hendiduras craneofaciales. Otro de las intervenciones necesarias es el tratamiento fonoaudiológico, a más tardar al tercer año de vida se debe iniciar el tratamiento del lenguaje, adicionalmente es necesario el control

periódico odontológico tanto para el control del desarrollo de caries como por el tratamiento ortodóntico y ortopédico. En cuanto al enfoque ortodóncico prequirúrgico, este se encamina a la adecuada formación de la arcada superior, preparándola para la primera intervención, además de promover una coordinación del crecimiento y la función, imitando el espacio oral fisiológico. Uno de los tratamientos ortopédicos destacados es la placa de separación oro-nasal que facilita el desarrollo normal del niño durante sus primeras etapas de vida, ayudándolo a beber, succionar, a promover la respiración nasal, separar la lengua de la zona fisurada, logra un apoyo normal en las mejillas y la lengua para la fonación entre otras. El tratamiento ortodóntico postquirúrgico es necesario en todos los casos de fisuras labio-alveolo-palatinas, se deben instaurar después del inicio de la erupción de la dentición definitiva es decir entre los 8 y 9 años, en las cuales trabajamos en las disgnatias, la erupción de dientes ectópicos, los problemas de posición de los incisivos en la región de la fisura. Finalmente se realizan intervenciones quirúrgicas secundarias que llevan a un mejoramiento principalmente estético del niño como pueden ser correcciones labiales, correcciones nasales e intervenciones para mejorar el lenguaje (2, 19).

En algunos casos es necesario la intervención de psicología para manejar la parte emocional y social del niño, pues normalmente estos aspectos se ven afectados por la disrupción de la normalidad facial a la cual se ven enfrentados, por tanto, el cambio quirúrgico debe ir acompañado de un cambio psicológico que le permita al niño mejorar su estado psicosocial, dejando atrás aquello que pudo haber marcado su crecimiento y desarrollo, afrontando una mejor relación consigo mismo y con los que lo rodean (2).

De esta forma es muy importante dilucidar qué factores nos pueden influir en el desarrollo de esta disrupción durante la formación embriológica, al conocer la importancia y la influencia que ejercen las interacciones genéticas con los factores ambientales, es imperante determinar qué aspectos, del medio ambiente natural nos afectan para la formación de las hendiduras faciales.

Contexto histórico geográfico

Con el renacer de las ciencias, la tecnología y las industrias, el ser humano tomó mano a todas sus habilidades, para desarrollar ciencias en pro de la humanidad, pero que desencadenaron desastres y daños para los seres vivos y el ambiente. Un ejemplo de ello es la energía nuclear y el desarrollo de bombas atómicas, basados en el interés por conocer la composición y la estructura de la materia.

El uso de energía nuclear, ha sido un tema muy controvertido, puesto que posee tanto ventajas como desventajas, y que, por los acontecimientos de la historia, esta ha dejado más huellas negativas en la humanidad y el medio ambiente, por su mal uso. Los incidentes ocurridos en Hiroshima y Nagasaki y el accidente en Chernobyl, muestran cómo ante un mundo que se desvive por crear armas nucleares más grandes y más potentes, queda la resistencia y el recuerdo: la historia ha mostrado que el uso de la energía nuclear de manera irresponsable trae tragedia y destrucción medioambiental (20).

En pleno siglo XX las ciudades de Hiroshima y Nagasaki fueron bombardeadas por orden de Harry Truman, presidente en ese entonces de los Estados Unidos, el 6 y 9 de agosto de 1945, poniendo punto final a la Segunda Guerra Mundial (20).

Hiroshima (Figura 1), es la capital de la prefectura de Hiroshima, en la región de Chūgoku, al oeste de Japón. La ciudad es casi totalmente llana y se encuentra levemente elevada sobre el nivel del mar. Por su parte Nagasaki (Figura 1) es la capital y la mayor ciudad de la prefectura de Nagasaki, ubicada sobre la costa sudoeste de Kyūshū en Japón (21).

Figura 1: Mapa de Japón (27)

Lo que tienen en común estas dos ciudades Japonesas, es que aquí ocurrieron hechos que marcaron la historia de todos los habitantes del mundo, sucesos lamentables que dejaron al descubierto el mal uso del poder del hombre adquirido por medio de la tecnología.

Finalizando la Segunda Guerra Mundial el 6 de agosto de 1945, la ciudad de Hiroshima padeció el primer bombardeo atómico de la historia por parte del ejército de los Estados Unidos. La acción de la bomba destruyó la ciudad casi en su totalidad; de 450.000 habitantes acabó con la vida de 120.000 personas aproximadamente y dejó heridas a otras 70.000. El bombardeo inició alrededor de las 8:15 de la mañana, al mando del piloto Paul W Tibbets, quien lanzó sobre la ciudad, la bomba Little boy de uranio, desde el avión Enola Gay de las fuerzas Aéreas de Estados Unidos. En el instante del impacto, un gran ruido marcó la explosión seguido de un resplandor que iluminó el cielo. Minutos después se apreció en el ambiente una columna de humo con más de un kilómetro de altura, un color gris morado y una temperatura aproximada a los 4000 grados centígrados. Una temperatura tan extremadamente alta que llegó a ocasionar un fenómeno conocido como el efecto sombra o sombra radioactiva que se produce en explosiones nucleares por el intenso brillo quemador de la explosión. Este impacto alcanzó el millón de grados centígrados e hizo que algunos cuerpos y objetos dejaran una sombra en la pared, plantas o piso (22).

Este hecho, se llevó a cabo con la justificación de que las relaciones diplomáticas entre Estados Unidos y Japón estaban en su peor momento, por una guerra económica entre ellos y por bloqueos petrolíferos por parte de Estados Unidos hacia Japón. Debido a esto, Japón decidió destruir una base naval estadounidense, destruyendo 12 buques de guerra, 188 aeronaves y dejando más de 2000 militares heridos y 68 ciudadanos muertos. Los estadounidenses indignados por el hecho y considerando a Japón como traicionero, le declararó la guerra, al tiempo que entró en la Segunda Guerra Mundial y se enfocó en el programa atómico junto con Gran Bretaña y Canadá. Este programa se mantuvo en secreto bajo el nombre de proyecto Manhattan, su objetivo consistía en crear la primera bomba atómica creándose varios centros de investigación, uno de los más importantes el distrito de ingeniería Manhattan en el laboratorio nacional Los Álamos en Nuevo México. Este proyecto agrupó a expertos físicos, químicos, pacifistas e izquierdistas, quienes tenían como fin aportar todos sus conocimientos para la creación de la bomba atómica, para lo que se hicieron necesarios ensayos para su posterior detonación en el objetivo (20).

Luego de la muerte del presidente Roosevelt, quien había apoyado estas investigaciones, el poder fue tomado por el norteamericano Harry Truman, que más tarde, lanzó a Japón la declaración Potsdam, una reunión llevada a cabo en Potsdam, Alemania, en la que se subrayó los términos de la rendición para Japón, dándole un ultimátum para su posterior rendición sin condiciones, advirtiéndole de una devastadora destrucción, si esto no se cumplía.

La meta de los estadounidenses era atacar ciudades que no hubiesen sido blancos de armas nucleares y de esta forma observar y medir el impacto real de los efectos de la bomba. Todo estuvo tan planeado, que semanas antes tripulaciones estadounidenses estuvieron entrenando con vuelos a la altura a la que se iba a realizar el ataque definitivo en la ciudad de Hiroshima.

Luego de verse una gran Ráfaga de fuego en el firmamento la mayoría de personas quedaron calcinadas por una fuerte ola de calor. Las personas que lograron sobrevivir al Impacto murieron a los 20 o 30 días como consecuencia de los mortales rayos Gamma. La onda expansiva luego de detonar la bomba, destruyó alrededor de 2.5 km de distancia, incinerando a quienes se encontraban en este sector. Las altas temperaturas acabaron de forma instantánea con seres humanos y animales, las plantas fueron arrancadas desde la raíz y quemados por el gran calor, y las edificaciones terminaron derribadas y carbonizadas. Se dice que 30 minutos luego de la explosión, empezó una lluvia negra que contenía carboncillo condensado del material orgánico quemado y del material reactivo de la bola de humo que se había levantado (20).

Estados Unidos siguió con su ataque preparado, esta vez en la ciudad de Nagasaki. El 9 de agosto, el avión ahora llamado Bock's Car, arrojó sobre el centro de esta ciudad la segunda bomba atómica, 'Fat man', destruyendo la ciudad en un 40%. De 270.000 habitantes, 173 .000 perdieron la vida y 60.000 resultaron heridos. De esta manera una semana después, el 15 de

agosto, el emperador japonés convenció al pueblo de rendirse asegurando que la guerra había culminado. Se oficializó la ceremonia el 2 de septiembre presidida por el general McArthur, comandante supremo de las potencias aliadas (20).

Aunque las bombas nucleares acabaron con mayor parte de Hiroshima y Nagasaki, las ciudades sufrieron efectos diferentes. Esto por su geografía y ubicación. En Hiroshima ubicada sobre un valle, las olas de fuego y radiación se expandieron más rápido y a mayor distancia que en Nagasaki, cuya geografía es montañosa (20).

Otro suceso de gran relevancia y relacionado con energía nuclear, fue el accidente ocurrido en el reactor 4 de la planta nuclear de Chernóbil, el 26 de abril de 1986; ubicada exactamente en Pripiat, a 18 kilómetros al noroeste de la ciudad de Chernobyl y a 17 km de la frontera entre Ucrania y Bielorrusia y a 120 km al norte de Kiev. Chernobyl está situada al norte de Ucrania en la provincia de Kiev, cerca de la frontera con Bielorrusia (23).

Figura 2: Mapa de Ucrania (28)

En la planta de Chernobyl ocurrió la catástrofe nuclear más grave conocida en la historia, la cual fue categorizada en nivel 7 de la escala internacional de accidentes nucleares. El suceso ocurrió, aproximadamente a la 1:23 de la mañana, aparentemente cuando personas

realizaban un experimento en el que se simulaba un corte de suministro eléctrico; un experimento que terminó con la vida de miles y miles de habitantes en esta ciudad (24).

En ese momento el reactor 4 de la planta nuclear explotó, liberando enormes cantidades de radiación y contaminando extensiones de Bielorrusia, la federación Rusa y Ucrania y afectando gravemente a la población local. Las llamas que se desencadenaron afectaron varios pisos y amenazaron a los otros reactores, pero gracias al control ejercido por los bomberos y militares, se evitó que el fuego se propagara al resto de la planta. La temperatura alcanzó los 2.500 grados centígrados y el humo radiactivo ascendió a una altura bastante considerable. Se dice que 31 personas perdieron la vida de inmediato y con el paso de los días la situación se fue agravando. La unión soviética trataba de esconder y no dar explicación a lo ocurrido, pero luego de que Suecia y otros países dieran aviso y mostrarán al mundo la magnitud del desastre, éste se vio obligado a explicar lo acontecido. La actitud de la unión soviética es cuestionada puesto que no tomó las medidas suficientes para alertar a la población (24).

Con el fin de contener la radiación, helicópteros del ejército arrojaron sobre el núcleo una mezcla de arena, arcilla, Plomo y Boro con el fin de absorber los neutrones. Las personas encargadas de realizar estas labores, no tuvieron los suficientes trajes o ropas protectoras y fueron expuestas directamente a la radioactividad generando más de 8.000 muertos y otros miles de enfermos. Luego de tomar medidas para evitar la propagación de la radiación utilizando materiales de relleno se tomó la decisión de iniciar el levantamiento de una estructura denominada sarcófago (25).

La ciudad más afectada por la explosión fue Pripiat, dado que el incidente emitió 400 veces más radiación que la bomba atómica en Hiroshima, esta debió ser evacuada de forma instantánea por la mayoría de los habitantes y trabajadores de la planta en contra de su voluntad. Muchos animales tanto domésticos, ganado y otros tuvieron que ser sacrificados por las consecuencias que la radiación les produjo.

La nube radiactiva se extendió por toda Europa, pero no lo hizo de forma uniforme en las regiones aledañas. Según informes divulgados, Bielorrusia recibió alrededor del 60% de la contaminación, sin embargo, señala que la mitad de las partículas volátiles se concentraron fuera de Ucrania, Bielorrusia y Rusia. Actualmente y en los últimos años se han concluido varios estudios sobre este suceso, uno de estos es el informe alemán TORCH 2006, quién en sus investigaciones concluyó que el 22% del área afectada por la explosión la tuvo Bielorrusia, seguida de Austria y otros países como Ucrania, Finlandia y Suecia también recibieron una pequeña cantidad de contaminación (24).

Radiación

Es esencial el entendimiento de cómo actúa la radiación y saber porque es de relevancia para los seres humanos, saber, en primera instancia que es; pues bien, la radiación es un fenómeno completamente natural, presente en el día a día de las personas, proveniente de muchas fuentes que nos rodean, como lo es el sol, los electrodomésticos, los rayos cósmicos, el suelo, el agua, la comida e incluso las personas. La radiación significa energía, es aquella energía que se encuentra en tránsito, en transporte y propagación en forma de partículas u ondas.

La radiación tiene diferentes clasificaciones, según su naturaleza la podemos dividir en electromagnética, aquella propagada por ondas y la corpuscular, que es representada por partículas subatómicas que se mueven a gran velocidad. También, se puede clasificar según su efecto biológico, en este caso se divide en radiación no ionizante y ionizante; la capacidad ionizante es la propiedad de extraer los electrones de un átomo. Por lo cual la radioactividad se va a dar gracias a núcleos inestables que emitirán espontáneamente, en intentos de estabilizarse, partículas cargadas o radiación ionizante, las cuales serán conocidas como radioisótopos.

Estos radioisótopos o partículas de radiación ionizante son de tres diferentes tipos, las alfa, que se dan gracias a la fisión de los núcleos inestables, liberando partículas de helio, producto de la descomposición del núcleo inicial en dos electrones y dos protones y otros elementos que quedan a partir de esta disociación. También encontramos las partículas Beta, que resultan de la descomposición del átomo inicial por medio del desdoblamiento de un neutrón del núcleo, en un protón y un electrón, el que será propiamente conocido como partícula Beta, más los elementos que derive esta descomposición radioactiva. Finalmente, está la radiación Gamma es aquella que como resultado de la fisión del átomo inicial va a descomponerse en dos elementos diferentes y en energía en forma de calor que será, propiamente la radiación Gamma.

Estas partículas están clasificadas dentro de la radiación ionizante y la corpuscular, es decir son aquellas que representan un mayor grado de peligro para las personas, dado que, esta propiedad ionizante al momento de ingresar o traspasar los cuerpos es la que puede llegar a generar disrupciones en la normalidad de las estructuras atómicas que componen nuestro organismo, trayendo como consecuencia daños en el ADN tales como rupturas del mismo, recombinaciones, deleciones y/o sustituciones de bases nitrogenadas; generando una modificación que podría desencadenar en daños directos, letales, in situ o llamados deterministas, como por ejemplo la muerte de un número determinado de células, que llevará a la pérdida de la función del órgano que componen, siendo el nivel de gravedad proporcional a la dosis de radiación recibida, que en este caso será mayor que la dosis umbral, es decir del límite que resisten las células. También se pueden generar daños subletales, a mediano - largo plazo, o bien llamados estocásticos que incluyen una modificación o mutación celular, estos efectos ocurren tras exposiciones moderadas y bajas y pueden ser o no reparadas, dando la

probabilidad de la supervivencia celular, en caso de una reparación exitosa; de una mutación celular, que traerá ciertos efectos en el genoma o en caso de no ser repara puede de igual forma llegar a la muerte, estos efectos pueden ser hereditarios o somáticos dependiendo del tipo celular mutado, es decir si la célula mutada es somática los efectos de dicha transgresión se verán en el portador de la célula, pero si por el contrario la mutación se da en una célula germinal el efecto se verá en la descendencia.

En cuanto al umbral de dosis, sabemos que el límite anual de radiación recibida es de 1 mSV, mas sin embargo se sabe que no hay efectos clínicos demostrables por debajo de los 200 mSV, y que entre 7000-10000 mSv se produce la muerte, es decir un efecto letal y determinístico.

Las diferentes radiaciones o tipos de radiaciones (Alfa, Beta y Gamma) no presentan el mismo grado de letalidad y/o peligrosidad, dicho grado se evidencia por factores tales como el tamaño de dichas partículas y la velocidad y movilidad que estas presenten, en orden ascendente tenemos primero las partículas alfa, de menor tamaño y menor energía, es decir menor velocidad, dichas partículas pueden ser detenidas por una hoja de papel, seguidamente están las partículas beta, de mediano tamaño, con mayor alcance y más movilidad, estas pueden ser detenidas por una hoja de aluminio; por último las Gamma, son el tipo con mayor letalidad, no solo por su movimiento y tamaño sino por las altas temperaturas que desprende, esta presenta la mayor fuerza y grado de letalidad, las puede bloquear un bloque de plomo.

En las plantas nucleares, donde se intenta utilizar esa radioactividad propia de los elementos presentes en la tierra para generar energía, como era el caso de la central nuclear de Chernobyl, se utiliza la modificación de elementos como el uranio natural que presenta una mezcla de tres isótopos 234U,235U y238U, de los cuales el 235U es fisionable y apto para las reacciones que generan energía, es por esto que dicha obtención de este uranio llamado enriquecido, genera la inestabilidad de su núcleo atómico, lo cual inicia los diferentes procesos de fisión nuclear para su estabilización, por esto se condensa en tubos metálicos sellados llamadas barras de combustión que serán introducidos en cantidades de más o menos 40000 varillas en un núcleo reactor que constara de una base llena de agua que actuara como refrigerante y como moderador, pues este reducirá la velocidad de los neutrones producidos por la fisión para sostener la reacción en cadena, esta fisión como ya lo sabemos genera calor que convierte el agua en vapor, y que hará que gire una turbina para producir electricidad.

Los efectos determinantes del accidente de Chernobyl están dados por las altas dosis de radiación, que afectó principalmente a trabajadores de emergencia y población residente cerca a la planta, alrededor de 1000 personas sufrieron los primeros daños, los cuales sufrieron consecuencias fatales. Sin embargo, para aquellas personas sobrevivientes, y sus descendencias, las consecuencias fueron diferentes tipos de cánceres y malformaciones.

Para ayudar a obtener un consenso científico sobre las consecuencias sanitarias del accidente de Chernobyl y promover una mejor comprensión frente a estos impactos,se estableció el foro

de Chernobyl, el cual es una invitación de la OIEA (Organismo Internacional de Energía Atómica), en cooperación con la OMS (Organización Mundial de la Salud), el PNUD(Programa de las Naciones Unidas para el Desarrollo), la FAO (Organización de las Naciones Unidas para la alimentación y la agricultura),PNUMA(programa de las Naciones Unidas para el Medio Ambiente), OCHA(Oficina para la Coordinación de Asuntos Humanitarios), la UNSCEAR(Comité Científico de las Naciones Unidas para el Estudio de los Efectos de las Radiaciones Atómicas), el Banco Mundial y el apoyo de los países más afectados(Bielorrusia, Rusia y Ucrania). Este foro se creó como una contribución a la estrategia decenal de las Naciones Unidas para Chernobyl, llamado "Human Consequences of the Chernobyl Nuclear Accident — A Strategy for Recovery".

La nube del reactor incendiado esparció diferentes materiales reactivos, especialmente radionucleidos de yodo y cesio sobre gran parte de Europa. El yodo radiactivo-131, tiene una vida media de 8 días, asociado con dosis que afectan la glándula tiroides; este elemento, se dice que se desintegró en gran medida en las primeras semanas del accidente. Por su parte el cesio radiactivo-137 tiene una vida media mucho más prolongada de 30 años y actualmente se puede medir en el suelo y algunos alimentos en muchas partes de Europa. Las mayores cantidades de radionucleidos se depositaron principalmente en los países de Bielorrusia, Rusia y Ucrania.En estos países más de 5 millones de personas fueron clasificadas como contaminadas debido a radionucleidos procedentes del accidente (más de 37 kBq m-2 of 137Cs). Alrededor de 400.000 personas que vivían en zonas más contaminadas, zonas de estricto control de radiación (por encima 555 kBq m-2 of 137Cs), tuvieron que ser evacuadas de las áreas que rodeaban la planta de energía llamada "zona de exclusión".

Las emisiones importantes de radionucleidos de la unidad 4 del reactor de Chernobyl continuaron durante diez días después de la explosión. Estos incluían gases radiactivos, aerosoles condensados y una gran cantidad de partículas de combustible. La liberación total de sustancias radiactivas fue de aproximadamente 14 EBq5, incluidos 1,8 EBq de yodo-131, 0,085 EBq de 137Cs, 0,01 EBq de 90Sr y 0,003 EBq de radioisótopos de plutonio. Los gases nobles contribuyeron con aproximadamente el 50% de la liberación total.

Más de 200 000 kilómetros cuadrados de Europa recibieron niveles de 137Cs por encima de 37 kBq m-2. Más del 70 por ciento de esta área estaba en los tres países más afectados. La deposición fue sumamente variada, ya que se realzó en las zonas donde llovía cuando pasaban las masas de aire contaminadas. La mayoría de los radioisótopos de estroncio y plutonio se depositaron a menos de 100 km del reactor destruido debido a los tamaños de partículas más grandes.

Muchos de los radionucleidos más importantes tenían una vida media física breve. Por tanto, la mayoría de los radionucleidos liberados por el accidente se han desintegrado. Las emisiones de yodo radiactivo causaron gran preocupación inmediatamente después del accidente. Durante las próximas décadas, el 137Cs seguirá siendo de gran importancia, con atención

secundaria al 90Sr. A largo plazo (de cientos a miles de años), los isótopos de plutonio y americio-241 permanecerán, aunque a niveles no significativos radiológicamente.

Tres grupos de población estuvieron expuestos al accidente de chernobyl:

- Trabajadores de la operación de emergencia y recuperación que trabajaban en la central eléctrica y en la zona de exclusión después del accidente.
- Habitantes evacuados de las áreas contaminadas.
- Habitantes de áreas contaminadas que no fueron evacuados.

Con la excepción del personal del reactor presente en el sitio y los trabajadores de emergencia que estaban presentes cerca del reactor destruido durante el tiempo del accidente y poco después, la mayoría de los trabajadores de operaciones de recuperación y las personas que vivían en los territorios contaminados recibieron un monto relativamente bajo, comparado a los niveles de radiación acumulados durante el período de 20 años desde el accidente.

Las dosis más altas fueron recibidas por los trabajadores de emergencia y el personal de campo durante los primeros días del accidente, que oscilaban entre los 2 y 20 Gy, resultando fatal para estos trabajadores. Las dosis recibidas por los trabajadores de la operación de recuperación que trabajan por periodos cortos durante cuatro años después del accidente, oscilaban entre los 500 y 1000 mSv según los registros de Bielorrusia, Rusia y Ucrania.

Se estimó que las dosis efectivas para las personas evacuadas de la zona de accidentes de Chernobyl en la primavera y el verano de 1986 eran del orden de 33 MSV en promedio, con la dosis más alta del orden de varios cientos de MSV.

El público en general ha estado expuesto durante los últimos veinte años después del accidente, tanto de fuentes externas (137C en el suelo, etc.) como a través de la ingesta de radionucleidos (principalmente 137Cs) con alimentos, agua y aire, ver. En promedio se estimó que las dosis efectivas para la población general de las áreas "contaminadas" acumuladas en 1986-2005 estaban entre 10 y 30 mSv en varias regiones de Bielorrusia, Rusia y Ucrania. En las áreas de estricto control radiológico, la dosis promedio fue de alrededor de 50 mSv y más. Algunos residentes recibieron hasta varios cientos de mSv. Cabe señalar que las dosis promedio recibidas por los residentes de los territorios 'contaminados' por la lluvia radiactiva de Chernobyl son generalmente más bajas que las recibidas por las personas que viven en algunas áreas de alta radiación natural de fondo en India, Irán, Brasil y China (100-200 mSv en 20 años).

La gran mayoría de personas que residen en áreas contaminadas de Bielorrusia, Rusia y Ucrania actualmente reciben dosis efectivas anuales de la lluvia radiactiva de Chernobyl de menos de 1 mSv, además de las dosis naturales. Sin embargo, alrededor de 100.000 residentes de las áreas más contaminadas todavía reciben más de 1 mSv al año de la lluvia radiactiva de Chernobyl. Aunque se espera que la reducción futura de los niveles de exposición sea bastante

lenta, es decir, de aproximadamente un 3 a un 5% anual, la gran mayoría de la dosis del accidente ya se ha acumulado.

La interacción de la radiación ionizante (alfa, beta, gamma y otros tipos de radiación) con la materia viva puede dañar las células humanas, provocando la muerte de algunas y modificando otras. La exposición a la radiación ionizante se mide en términos de energía absorbida por unidad de masa, es decir, dosis absorbida. La unidad de dosis absorbida es el gray (Gy), que es un joule por kilogramo (J / kg). La dosis absorbida en un cuerpo humano de más de un Gy puede causar síndrome de radiación aguda (ARS) como sucedió con algunos de los trabajadores de emergencia de Chernobyl.

Debido a que muchos órganos y tejidos quedaron expuestos como resultado del accidente de Chernobyl, ha sido muy común utilizar un concepto adicional, el de dosis efectiva, que caracteriza el riesgo general para la salud debido a cualquier combinación de radiación. La dosis efectiva tiene en cuenta tanto la energía absorbida y el tipo de radiación como la susceptibilidad de varios órganos y tejidos al desarrollo de un cáncer o efecto genético grave inducido por radiación. La unidad de dosis efectiva es el sievert. Un sievert es una dosis bastante grande, por lo que el milisievert o mSv (una milésima de Sv) se usa comúnmente para describir exposiciones normales.

Los organismos vivos están continuamente expuestos a la radiación ionizante de fuentes naturales, que incluyen rayos cósmicos, radionúclidos cosmogénicos y terrestres (como 40K, 238U, 232Th y su progenie, incluido el 222Rn). La UNSCEAR ha estimado que las dosis naturales anuales de los seres humanos en todo el mundo en un promedio de 2,4 mSv, con un rango típico de 1 a 10 mSv. Las dosis de por vida debidas a la radiación natural serían, por tanto, de 100 a 700 mSv.

En Hiroshima y Nagasaki, se presenta el otro gran hito de la radiación a nivel histórico, con un componente más bélico en el contexto de la guerra, Estados Unidos decide lanzar bombas atómicas a Japón, como medio para ganar la guerra. Dichas bombas atómicas, *Little Boy* (Hiroshima) que mató a unas 80000 personas y *Fat Man* (Nagasaki) que mató de inmediato a 40000 personas; presentaban el mismo modo de funcionamiento, la fisión, es decir la fracción del núcleo atómico para lograr la liberación de energìa como se mencionaba anteriormente, para lograr este fenómeno es necesario lanzar un neutrón contra un núcleo inestable, en las bombas atómicas el factor que determina su efecto perjudicial masivo es dicho fenómeno pero en cadena, es decir en fracciones de segundo la incidencia de un neutrón en uno de los núcleos atómicos inestables genera la diseminación de energìa, pero adicionalmente hay también la liberación de más neutrones, que en presencia de más núcleos atómicos generará múltiples fisiones nucleares consecutivas de todos los núcleos atómicos que presente la bomba.

A pesar de que ambas bombas nucleares utilizan la fisión como forma de acción, pero su mecanismo interno era distinto, Little Boy utilizaba uranio 235 y Fat Man plutonio 239, los

núcleos de estos materiales tienen la propiedad de al dividirse liberan gran cantidad de neutrones fusionando más núcleos.

En Little Boy se utiliza una estructura en forma de pistola donde internamente se dispara un proyectil de Uranio 235 que iba a incidir en una masa que se encontraba contraria a esta del mismo material, desatando una reacción en cadena, a la hora de la explosion solo el el 1% del total de los 64 kilos de uranio con los cuales estaba cargada se logró fisionar

Por otro lado, Fat man se diseñó como una bomba de implosión, donde en una posición central se ubicaba una más de plutonio 239 que estaba rodeada por explosivos dirigidos a la explosion interna de la esfera de plutonio para generar la fisión en cadena, por medio de la compresión de la misma, duplicando su densidad, presionando los núcleos atómicos unos contra otros, generando su división en masa. Estaba compuesta por 6 kilos de plutonio 239 de los cuales solo se fusionó 1 kilo del material.

Como ya lo hemos visto dichas fisiones no conlleva solo a la explocion y a la liberación de calor en miles de grados sino también a la liberación de radiación ionizante, que impactará todo lo que encuentre a su paso destruyendo las células o alterar la forma fisiológica de la misma.

Objetivos

Recopilar e integrar la información sobre la radiación como factor etiológico de las malformaciones craneofaciales y más específicamente de tipo labio paladar fisurado en poblaciones afectadas por dos eventos históricos asociados a radiación, como fueron las bomba atómica en Hiroshima y Nagasaki (Japón) y el accidente por explosión del núcleo de una central nuclear en Chernobyl, y sus efectos en la población, por medio de una revisión narrativa.

Objetivos específicos

A partir de la evidencia científica:

- Actualizar y sintetizar la información de la radiación como factor etiológico para las malformaciones craneofaciales de tipo labio paladar fisurado en las poblaciones afectadas por las bombas atómicas de Hiroshima y Nagasaki en el año 1945 y en adelante por medio del índice de incidencia y prevalencia
- Actualizar y sintetizar la información de la radiación como factor etiológico para las malformaciones craneofaciales de tipo labio paladar fisurado en las poblaciones afectadas por el accidente de Chernobyl en el año 1986 y en adelante por medio del índice de incidencia y prevalencia.
- Con base en la literatura recopilada, establecer la posible asociación entre la presencia de la anomalía craneofacial de tipo labio y paladar hendidos y dos diferentes tipos de radiación, que afectaron zonas geográficas distintas y en épocas diferentes.

Materiales y métodos

Tipo de estudio: Revisión Narrativa

Muestra: Artículos científicos donde se determine a partir de la investigación datos de prevalencia, incidencia y/o epidemiología del labio paladar hendido en poblaciones expuestas a la radiación después de las bombas atómicas de Hiroshima y Nagasaki, en 1945 y en adelante.

Artículos científicos donde se determine a partir de la investigación datos de prevalencia, incidencia y/o epidemiología del labio paladar hendido en poblaciones expuestas a la radiación después del accidente de Chernobyl en 1986 y en adelante.

Variables

- Tipo de radiación proveniente de las bombas atómicas en Hiroshima y Nagasaki
- Tipo de radiación proveniente del accidente de Chernobyl
- Malformaciones craneofaciales tipo labio y paladar fisurados
- Índice de prevalencia
- Índice de incidencia
- Habitantes de poblaciones japonesas de Hiroshima y Nagasaki y sus alrededores
- Habitantes de la población de Ucrania, específicamente de Chernobyl y alrededores.

Búsqueda de información:

Palabras clave

Hendiduras orales	**Variables**	**Términos clave**
	Palabra clave	Oral cleft
	Término [MeSH]	Orofacial Cleft
	Término [Emtree]	oral cleft
	Sinonimo términos relacionados	Brain/abnormalities Cleft Lip Cleft Palate
Prevalencia/Incidencia/Epidemiología	**Variables**	**Términos clave**
	Palabra clave	Prevalence/Incidence/Epidemiology
	Término [MeSH]	Epidemiology

	Término [Emtree]	Epidemiology
	Sinonimo términos relacionados	Prevalence Incidence Epidemiology
Japón	**Variables**	**Términos clave**
	Palabra clave	Japan
	Término [MeSH]	Japan
	Término [Emtree]	Japan
	Sinonimo términos relacionados	Asia Far East
Malformaciones congénitas	**Variables**	**Términos clave**
	Palabra clave	Congenital malformations
	Término [MeSH]	Congenital Abnormalities
	Término [Emtree]	Congenital malformations
	Sinonimo términos relacionados	Abnormality, Congenital Congenital Abnormality Deformities Deformity Congenital Defects Defect, Congenital Defect, Birth
Anormalidades inducidas por la radiación	**Variables**	**Términos clave**
	Palabra clave	Radiation-Induced Abnormalities
	Término [MeSH]	Radiation-Induced Abnormalities

	Término [Emtree]	Radiation-Induced Abnormalities
	Sinonimo términos relacionados	Abnormalities, Radiation Induced Abnormality, Radiation-Induced Radiation Induced Abnormalities Radiation-Induced Abnormality
Hiroshima	**Variables**	**Términos clave**
	Palabra clave	Hiroshima
	Término [MeSH]	Hiroshima
	Término [Emtree]	Hiroshima
	Sinonimo términos relacionados	Japan Hiroshima accident
Nagasaki	**Variables**	**Términos clave**
	Palabra clave	Nagasaki
	Término [MeSH]	Nagasaki
	Término [Emtree]	Nagasaki
	Sinonimo términos relacionados	Nagasaki bomb Japan
Chernobyl	**Variables**	**Términos clave**
	Palabra clave	Chernobyl
	Término [MeSH]	Chernobyl Nuclear Accident
	Término [Emtree]	Chernobyl accident
	Sinonimo términos relacionados	Chernobyl atomic energy station accident

		Chernobyl atomic power station accident Chernobyl disaster
Labio fisurado	**Variables**	**Términos clave**
	Palabra clave	Cleft lip
	Término [MeSH]	Cleft Lip
	Término [Emtree]	cleft lip
	Sinonimo términos relacionados	Cleft Lips Lip, Cleft Lips, Cleft Harelip

Estructura de las estrategias de búsqueda

#1	**Oral Cleft**
#2	prevalence OR incidence OR epidemiology
#3	Japan
#4	**#1 + #2 + #3** ((oral cleft)AND(prevalence OR incidence OR epidemiology) AND (Japan))
#5	Congenital malformations
#6	Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality
#7	Hiroshima
#8	Nagasaki
#9	chernobyl
#10	#5 AND #6
#11	#10 AND #7 AND #8

#12	#10 AND #9
#13	Cleft lip
#14	#13+#2+#9 ('cleft lip'/exp OR 'cleft lip') AND ('prevalence'/exp OR prevalence OR 'incidence'/exp OR incidence OR 'epidemiology'/exp OR epidemiology) AND ('chernobyl'/exp OR chernobyl)

Resultados de la aplicación de la estrategia de búsqueda

Base de datos	**Web of Science**		
Búsqueda	**Algoritmo**	**Cantidad de artículos encontrados**	**Cantidad de artículos seleccionados por Título/ abstract**
#1	Oral Cleft	3.981	
#2	prevalence OR incidence OR epidemiology	1.448.640	
#3	Japan	212.743	
#4	#1 + #2 + #3 ((oral cleft)AND(prevalence OR incidence OR epidemiology) AND (Japan))	11	2
#5	Congenital malformations	23.468	
#6	Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality	880	
#7	Hiroshima	2.203	
#8	Nagasaki	1.371	
#9	chernobyl	4.955	
#10	#5 AND #6 (((Congenital malformations) AND(Abnormalities, Radiation Induced OR Radiation-Induced	11	

	Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality)))		
#11	#10 AND #7 AND #8 ((Congenital malformations) AND(Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality)AND(Hiroshima)AND(Nagasaki))	0	
#12	#10 AND #9 (((Congenital malformations) AND(Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality)AND(chernobyl)))	1	
#13	Cleft lip	10.031	
#14	#13+#2+#9 ('cleft lip'/exp OR 'cleft lip') AND ('prevalence'/exp OR prevalence OR 'incidence'/exp OR incidence OR 'epidemiology'/exp OR epidemiology) AND ('chernobyl'/exp OR chernobyl)	2	

Base de datos	**PUBMED**		
Búsqueda	**Algoritmo**	**Cantidad de artículos encontrados**	**Cantidad de artículos seleccionados por** **Título/ abstract**
#1	Oral Cleft	12.451	
#2	prevalence OR incidence OR epidemiology	3.342.218	

#3	Japan	1.293.844	
#4	#1 + #2 + #3 ((oral cleft)AND(prevalence OR incidence OR epidemiology) AND (Japan))	68	8
#5	Congenital malformations	627.533	
#6	Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality	3.856	
#7	Hiroshima	31.484	
#8	Nagasaki	20.923	
#9	chernobyl	5.088	
#10	#5 AND #6 (((Congenital malformations) AND(Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality)))	1.845	
#11	#10 AND #7 AND #8 ((Congenital malformations) AND(Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality)AND(Hiroshima)AND(Nagasaki))	30	6
#12	#10 AND #9 (((Congenital malformations) AND(Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality)AND(chernobyl)))	94	16
#13	Cleft lip	19.062	
#14	#13+#2+#9	3	

	('cleft lip'/exp OR 'cleft lip') AND ('prevalence'/exp OR prevalence OR 'incidence'/exp OR incidence OR 'epidemiology'/exp OR epidemiology) AND ('chernobyl'/exp OR chernobyl)		

Base de datos	**EMBASE**		
Búsqueda	**Algoritmo**	**Cantidad de artículos encontrados**	**Cantidad de artículos seleccionados por Título/ abstract**
#1	Oral Cleft	2	
#2	prevalence OR incidence OR epidemiology	3.407.080	
#3	Japan	335	
#4	#1 + #2 + #3 ((oral cleft)AND(prevalence OR incidence OR epidemiology) AND (Japan))	126	
#5	Congenital malformations	51.576	
#6	Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality	232	
#7	Hiroshima	52.442	
#8	Nagasaki	34.708	
#9	chernobyl	0	
#10	#5 AND #6 (((Congenital malformations) AND(Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality)))	34	

#11	#10 AND #7 AND #8 ((Congenital malformations) AND(Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality)AND(Hiroshima)AND(Nagasaki))	1	
#12	#10 AND #9 (((Congenital malformations) AND(Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality)AND(chernobyl)))	2	
#13	Cleft lip	22.886	
#14	#13+#2+#9 ('cleft lip'/exp OR 'cleft lip') AND ('prevalence'/exp OR prevalence OR 'incidence'/exp OR incidence OR 'epidemiology'/exp OR epidemiology) AND ('chernobyl'/exp OR chernobyl)	7	4

Preselección de artículos por algoritmos de búsqueda y bases de datos

Base de datos	**Web of science**
Algoritmo final	**((oral cleft)AND(prevalence OR incidence OR epidemiology) AND (Japan))**

Updating the Epidemiology of Cleft Lip With or Without Cleft Palate

Shoichiro A Tanaka , Raman C Mahabir, Daniel C Jupiter, John M Menezes

Background: Much of the literature on the epidemiology of cleft lip with or without cleft palate is more than three decades old. The question arose as to whether there has been any recent change or trend in its rate of occurrence.

Methods: The number of live births with cleft lip or other congenital anomalies was solicited from national and international organizations. Data were collected for 34 states and 30 countries for the years 2002 to 2006. All data were normalized and reported per 10,000 live births. Descriptive statistics, in addition to correlation and regression, were used to analyze the data.

Results: Data for the 5-year period demonstrated that the overall congenital anomaly rate increased in the United States and decreased internationally. The states with the highest and lowest rates were Maryland (21.46) and West Virginia (2.59), respectively. The United States cleft lip national rate averaged 7.75. Countries with the highest and lowest rates were Japan (19.05) and South Africa (3.13), respectively. Internationally, the rate of cleft lip declined, with an average overall prevalence of 7.94.

Conclusions: The average prevalence of cleft lip with or without cleft palate was 7.75 per 10,000 live births in the United States and 7.94 per 10,000 live births internationally. The trends diverged over the 5-year period, as the rate was stable in the United States and the international rate declined.

Questionnaire Results on Exposure Characteristics of Pregnant Women Participating in the Japan Environment and Children Study (JECS)

Miyuki Iwai-Shimada , Shoji F Nakayama , Tomohiko Isobe , Takehiro Michikawa , Shin Yamazaki , Hiroshi Nitta , Ayano Takeuchi , Yayoi Kobayashi , Kenji Tamura , Eiko Suda , Masaji Ono , Junzo Yonemoto , Toshihiro Kawamoto , Japan Environment and Children's Study Group

Abstract:

Background: The Japan Environment and Children's Study (JECS) is a nation-wide birth cohort study investigating environmental effects on children's health and development. In this study, the exposure characteristics of the JECS participating mothers were summarized using two questionnaires administered during pregnancy.

Methods: Women were recruited during the early period of their pregnancy. We intended to administer the questionnaire during the first trimester (MT1) and the second/third trimester (MT2). The total number of registered pregnancies was 103,099.

Results: The response rates of the MT1 and MT2 questionnaires were 96.8% and 95.1%, respectively. The mean gestational ages (SDs) at the time of the MT1 and MT2 questionnaire responses were 16.4 (8.0) and 27.9 (6.5) weeks, respectively. The frequency of participants who reported "lifting something weighing more than 20 kg" during pregnancy was 5.3% for MT1 and 3.9% for MT2. The Cohen kappa scores ranged from 0.07 to 0.54 (median 0.31) about the occupational chemical use between MT1 and MT2 questionnaires. Most of the partici pants (80%) lived in either wooden detached houses or steel-frame collective housing. More than half of the questionnaire respondents answered that they had "mold growing somewhere in the house".

Insect repellents and insecticides were used widely in households about 60% used "moth repellent for clothes in the closet," whereas 32% applied "spray insecticide indoors" or "mosquito coil or an electric mosquito repellent mat."

Conclusions: We summarized the exposure characteristics of the JECS participants using two maternal questionnaires during pregnancy.

Base de datos	**PUBMED**
Algoritmo final	((oral cleft)AND(prevalence OR incidence OR epidemiology) AND (Japan))

Epidemiologic Research on Malformations Associated With Cleft Lip and Cleft Palate in Japan

Hiroshi Koga, Koichi Iida, Tomoki Maeda, Mizuho Takahashi, Naoki Fukushima , Terufumi Goshi

Abstract

To investigate malformations associated with cleft lip and cleft palate, we conducted surveys at neonatal intensive care units (NICUs) and other non-NICU facilities and to determine whether there are differences among facilities. The regional survey investigated NICU facilities located in Oita Prefecture, including 92 patients with cleft lip and palate (CLP) or cleft palate (CP) that occurred between 2004 and 2013, and the national survey investigated oral surgery, plastic surgery, and obstetrics and gynecology facilities located in Japan, including 16,452 patients with cleft lip (CL), CLP, or CP that occurred since 2000. The incidence per 10,000 births was 4.2, 6.2, and 2.8 for CL, CLP, and CP, respectively, according to the national survey, and 6.3 and 2.9 for CLP and CP, respectively according to the regional survey. These results indicated comparable incidences between the two surveys. In contrast, when the survey results on malformations associated with CLP and CP according to the ICD-10 classification were compared between the national survey conducted at oral surgery or plastic surgery facilities and the regional survey conducted at NICU facilities, the occurrence of associated malformations was 19.8% vs. 41.3% for any types of associated malformation, 6.8% vs. 21.7% for congenital heart disease, and 0.5% vs. 16.3% for chromosomal abnormalities. These results indicated that the incidences of all of these associated malformations were significantly

greater in the survey conducted at NICU facilities and similar to the findings from international epidemiological surveys. When comparing the survey conducted at obstetrics facilities vs. NICU facilities, the occurrence of associated malformations was similar results as above. The incidence of CLP and CP was not different between surveys conducted at NICU facilities vs. non-NICU facilities; however, when conducting surveys on associated malformations, it is possible to obtain accurate epidemiological data by investigating NICU facilities where detailed examinations are thoroughly performed.

Incidence of Cleft Lip or Palate in 303738 Japanese Babies Born Between 1994 and 1995

N Natsume, T Kawai, G Kohama, T Teshima, S Kochi, Y Ohashi, S Enomoto, M Ishii, Y Nakano, T Matsuya, M Kogo, Y Yoshimura, M Ohishi, N Nakamura, T Katsuki, M Goto, M Shimizu, S Yanagisawa, T Mimura, H Sunakawa

Abstract

To investigate the incidence of cleft lip or palate or both (CLP) in Japan, 303738 babies born in 1532 institutions between 1994 and 1995 were examined and 437 (0.14%) were found to have abnormalities. Of these babies, 32.1% had cleft lip, 43.3% had cleft lip and palate, and 24.8% had cleft palate (Table 2). These results show that the incidence of cleft lip and palate has declined compared with the period from 1981 to 1982.

Craniofacial and Oral Malformations in an Autopsy Population of Japanese Human Fetuses and Newborns

N Akimoto, T Ikeda, Y Satow, J Y Lee, N Okamoto

Abstract

A review of the autopsy records of the Department of Pathology of Nagasaki University and the Department of Geneticopathology of Hiroshima University from 1944 through 1982 revealed that during this period there were 11,050 cases of fetuses and newborns, including 432 cases with craniofacial and oral malformations and 22 cases with amniogenous malformations. Among the cranial malformations, there were 202 (46.8%) anencephaly cases, 38 (8.8%) holoprosencephaly, 28 (6.48%) hydrocephaly, 27 (6.25%) meningoencephalocele, and 13 other cranial malformations (seven microcephaly and two each of macrocephaly, dolichocephaly, and iniencephaly). Among the oral malformations, there were 25 (5.78%) cleft lip cases, 23 (5.32%) cleft palate, and 76 (17.6%) cleft lip and palate. Among the facial malformations, there were 12 (2.78%) anomicrophthalmia cases, 37 (8.56%) ear malformations, 15 (3.47%) micrognathia, and 8 (1.85%) nose malformations. One cranial malformation was found that was complicated with anencephaly and holoprosencephaly. Of 307 cranial malformations, 38 (12.4%) were complicated with oral malformations and 4 (4.6%) with facial malformations. Among the 124 cases of oral malformations, 38 (30.6%) were complicated with cranial malformations. The complicating cranial malformations were anencephaly in 16 cases, holoprosencephaly in seven, hydrocephaly in six, meningoencephalocele in seven, other cranial malformations in two, and with facial malformations in 19 cases. Among the 72 cases of facial malformations, 14 were complicated with cranial malformations and 19 with oral malformations. Four cases showed three or more cranial, facial, and/or oral malformations at the same time. Recently, experimental embryological studies have shown that the neural crest cell-derived mesectoderm participates largely in the morphogenesis of the face and the cardiovascular system. It may be said that neural crest cells are deeply involved in the teratogenesis.

Incidence of cleft lip and cleft palate in 39,696 Japanese babies born during 1983

NagatoNatsume, TsuyoshiKawai

Abstract

To estimate the incidence of cleft lip and/or cleft palate among the Japanese, 39696 Japanese babies born during the period from January 1, 1983 to December 31, 1983, were investigated. It was found that 65 babies (0.163%) had these abnormalities, and that the ratio of the birth of such babies was approximately one per 611 in the population. Of the 65 affected babies, 41.3% presented cleft lip (CL), 46.0% cleft lip and palate (CL/P), and 12.7% cleft palate (CP). These results suggest that the incidence of CL/P in the Japanese is higher than that observed among other races.

The Prevalence of Cleft Lip and Plate in Japanese

N Natsume , T Suzuki, T Kawai

Abstract

To determine the prevalence of cleft lip and palate (CL/P) among the Japanese, 43,821 babies born between 1 January, 1985, and 31 December, 1985, were investigated. Sixty-four infants (0.146%) were found to demonstrate these abnormalities, a birth prevalence rate of 1.46/1000. Among 326 infants in whom it was possible to classify the types of cleft, born between 1 January, 1981, and 31 December, 1985, there were 111 (34.0%) with cleft lip (CL), 154 (47.3%) with cleft lip and palate (CLP) and 61 (18.7%) with cleft palate (CP).

The Prevalence of Cleft Lip and Palate in the Japanese: Their Birth Prevalence in 40,304 Infants Born During 1982

N Natsume, T Suzuki, T Kawai

Abstract

To determine the prevalence of cleft lip and palate (CL/P) among the Japanese, 40,304 infants born between Jan. 1, 1982, and Dec. 31, 1982, were investigated. Eighty-three infants (0.206%) were

found with these abnormalities in approximately 2.06/1000 live births. Among fifty-two infants in whom it was possible to classify the types of cleft, seventeen (32.7%) had cleft lip only (CL), twenty-four (46.1%) had cleft lip and palate (CLP), and eleven (21.2%) had isolated cleft palate (CP).

Survey of Congenital Anomalies Associated With Cleft Lip and/or Palate in 701,181 Japanese People

N Natsume , T Niimi, H Furukawa, T Kawai, N Ogi, Y Suzuki, T Kawai

Abstract

There have been many reports on congenital anomalies associated with cleft lip and/or palate (CL/CLP) in Japan. However, these reports included data only on patients who came to hospitals; thus the real situation regarding these anomalies remains unclear. Therefore, we surveyed newborns at all delivery facilities in the central area of Japan for the presence of these anomalies, following their progress for 12 consecutive years; at the end of that time, questionnaires were collected and analyzed. In this article, we describe our results.

Loss of Teratogenic Response to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in Mice Lacking the Ah (Dioxin) Receptor

J Mimura , K Yamashita, K Nakamura, M Morita, T N Takagi, K Nakao, M Ema, K Sogawa, M Yasuda, M Katsuki, Y Fujii-Kuriyama

Abstract

Background: The aryl hydrocarbon receptor (AhR or dioxin receptor) is a ligand-activated

transcription factor that is considered to mediate pleiotropic biological responses such as teratogenesis, tumour promotion, epithelial hyperplasia and the induction of drug-metabolizing enzymes to environmental contaminants usually represented by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). In contrast to the role of AhR in the regulatory mechanism of xenobiotic-metabolizing enzymes, there is no direct proof that the AhR is involved in the teratogenic effects of TCDD.

Results: To gain insight into the physiological and teratogenic role of the AhR, we have used gene targeting in mice to disrupt the murine Ahr gene by homologous recombination. Ahr-null mice were viable and fertile and were apparently normal at birth, but displayed a slightly slower growth rate than wild-type mice for the first few weeks of life. When pregnant dams were administered with TCDD by gavage, at a dose of 40 microg/kg body weight at gestation day 12.5, none of the Ahr-null mutant foetuses were sensitive to the teratogenic effects of TCDD, although almost all wild-type foetuses suffered from cleft palate and hydronephrosis. In heterozygous Ahr+/- genotypes, nearly all foetuses suffered from hydronephrosis in response to TCDD treatment, while haplo-insufficiency was observed in the incidence of cleft palate.

Conclusion: These results clearly show that the AhR is involved in the malformation of the palate and kidney in mouse embryos caused by TCDD and suggests that the mechanism of its involvement differs between the cleft palate and hydronephrosis.

Base de datos	**PUBMED**
Algoritmo final	(((Congenital malformations) AND(Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality)AND(chernobyl)))

Fallout From the Chernobyl Nuclear Disaster and Congenital Malformations in Europe

W Hoffmann

Abstract

Investigators estimate that the population exposure that resulted from the Chernobyl fallout is in the range of natural background radiation for most European countries. Given current radiobiologic knowledge, health effects-if any-would not be measurable with epidemiologic tools. In several independent reports, however, researchers have described isolated peaks in the prevalence of congenital malformations in the cohort conceived immediately after onset of the fallout. The consistency of the time pattern and the specific types of malformation raise concern about their significance. In this study, the author summarizes findings from Turkey, Belarus, Croatia, Finland, Germany, and other countries, and implications for radiation protection and public health issues are discussed.

Congenital Malformations Among Offspring of the Liquidators of the Consequences From Chernobyl Accident

A M Liaginskaia, A R Tukov, V A Osipov, A P Ermalitskiĭ, O N Prokhorova

Abstract

The frequency and the structure of congenital malformations at children of the liquidators of the consequences from Chernobyl accident, undergone to an external scale gamma-irradiation in dozes up to 25 cGy. In total is surveyed 2379 newborn at which is revealed 318 intrauterine development defects. The received results are compared to the earlier published data on birth of congenital malformations in families of the fathers who have undergone to an irradiation in connection with professional activity at the enterprises of a nuclear industry, with emergency irradiation, with irradiation as a result of explosions of nuclear bombs in Japan, and are discussed from positions of the basic rules (situations) of radiating genetics. Total frequency, the frequency of forms 21 of inherent defects of development, taken into account in the International register of congenital malformations and frequency 9 forms heaviest of congenital intrauterine development defects with the high contribution mutation components at children of the liquidators authentically is higher than on the average on Russian Federation. The dependence of the frequency congenital malformations at children from dozes of an irradiation of the fathers--liquidators is revealed. The curve of dependence of the frequency of congenital malformations from time, past after work up to

copulation carries arched character with peak of rise of frequency of congenital malformations in 2-3 years and decrease in 6-7 years.

Congenital Malformations Among Newborns and Developmental Abnormalities Among Human Embryos in Belarus After Chernobyl Accident

Sergei P Feshchenko , Heinz C Schröder, Werner E G Müller, Gennady I Lazjuk

Abstract

Evaluation of the effects of radioactive contamination on human populations is important for an understanding of the present and future risk for human health, including the genetic risk. This review centers on the results of population monitoring of developmental anomalies among human embryos and congenital malformations among newborn in the Republic of Belarus before and after Chemobyl accident. The data revealed that the incidences of developmental anomalies and congenital malformation from the mostly radionuclide-contaminated rural regions of Belarus reliably exceed the indices in control areas.

Teratogen Update: Radiation and Chernobyl

F P Castronovo Jr

Abstract

The 1986 nuclear reactor accident at Chernobyl caused nonuniform radiocontamination of air and land, primarily within regions of the former Soviet Union and Western Europe. Major exposure groups included the reactor workers, villagers evacuated from within 30 km of the accident, the

"liquidators" who decontaminated the evacuation zone afterward, those in radiocontaminated villages not evacuated, and "others" not in the latter categories. The possibility of being exposed to radiation caused considerable anxiety, especially among pregnant women. Were teratogenic levels of radiation (> or = 0.1 Gy) exposure attained? To date there is no consistent proof that this level of radiation exposure was received. Nevertheless, thousands of induced abortions were performed. Radioiodine (I-131) caused thyroid cancer in young children in portions of Belarus, the Ukraine, and Russia. It is not known but very possible that I-131 fetal thyroid exposure contributed to this observation. The relationship between mental retardation and radiation exposure has not been confirmed. Leukemia and other cancers, while predicted for the liquidators (mainly males), has not been found in the other exposure groups at this time. Investigations of aborted fetuses and newborns in Belarus showed an increase in the frequency of both congenital and fetal abnormalities in high and low Cs-137 contaminated regions. This study is unreliable due to detection and selection biases. Accident and environmental factors unrelated to radiation doses may have contributed to these observations. Occasional positive teratogenic studies in less contaminated regions of Western Europe are suspect because of the low radiation doses received. There is no substantive proof regarding radiation-induced teratogenic effects from the Chernobyl accident.

Chronic Radiation Exposure in the Rivne-Polissia Region of Ukraine: Implications for Birth Defects

Kelsey Needham Dancause , Lyubov Yevtushok, Serhiy Lapchenko, Ihor Shumlyansky, Genadiy Shevchenko, Wladimir Wertelecki, Ralph M Garruto

Abstract

Objectives: The health effects of chronic low-dose radiation exposure remains a controversial question. Monitoring after the Chernobyl nuclear accident in Ukraine suggested that chronic low-dose radiation exposure was not linked to cancer mortality among the general population. However, elevated rates of birth defects in contaminated compared to uncontaminated regions suggest that exposure to radiation in utero might impact development and that chronic radiation exposure might

represent an underestimated risk to human health.

Iodine 131: Biokinetics, Radiation Exposure and Risk Assessment With Reference to the Reactor Accident at Chernobyl

E Moser, H D Roedler

Abstract

Following the reactor accident at Chernobyl, this paper describes the biokinetics of radioiodine in man and discusses the radiation exposure resulting from intake of 131I. The risk of radiation-induced thyroid carcinomas and of congenital abnormalities is evaluated. Assuming a linear dose/risk relationship, one can calculate an increase in mortality from thyroid carcinomas amongst children in southern Germany of 100 to 101 per million children. For adults in southern Germany, and for the rest of the population in Germany, the figure is considerably lower. Gonadal dose from the 131I released is so small, compared with the annual natural radiation exposure, that it is not appropriate to discuss genetic effects.

Geburtsprävalenz ausgewählter Fehlbildungen bei Lebendgeborenen in Bayern von 1984–1991

Cornelia Irl, Angela Schoetzau, Fredericus van Santen & Bernd Grosche

Abstract

The study presents data on birth prevalences of selected congenital malformations in livebirths with residence in Bavaria, born between 1984 and 1991. Cases have been ascertained retrospectively by reviewing hospital records of all children being referred to a Bavarian children's hospital up to two years of age. The calculations of prevalences give rates both of malformed children (child with multiple malformations was counted only once according to his malformation class) and of malformation diagnoses (child with multiple malformations was counted under each of his malformation diagnoses). 8,527 children with isolated malformations and 3,513 children with multiple malformations were included. Boys were more often affected than girls (m:f=1,4:1, without hypospadia). While prevalences of most malformations remained relatively constant between 1984 and 1991, the rate of isolated spina bifida has decreased slightly, whereas the rates of isolated

ventricular septal defects and isolated obstructive defects of the urinary tract (ICD9 753.2+753.6) have increased considerably. The Bavarian prevalences were compared with those of the EUROCAT registry.

Ten Years After Chernobyl

T Rytömaa

Abstract

This review focuses on current findings on the health consequences of the accident at the Chernobyl nuclear power plant in 1986. Acute radiation damage caused by exposure to high doses of ionizing radiation involved a few hundred people, apparently with fewer than 100 deaths within the first few months. Epidemiologically detectable increases in congenital abnormalities have not been reported thus far, with the possible exception of Down's syndrome. Owing to the long latency period of radiation-induced cancer, discernible increases in cancer incidence and mortality are not yet expected for most tumour types, especially among adults. However, dramatic increases in the number of childhood thyroid cancers have already been observed in Belarus and Ukraine and the Bryansk regions of Russia. The increase has been over 100-fold in some areas with heavy contamination. From the viewpoint of overall public health, the outlook of direct health effects of the Chernobyl accident are likely to be severe only among some limited subgroups, such as young children exposed to high levels of fallout nuclides. In absolute terms, the global number of Chernobyl-associated cancer cases can be estimated to be tens of thousands, but only a small fraction of these is likely to be discernible epidemiologically.

Changes in Registered Congenital Anomalies in the Republic of Belarus After the Chernobyl Accident

G I Lazjuk, D L Nikolaev, I V Novikova

Abstract

A descriptive analysis of birth defects and malformations was performed to assess whether the rates of these defects correlate with the geographic areas of Belarus that received different levels of 137Cs contamination resulting from the Chernobyl catastrophe. Since this accident in 1986, the frequency of both congenital and fetal abnormalities in the Republic of Belarus has apparently increased. This increase is most prominent in areas with at least 555 9Bq/m2 radioactive contamination, although it has not been possible to correlate the individual dose received by a pregnant woman with the incidence of congenital malformations. The types of anomalies that were most increased in frequency were multiple congenital malformations, polydactyly, and reduction limb defects. These malformations are commonly associated with dominant new mutations. Chromosomal disorders such as occur in Down syndrome were not increased in frequency, nor could teratogenic effects be attributed to exposure to ionizing radiation. Preventive measures have apparently reduced the number of births with congenital abnormalities but have had no apparent effect on the frequency of fetal defects. Results of our analysis are consistent with the hypothesis that ionizing radiation released during the Chernobyl accident may have placed fetuses and neonates at risk for congenital malformations. Epidemiological studies are now required to determine whether a mother's radiation dose correlates with congenital malformations in her children.

Radiation Effects on the Population of Belarus After the Chernobyl Accident and the Prediction of Stochastic Effects

J E Kenigsberg , V F Minenko, E E Buglova

Abstract

Evaluation of conditions of exposure during the post-accident period makes it possible to identify two periods in the radiation exposure of Belarus's population. As a result of our investigations we

obtained data about doses for four different categories in the exposed population: people who lived in the contaminated territories without evacuation and relocation; evacuated people: cleanup workers ("liquidators"); and people who were exposed in childhood, especially for thyroid exposure. The total doses for these categories in different time periods were analysed. Evaluation of doses received by the Belarusian population due to the Chernobyl accident shows no evidence of doses, that could lead to the deterministic consequences of radiation exposure. For all exposed groups we made predictions about different types of stochastic consequences of exposure.

Cleft lip and cleft palate birth rate in Bavaria before and after the Chernobyl nuclear power plant accident

Background Cleft lip and palates (CLP) occur with a frequency of between 1 and 2 cases in 1000 live births and thus belong to the most frequent congenital anomalies. In the former German Democratic Republic (GDR), records covering 1967–1989 for CLP newborns show a 9.4% increase of the prevalence of CLP from 1987 to 1989, possibly due to Chernobyl. Data and statistical method In Bavaria, all congenital malformations in children's hospitals have been recorded from 1984 to 1991. Among these data, 1324 cases with CLP were found. A spatial-temporal analysis aimed at uncovering a possible association of the CLP occurrence with the Chernobyl fallout on a district level, as well as a synoptic analysis of the GDR and Bavarian data, were carried out. Results In Bavaria, from October 1986 to December 1990, the CLP frequency increased by 9.5% (p=0.10) relative to the trend as computed from the remaining years. The association of CLP rates with fallout on a district level is reflected by a significant relative risk (RR) per kBq/m2 of RR=1.008 (p=0.03). A synoptic analysis of the Bavarian data and the GDR data restricted to the overlapping time window from 1984 to 1989 discloses a simultaneous significant jump of the CLP prevalence by 8.6% (p=0.02) after 1986. Conclusion The presumption of a long-term increase of CLP after exposure to Chernobyl fallout is corroborated by the analysis of the Bavarian congenital malformation data.

Overview of 1993 Research Activities in Belarus Related to the Chernobyl Accident

N Krissenko

Abstract

This overview describes the medical and biological consequences of the Chernobyl nuclear power plant accident that had been assessed by Belarus scientists as of 1993. In particular, childhood thyroid cancer has increased in both frequency and severity. Other malignant tumors may have also increased, as may have childhood diseases that result from impaired immune function. It is unknown whether these increases in human disease (other than thyroid cancer) are due to improved methods of reporting or to exposure to ionizing radiation. In addition to the medical consequences of radiation damage, there are also significant psychological problems endured by the population living in contaminated areas. The Republic of Belarus has participated in several international programs for the study and management of widespread radiation exposure, and will continue to do so. Programs to address issues of radiation protection and population safety are being implemented wherever possible.

Facial Cleft Birth Rate in Former East Germany Before and After the Reactor Accident in Chernobyl

V Zieglowski , A Hemprich

Abstract

Cleft lip palates (CLP) are caused by a variety of factors. Ionizing radiation is only one of these factors. The meltdown of the nuclear reactor at Chernobyl on April 26, 1986, and the subsequent radioactive fallout did not cause any acute radiation sickness in Germany. Nevertheless, in West Berlin a significant increase of trisomy-21 cases was reported in births 9 months after the Chernobyl reactor

accident. In our study we analyzed the influence of the radioactive fallout after the Chernobyl disaster on the rate and regional distribution of CLP newborns in the former German Democratic Republic (GDR). In contrast to the Federal Republic of Germany an ongoing malformation register for CLP newborns had existed in the former GDR since 4 July 1967. Environmental data were collected from national and international environmental authorities and atomic energy agencies. Population statistics were taken from the statistical year-book of the former GDR. During a 10-year period from 1980 to 1989, the average number of CLP newborns in the GDR was 1.88 per 1,000 live births. A significant prevalence increase was recorded in 1983, 1987 und 1988. In comparison to the mean rate in the period from 1980 until 1986, 1987 demonstrated an increase of 9.4%. Regional prevalence increases were seen in the three northern districts of Schwerin, Rostock and Neubrandenburg, where the radioactivity measurements in general showed higher levels of the radionuclides caesium-137 und strontium-90 than in other districts. Owing to the comprehensive malformation register for CLP patients in the GDR, this is the first study for Germany, analyzing the CLP rate before and after the fallout in Chernobyl. The results support the allegation of the influence of radiation-induced increase of CLP newborns after the Chernobyl reactor accident.

The Morphological Status of the Maxillodental System in Children Living in an Area Contaminated by Radionuclides as a Result of the Accident at the Chernobyl Atomic Electric Power Station

A V Sevbitov, L S Persin, A B Slabkobskaia, N V Pankratova

Abstract

The present study has been done in the framework of federal programme "Children of Che rnobyl" with the aim to determine spread and structure of dental jaw abnormalities in children born and living in the radiation polluted regions after Chernobyl accident in 1986. 183 children have been examined in Donskoi town of Tula Province with the polluted soil by Cs-137 up to 5 Ci/km. All the

examined children were divided into 2 groups: group 1--born in 1980-1986 and group 2--born in 1987-1994. It was determined that 76.5% of children have dental jaw system abnormalities. The most spread ones were occlusion abnormalities in combination with teeth abnormalities (28.9% cases) while the state of dental jaw system corresponding to the age standard was 2 times rarer in children born after the Chernobyl accident.

The Genetic Consequences of the Chernobyl Accident. The Monitoring of Congenital Developmental Defects in Newborn Infants in Kaluga Province

G G Guzeev, B A Kalabushkin

Abstract

The study concentrates on the genetic after-effects of the Chernobyl accident in some districts of Kaluga Province. The frequencies and range of congenital malformations, prematurely death-rate in the radionuclear polluted districts were compared with the control districts. Prematurely death-rate in compared regions is the same. The increase of the congenital malformation frequency is revealed in one the polluted districts (256/10,000) as compared with the control one (27/10,000). We assume that the observed effect is mainly connected with the professional activity of the population.

Incidence of Developmental Defects in Human Embryos in the Territory of Byelarus After the Accident at the Chernobyl Nuclear Power Station

G I Laziuk, I A Kirillova, Iu E Dubrova, I V Novikova

Abstract

The incidence of developmental abnormalities (DA) among 5 to 12-week human embryos collected

in Minsk during abortions before the Chernobyl' accident was compared to that in Minsk, Mogilev, and southeastern districts of Gomel' and Mogilev regions before and after the accident. The incidence of DA among human embryos from the most radionuclide-contaminated rural regions of Byelarus exceeds that of the control group and of the urban population after the Chernobyl' accident by a factor of 1.5-2. The mutagenic effect of irradiation is the most probable cause of the increased DA frequency. These data suggest that recording of DA in embryos obtained by medical abortions is a new promising approach to the monitoring of genetic consequences of irradiation in human populations.

Base de datos	**PUBMED**
Algoritmo final	((Congenital malformations) AND(Abnormalities, Radiation Induced OR Radiation-Induced Abnormalities OR Abnormality, Radiation-Induced OR Radiation Induced Abnormalities OR Radiation-Induced Abnormality)AND(Hiroshima)AND(Nagasaki))

Implications of the Hiroshima-Nagasaki Genetic Studies for the Estimation of the Human "Doubling Dose" of Radiation

J V Neel , W J Schull, A A Awa, C Satoh, M Otake, H Kato, Y Yoshimoto

Abstract

Since 1946 a continuous effort to evaluate the potential genetic effects of the atomic bombs has been sustained. Observations on children born in Hiroshima and Nagasaki include sex ratio, congenital malformations, stillbirths, survival of liveborn infants, chromosomal abnormalities (sex chromosomal abnormalities and balanced chromosomal rearrangements), mutations altering protein structure or activity, and physical growth and development. There are no statistically significant differences between the children of parents who received increased amounts of radiation at the time of the bombings and those whose parents did not. However, the difference between the

two sets of children is consistent with the hypothesis of a genetic effect of the exposure, but its magnitude suggests humans are not as sensitive to the genetic effects of radiation as projected from the mouse paradigm.

Genetic Effects of Radiation in Atomic-Bomb Survivors and Their Children: Past, Present and Future

Nori Nakamura

Abstract

Genetic studies in the offspring of atomic bomb survivors have been conducted since 1948 at the Atomic Bomb Casualty Commission and its successor, the Radiation Effects Research Foundation, in Hiroshima and Nagasaki. Past studies include analysis of birth defects (untoward pregnancy outcome; namely, malformation, stillbirth, and perinatal death), chromosome aberrations, alterations of plasma and erythrocyte proteins as well as epidemiologic study on mortality (any cause) and cancer incidence (the latter study is still ongoing). There is, thus far, no indication of genetic effects in the offspring of survivors. Recently, the development of molecular biological techniques and human genome sequence databases made it possible to analyze DNA from parents and their offspring (trio-analysis). In addition, a clinical program is underway to establish the frequency of adult-onset multi-factorial diseases (diabetes mellitus, high blood pressure, and cardiovascular disease etc) in the offspring. The complementary kinds of data that will emerge from this three-pronged approach (clinical, epidemiologic, and molecular aspects) promise to shed light on health effects in the offspring of radiation-exposed people.

Effects and Consequences of Prenatal Irradiation

O Vos

Abstract

After a brief introduction about the historic development of risk estimates and maximum permissible doses of ionizing radiation, the risks of prenatal irradiation are discussed. Experimental data mainly obtained with mice indicate that the most important risk exists during the period of organogenesis and concerns the induction of malformations. Although in man this period lies between about 10 and 80 days after fertilization for most organs, the main development of the brain occurs later, namely between the 8th and 15th week after conception. Data from Japanese victims of the atomic bomb explosions above Hiroshima and Nagasaki indicate that during development the brain is the most sensitive organ to irradiation and maximal sensitivity is found between the 8th and 15th week after fertilization. A dose of one Gray received during this period induces a severe mental retardation in about 45% of the newborns. The dose response relationship is not significantly different from a linear one without a threshold dose. Studies of intelligence and school performance have shown that 1 Gray received during the 8th-15th week causes a shift of the average intelligence of about 30 points. Irradiation before the 8th week and after the 25th week had no effect on intelligence or mental retardation. During the 16th and 25th week sensitivity was about one fourth of that during the 8th-15th week. Although the irradiation of the embryo and fetus should be avoided as much as possible, the new data have led to an abandonment of the so-called 10-day rule. Generally an accidental irradiation of the embryo or fetus of less than 5 cGy is not considered as a medical indication for abortion. Retrospective studies showed that mothers from children who died from leukemia or other childhood tumors, had been subjected to a diagnostic irradiation of the pelvis or lower abdomen more frequently than mothers from children that did not develop a tumor. It has been estimated that prenatal sensitivity for induction of leukemia and tumors is higher than sensitivity after birth. However, it is still in discussion, whether the relationship between prenatal irradiation and a higher incidence of tumors is of a causal nature.

The Children of Atomic Bomb Survivors: A Synopsis

William J Schull

Abstract

When the atomic bombing of Hiroshima and Nagasaki occurred in the summer of 1945, most members of the public presumed that many of the children conceived by the survivors would be grossly deformed or seriously damaged in other ways as a consequence of radiation-induced mutations. Although the experimental data then available, largely limited to studies of Drosophila melanogaster, the common fruit fly, did not support this perception, the limitations of the data and the depth of public concern warranted a careful follow-up of the children born to the survivors. To this end a surveillance was begun in 1947 of all pregnancy outcomes after 20 weeks of gestation in these two cities. Over the half century subsequent to the initiation of this surveillance, some 80-odd thousand pregnancy outcomes have been studied and a variety of potential indicators of mutational damage measured. This report summarises the findings of these studies and offers an estimate of the genetic risk based on these findings.

The Evidence of Radiation Effects in Embryos and Fetuses Exposed to Chernobyl Fallout and the Question of Dose Response

Chris Busby , Edmund Lengfelder, Sebastian Pflugbeil, Inge Schmitz-Feuerhake

Abstract

Current legal frameworks for radiation exposure limits are based on the risk models of the International Commission on Radiological Protection (ICRP). In Publication 90 (2003), ICRP presents a safe (threshold) dose range of up to 100 mSv for radiogenic effects resulting from in utero exposure and bases this conclusion on the findings in Hiroshima and Nagasaki. However, a variety of observations of congenital malformations, fetal loss, stillbirths and infant deaths, as well as of Down's syndrome and other health defects in children after the Chernobyl accident exposures

suggest that the A-bomb survivor data are incomplete. The Chernobyl findings are generally marginalized or even denied because of the low values of the estimated human exposures and the inconsistency of the results with the accepted risk models. One explanation for the observations is that physical dosimetric models have underestimated the effective exposure. This possibility is supported by biological dosimetry in the contaminated regions. The assumptions about effects after in utero exposure by incorporated radionuclides need to be revised.

Quantification of Radiation-Induced Genetic Risk

U H Ehling

Abstract

Associated with technical advances of our civilization is a radiation- and chemically-induced increase in the germ cell mutation rate in man. This would result in an increase in the frequency of genetic diseases and would be detrimental to future generations. It is the duty of our generation to keep this risk as low as possible. The estimation of the radiation-induced genetic risk of human populations is based on the extrapolation of results from animal experiments. Radiation-induced mutations are stochastic events. The probability of the event depends on the dose; the degree of the damage does not. The different methods to estimate the radiation-induced genetic risk will be discussed. The accuracy of the predicted results will be evaluated by a comparison with the observed incidence of dominant mutations in offspring born to radiation exposed survivors of the Hiroshima and Nagasaki atomic bombings. These methods will be used to predict the genetic damage from the fallout of the reactor accident at Chernobyl. For the exposure dose we used the upper limits of the mean effective life time equivalent dose from the fallout values in the Munich region. According to the direct method for the risk estimation we will expect for each 100 to 500 spontaneous dominant mutations one radiation-induced mutation in the first generation. With the indirect method we estimate a ratio of 100 dominant spontaneous mutations to one radiation-induced dominant mutation. The possibilities and the limitations of the different methods to estimate the genetic risk will be discussed. The discrepancy between the high safety standards for radiation protection and

the low level of knowledge for the toxicological evaluation of chemical mutagens will be emphasized.

Base de datos	Embase
Algoritmo final	('cleft lip'/exp OR 'cleft lip') AND ('prevalence'/exp OR prevalence OR 'incidence'/exp OR incidence OR 'epidemiology'/exp OR epidemiology) AND ('chernobyl'/exp OR chernobyl)

Cleft Lip and Cleft Palate Birth Rate in Bavaria Before and After the Chernobyl Nuclear Power Plant Accident

H Scherb , E Weigelt

Abstract

Background: Cleft lip and palates (CLP) occur with a frequency of between 1 and 2 cases in 1000 live births and thus belong to the most frequent congenital anomalies. In the former German Democratic Republic (GDR), records covering 1967-1989 for CLP newborns show a 9.4% increase of the prevalence of CLP from 1987 to 1989, possibly due to Chernobyl. DATA AND STATISTICAL METHOD: In Bavaria, all congenital malformations in children's hospitals have been recorded from 1984 to 1991. Among these data, 1324 cases with CLP were found. A spatial-temporal analysis aimed at uncovering a possible association of the CLP occurrence with the Chernobyl fallout on a district level, as well as a synoptic analysis of the GDR and Bavarian data, were carried out.

Results: In Bavaria, from October 1986 to December 1990, the CLP frequency increased by 9.5% (p=0.10) relative to the trend as computed from the remaining years. The association of CLP rates with fallout on a district level is reflected by a significant relative risk (RR) per kBq/m(2) of RR=1.008 (p=0.03). A synoptic analysis of the Bavarian data and the GDR data restricted to the overlapping time window from 1984 to 1989 discloses a simultaneous significant jump of the CLP prevalence

by 8.6% (p=0.02) after 1986.

Conclusion: The presumption of a long-term increase of CLP after exposure to Chernobyl fallout is corroborated by the analysis of the Bavarian congenital malformation data.

The Congenital Anomalies Registry in Belarus: A Tool for Assessing the Public Health Impact of the Chernobyl Accident

G Lazjuk , P Verger, B Gagnière, Zh Kravchuk, I Zatsepin, E Robert-Gnansia

Abstract

A national population-based malformation registry (BNR) has been in operation since 1979 in Belarus, one of the countries most heavily exposed to the contamination from the Chernobyl accident of 26 April 1986. We describe its methodology and its compliance with established criteria, evaluate the completeness of its reporting, and analyze the data collected in four administrative regions with contrasting contamination levels from 1983 through 1999. Nine easily diagnosed malformations have been monitored since 1983. Reporting completeness exceeds 85% for all periods and all regions. In all periods, the prevalence at birth of these malformations was lower in the most contaminated regions and showed a similar positive time trend in areas of low and high contamination. We conclude that the BNR is a reliable tool for studying the possible effects on congenital malformations caused by the Chernobyl accident. Although the trend we observed may be explained by better ascertainment and prenatal diagnosis, a real increase cannot be ruled out.

Teratology in the 20th Century: Environmental Causes of Congenital Malformations in Humans and How They Were Established

Harold Kalter

Discusses the teratology of congenital malformations in humans and the establishment of their environmental causes. The article first explores various aspects of congenital malformations and their teratology and also, early human studies and experiments. The article then focuses on various diseases like phenylketonuria, insulin dependent diabetes mellitus and hyperthermia as teratogens and discusses various environmental hazards and disasters. The article also discusses the effects of disease medications, alcohol consumption during pregnancy and various chemicals like folic acid and thalidomide on human malformations. The article concludes that the causes of major congenital malformations of external origin that have been discovered and are now known are relatively few, and questions that whether it is encouraging that maybe, further discovery of environmental causes of congenital malformations with major significance has reached a plateau or perhaps a breathing spell.

Facial Cleft Birth Rate in Former East Germany Before and After the Reactor Accident in Chernobyl

V Zieglowski , A Hemprich

Abstract

Cleft lip palates (CLP) are caused by a variety of factors. Ionizing radiation is only one of these factors. The meltdown of the nuclear reactor at Chernobyl on April 26, 1986, and the subsequent radioactive fallout did not cause any acute radiation sickness in Germany. Nevertheless, in West Berlin a significant increase of trisomy-21 cases was reported in births 9 months after the Chernobyl reactor accident. In our study we analyzed the influence of the radioactive fallout after

the Chernobyl disaster on the rate and regional distribution of CLP newborns in the former German Democratic Republic (GDR). In contrast to the Federal Republic of Germany an ongoing malformation register for CLP newborns had existed in the former GDR since 4 July 1967. Environmental data were collected from national and international environmental authorities and atomic energy agencies. Population statistics were taken from the statistical year-book of the former GDR. During a 10-year period from 1980 to 1989, the average number of CLP newborns in the GDR was 1.88 per 1,000 live births. A significant prevalence increase was recorded in 1983, 1987 und 1988. In comparison to the mean rate in the period from 1980 until 1986, 1987 demonstrated an increase of 9.4%. Regional prevalence increases were seen in the three northern districts of Schwerin, Rostock and Neubrandenburg, where the radioactivity measurements in general showed higher levels of the radionuclides caesium-137 und strontium-90 than in other districts. Owing to the comprehensive malformation register for CLP patients in the GDR, this is the first study for Germany, analyzing the CLP rate before and after the fallout in Chernobyl. The results support the allegation of the influence of radiation-induced increase of CLP newborns after the Chernobyl reactor accident.

Materiales y métodos

Tipo de estudio: Revisión Narrativa

Muestra: Artículos científicos donde se determine a partir de la investigación datos de prevalencia, incidencia y/o epidemiología del labio paladar hendido en poblaciones expuestas a la radiación después de las bombas atómicas de Hiroshima y Nagasaki, en 1945 y en adelante.

Artículos científicos donde se determine a partir de la investigación datos de prevalencia, incidencia y/o epidemiología del labio paladar hendido en poblaciones expuestas a la radiación después del accidente de Chernobyl en 1986 y en adelante.

Pregunta

Se estableció la pregunta. la cual orienta la revisión y es la que la revisión pretende responder:

¿Es la radiación un agente causal para el desarrollo de Labio Paladar Hendido, teniendo como base las poblaciones expuestas en el accidente de Chernobyl y las bombas atómicas en Hiroshima y Nagasaki?

Estructura de la revisión:

Teniendo en cuenta la pregunta, se estableció la estructura de la revisión de acuerdo a las siguientes subtemáticas:

- Chernobyl

  a) Efectos estocásticos:

  b) Nivel de contaminación

  c)Prevalencia de Labio Paladar Fisurado

  d)Tiempo

  e) Distancia

- Hiroshima

  a) Efectos estocásticos

  b) Nivel de contaminación

  c)Prevalencia de Labio Paladar Fisurado

  d)Tiempo

  e) Distancia

- Nagasaki

  a) Efectos estocásticos

  b) Nivel de contaminación

c)Prevalencia de Labio Paladar Fisurado

d)Tiempo

e) Distancia

Definición de las variables

Variable	Definición	Unidad de medida
Efectos estocásticos	Modificaciones en el DNA que podrán o no producir daños en la salud y/o integridad corporal producto de la radiación a largo y mediano plazo	Diferentes patologías presentes en las personas expuestas y en su descendencia
Nivel de contaminación	Concentración de elementos químicos radiactivos en el entorno de los diferentes países afectados	● mSv : Unidad de dosis equivalente de radiación absorbida ● Gy: Dosis absorbida de radiación ● Roetgen:medida de la exposición a la radiación
Prevalencia de labio paladar fisurado	Proporción de individuos que presentan labio paladar fisurado en las diferentes poblaciones expuestas a la radiación	Porcentaje (%)
Tiempo	Años transcurridos a partir de la radiación donde se presentaron efectos	Años
Distancia	Alcance de la nube radioactiva a lo largo de los diferentes paises	Kilómetros

Búsqueda de información:

Se establecieron las variables para cada temática a ser tratada en la revisión a partir de las de las cuales se establecieron las palabras claves para poder elaborar estrategias de búsqueda de cada una de las temáticas propuestas.

Palabras clave

Chernobyl	**Variables**	**Términos clave**
	Palabra clave	Chernobyl
	Término [MeSH]	Chernobyl Nuclear Accident
	Término [Emtree]	Chernobyl accident
	Sinonimo términos relacionados	Chernobyl atomic energy station accident Chernobyl atomic power station accident Chernobyl disaster
Efectos estocásticos	**Variables**	**Términos clave**
	Palabra clave	stochastic effects
	Término [MeSH]	Effect, Radiation
	Término [Emtree]	stochastic effects
	Sinonimo términos relacionados	Radiation Effect Effects, Radiation
Nivel de contaminación	**Variables**	**Términos clave**
	Palabra clave	Level Pollution
	Término [MeSH]	Air Pollutants, Radioactive
	Término [Emtree]	Air pollution
	Sinonimo términos relacionados	Pollutants, Radioactive Air Radioactive Air Pollutants
Prevalencia	**Variables**	**Términos clave**
	Palabra clave	Prevalence/Incidence/Epidemiology

	Término [MeSH]	Epidemiology
	Término [Emtree]	Epidemiology
	Sinonimo términos relacionados	Prevalence Incidence Epidemiology
Labio Paladar Fisurado	**Variables**	**Términos clave**
	Palabra clave	Cleft lip
	Término [MeSH]	Cleft Lip
	Término [Emtree]	cleft lip
	Sinonimo términos relacionados	Cleft Lips Lip, Cleft Lips, Cleft Harelip
Tiempo	**Variables**	**Términos clave**
	Palabra clave	Time
	Término [MeSH]	Time
	Término [Emtree]	Time
	Sinonimo términos relacionados	Longterm Effects Effects, Longterm Effect, Longterm Longterm Effect Long-Term Effects Long Term Effects Effects, Long-Term Effect, Long-Term

		Effects, Long Term Long-Term Effect
Distancia	**Variables**	**Términos clave**
	Palabra clave	Distance
	Término [MeSH]	Distance
	Término [Emtree]	Distance
	Sinonimo términos relacionados	Distant disease free survival
Hiroshima	**Variables**	**Términos clave**
	Palabra clave	Hiroshima
	Término [MeSH]	Hiroshima
	Término [Emtree]	Hiroshima
	Sinonimo términos relacionados	Japan Hiroshima accident
Nagasaki	**Variables**	**Términos clave**
	Palabra clave	Nagasaki
	Término [MeSH]	Nagasaki
	Término [Emtree]	Nagasaki
	Sinonimo términos relacionados	Nagasaki bomb Japan

Estructura de la estrategia de búsqueda (Algoritmos)

- **Chernobyl**

#1	Chernobyl
#2	Effect, Radiation OR stochastic model
#3	**#1+#2** ('chernobyl accident'/exp OR 'chernobyl accident') AND 'stochastic model'
#4	Air Pollutants, Radioactive OR Air pollution

#5	**#1+#4** ('chernobyl accident'/exp OR 'chernobyl accident') AND 'air pollution'
#6	prevalence OR incidence OR epidemiology
#7	Cleft lip palate OR malformations
#8	**#1+#6+#7** ('chernobyl accident'/exp OR 'chernobyl accident') AND prevalence AND 'cleft lip'
#9	**#1+#6+#7** (((Chernobyl) AND (((Prevalence) OR Incidence) OR Epidemiology)) AND Cleft lip palate) OR malformations
#10	**#1+#2+#7** ((Chernobyl) AND (Effect, Radiation OR stochastic model)) AND (Cleft lip palate OR malformations)
#11	**#1+#7+#5** ((Chernobyl) AND (Cleft lip palate OR malformations)) AND (('chernobyl accident'/exp OR 'chernobyl accident') AND 'air pollution' AND 'cleft lip')
#12	**#1+#7+#4** ((Chernobyl) AND (Cleft lip palate OR malformations)) AND (Air PollutaAir Pollutants, Radioactive OR Air pollutionnts, Radioactive OR Air pollution)

- **Hiroshima**

#1	Hiroshima
#2	Effect, Radiation OR stochastic model
#3	**#1+#2** (hiroshima AND (effect, AND radiation OR stochastic) AND model) (Effect, Radiation OR stochastic model) AND (Hiroshima)
#4	Air Pollutants, Radioactive OR Air pollution
#5	**#3+#4** ((Effect, Radiation OR stochastic model) AND (Hiroshima)) AND (Air Pollutants, Radioactive OR Air pollution)
#6	Cleft lip palate OR malformations
#7	#3+#6

	(hiroshima AND (effect, AND radiation OR stochastic) AND model AND 'congenital malformation')
#8	Prevalence OR incidence OR Epidemiology
#9	**#5+#6+#8** ((((Effect, Radiation OR stochastic model) AND (Hiroshima)) AND (Air Pollutants, Radioactive OR Air pollution)) AND (Cleft lip palate OR malformations)) AND (Prevalence OR incidence OR Epidemiology)

- **Nagasaki**

#1	Nagasaki
#2	Effect, Radiation OR stochastic model
#3	**#1+#2** (Effect, Radiation OR stochastic model) AND (Nagasaki)
#4	Air Pollutants, Radioactive OR Air pollution
#5	**#3+#4** ((Effect, Radiation OR stochastic model) AND (Nagasaki)) AND (Air Pollutants, Radioactive OR Air pollution)
#6	Cleft lip palate OR malformations
#7	**#3+#6** (Nagasaki AND (effect, AND radiation OR stochastic) AND model AND 'congenital malformation')
#8	Prevalence OR incidence OR Epidemiology
#9	**#5+#6+#8** ((((Effect, Radiation OR stochastic model) AND (Nagasaki)) AND (Air Pollutants, Radioactive OR Air pollution)) AND (Cleft lip palate OR malformations)) AND (Prevalence OR incidence OR Epidemiology)

Resultados de la aplicación de la estrategia de búsqueda

- **Chernobyl**

Base de datos	**EMBASE**		
Búsqueda	**Algoritmo**	**Cantidad de artículos encontrados**	**Cantidad de artículos seleccionados por Título/ abstract**
#1	Chernobyl	5.347	
#2	Effect, Radiation OR stochastic model	5.347	
#3	('chernobyl accident'/exp OR 'chernobyl accident') AND 'stochastic model'	9	3
#4	Air Pollutants, Radioactive OR Air pollution	126,887	
#5	('chernobyl accident'/exp OR 'chernobyl accident') AND 'air pollution'	155	8
#6	prevalence OR incidence OR epidemiology	3,487,091	
#7	Cleft lip palate OR malformations	105.592	
#8	('chernobyl accident'/exp OR 'chernobyl accident') AND prevalence AND 'cleft lip'	3	1
#9	(((Chernobyl) AND (((Prevalence) OR Incidence) OR Epidemiology)) AND Cleft lip palate) OR malformations	87.283	
#10	((Chernobyl) AND (Effect, Radiation OR stochastic model)) AND (Cleft lip palate OR malformations)	0	
#11	((Chernobyl) AND (Cleft lip palate OR malformations)) AND (('chernobyl accident'/exp OR 'chernobyl accident') AND 'air pollution' AND 'cleft lip')	1	1
#12	(Chernobyl) AND (Cleft lip palate OR malformations)) AND (Air PollutaAir Pollutants,	1	1

	Radioactive OR Air pollutionnts, Radioactive OR Air pollution)		

Base de datos	**PUBMED**		
Búsqueda	**Algoritmo**	**Cantidad de artículos encontrados**	**Cantidad de artículos seleccionados por Título/ abstract**
#1	Chernobyl	5.106	-
#2	Effect, Radiation OR stochastic model	418.566	-
#3	('chernobyl accident'/exp OR 'chernobyl accident') AND 'stochastic model'	14	2
#4	Air Pollutants, Radioactive OR Air pollution	84.784	-
#5	('chernobyl accident'/exp OR 'chernobyl accident') AND 'air pollution'	165	8
#6	prevalence OR incidence OR epidemiology	3.402.244	-
#7	Cleft lip palate OR malformations	1,012,464	-
#8	('chernobyl accident'/exp OR 'chernobyl accident') AND 'air pollution' AND 'cleft lip'	2	1
#9	(((Chernobyl) AND (((Prevalence) OR Incidence) OR Epidemiology)) AND Cleft lip palate) OR malformations	1,010,956	-
#10	((Chernobyl) AND (Effect, Radiation OR stochastic model)) AND (Cleft lip palate OR malformations)	193	31
#11	((Chernobyl) AND (Cleft lip palate OR malformations)) AND (('chernobyl accident'/exp OR 'chernobyl accident') AND 'air pollution' AND 'cleft lip')	2	1

#12	((Chernobyl) AND (Cleft lip palate OR malformations)) AND (Air PollutaAir Pollutants, Radioactive OR Air pollutionnts, Radioactive OR Air pollution)	18	8

- **Hiroshima**

Base de datos	**EMBASE**		
Búsqueda	**Algoritmo**	**Cantidad de artículos encontrados**	**Cantidad de artículos seleccionados por Título/ abstract**
#1	Hiroshima	53.424	-
#2	Effect, Radiation OR stochastic model	69.399	-
#3	**#1+#2** 'hiroshima accident' OR (('accident'/exp OR accident) AND hiroshima AND (effect, AND ('radiation'/exp OR radiation) OR stochastic) AND ('model'/exp OR model))	7	1
#4	Air Pollutants, Radioactive OR Air pollution	126,887	-
#5	**#3+#4** ((Effect, Radiation OR stochastic model) AND (Hiroshima)) AND (Air Pollutants, Radioactive OR Air pollution)	0	-
#6	Cleft lip palate OR malformations	3,487,091	-
#7	**#3+#6** ('hiroshima bomb' OR (hiroshima AND ('bomb'/exp OR bomb))) AND (effect, AND radiation OR 'stochastic model') AND (cleft AND lip AND palate OR malformations)	5	3

#8	Prevalence OR incidence OR Epidemiology	3	0
#9	**#5+#6+#8** ((((Effect, Radiation OR stochastic model) AND (Hiroshima)) AND (Air Pollutants, Radioactive OR Air pollution)) AND (Cleft lip palate OR malformations)) AND (Prevalence OR incidence OR Epidemiology)	0	-

Base de datos	**PUBMED**		
Búsqueda	**Algoritmo**	**Cantidad de artículos encontrados**	**Cantidad de artículos seleccionados por** **Título/ abstract**
#1	Hiroshima	32.352	**-**
#2	Effect, Radiation OR stochastic model	418.566	**-**
#3	**#1+#2** (hiroshima AND (effect, AND radiation OR stochastic) AND model) (Effect, Radiation OR stochastic model) AND (Hiroshima)	2.153	**-**
#4	Air Pollutants, Radioactive OR Air pollution	84.438	-
#5	**#3+#4** ((Effect, Radiation OR stochastic model) AND (Hiroshima)) AND (Air Pollutants, Radioactive OR Air pollution)	19	4
#6	Cleft lip palate OR malformations	1.012464	**-**
#7	#3+#6 (hiroshima AND (effect, AND radiation OR stochastic) AND model AND 'congenital malformation')	121	10
#8	Prevalence OR incidence OR Epidemiology	3.402.244	-

#9	**#5+#6+#8** ((((Effect, Radiation OR stochastic model) AND (Hiroshima)) AND (Air Pollutants, Radioactive OR Air pollution)) AND (Cleft lip palate OR malformations)) AND (Prevalence OR incidence OR Epidemiology)	1	0

- **Nagasaki**

Base de datos	**EMBASE**		
Búsqueda	**Algoritmo**	**Cantidad de artículos encontrados**	**Cantidad de artículos seleccionados por** **Título/ abstract**
#1	Nagasaki	35.342	-
#2	Effect, Radiation OR stochastic model	5.347	-
#3	**#1+#2** (Effect, Radiation OR stochastic model) AND (Nagasaki)	99	1
#4	Air Pollutants, Radioactive OR Air pollution	126,887	-
#5	**#3+#4** ((Effect, Radiation OR stochastic model) AND (Nagasaki)) AND (Air Pollutants, Radioactive OR Air pollution)	1	0
#6	Cleft lip palate OR malformations	3,487,091	**-**
#7	**#3+#6** (Nagasaki AND (effect, AND radiation OR stochastic) AND model AND 'congenital malformation')	1	0

#8	Prevalence OR incidence OR Epidemiology	3	-
#9	**#1+#6+#8** ('nagasaki bomb' OR (nagasaki AND ('bomb'/exp OR bomb))) AND 'congenital malformation' AND radiation AND epidemiology	13	9

Base de datos	**PUBMED**		
Búsqueda	**Algoritmo**	**Cantidad de artículos encontrados**	**Cantidad de artículos seleccionados por** **Título/ abstract**
#1	Nagasaki	21.457	**-**
#2	Effect, Radiation OR stochastic model	418.566	**-**
#3	**#1+#2** (Effect, Radiation OR stochastic model) AND (Nagasaki)	1,084	**-**
#4	Air Pollutants, Radioactive OR Air pollution	86,438	-
#5	**#3+#4** ((Effect, Radiation OR stochastic model) AND (Nagasaki)) AND (Air Pollutants, Radioactive OR Air pollution)	13	1
#6	Cleft lip palate OR malformations	1,012,464	-
#7	**#3+#6** ((Effect, Radiation OR stochastic model) AND (Nagasaki)) AND (Cleft lip palate OR malformations)	75	4
#8	Prevalence OR incidence OR Epidemiology	3,402,244	-
#9	**#5+#6+#8** ((((Effect, Radiation OR stochastic model) AND (Nagasaki)) AND (Air Pollutants, Radioactive OR Air pollution)) AND (Cleft lip palate OR	1	0

	malformations)) AND (Prevalence OR incidence OR Epidemiology)		

Selección de artículos por algoritmos de búsqueda y bases de datos

- **Chernobyl**

Base de datos	**PUBMED**
Algoritmo	(Chernobyl) AND (Cleft lip palate OR malformations)) AND (Air PollutaAir Pollutants, Radioactive OR Air pollutionnts, Radioactive OR Air pollution)

Chornobyl 30 years later: Radiation, pregnancies, and developmental anomalies in Rivne, Ukraine

In the 30 years since the Chornobyl nuclear power plant disaster, there is evidence of persistent levels of incorporated ionizing radiation in adults, children and pregnant women in the surrounding area. Measured levels of Cesium-137 vary by region, and may be influenced by dietary and water sources as well as proximity to nuclear power plants. Since 2000, comprehensive, population-based birth defects monitoring has been performed in selected regions of Ukraine to evaluate trends and to generate hypotheses regarding potential causes of unexplained variations in defect rates. Significantly higher rates of microcephaly, neural tube defects, and microphthalmia have been identified in selected regions of Ukraine collectively known as Polissia compared to adjacent regions collectively termed non-Polissia, and these significantly higher rates were evident particularly in the years 2000-2009. The Polissia regions have also demonstrated higher mean whole body counts of Cesium-137 compared to values in individuals residing in other non-Polissia regions. The potential causal relationship between persistent ionizing radiation pollution and selected congenital anomaly rates supports the need for a more thorough, targeted investigation of the sources of persistent ionizing radiation and the biological plausibility of a potential teratogenic effect.

Birth defects on Chernobyl radionuclide polluted territories

147318 pregnancy outcomes were analyzed in Zhytomyrska Oblast during 2000-2010; the descriptive analysis was performed. The frequency of birth defects was estimated among newborns, still-born babies and abortions due to genetic disorders of a fetus on "clean" and polluted territories. There was an increase of all birth defects on the polluted territories; among newborns it was (26.10 ± 0.80) per thousand and (24.23 ± 0.47) per thousand, $p < 0.05$; among newborns and still-born babies it was (26.54 ± 0.81) per thousand and (24.78 ± 0.48) per thousand, $p < 0.06$. The increase in the birth defects of the nervous system was detected: among newborns it was (1.09 ± 0.17) per thousand and (0.75 ± 0.08) per thousand, $p < 0.05$; among newborns and still-born babies it was (1.22 ± 0.18) per thousand and (0.81 ± 0.09) per thousand, p. < 0.05; among newborns, still-born babies and genetically caused abortions it was 2.76 ± 0.26) per thousand and (2.34 ? 0.15) per thousand, $p = 0.165$. X2 criteria confirmed the difference between the frequency of birth defects on "clean" and polluted territories. Estimation by Bayes did not confirm the hypothesis about the difference between the frequency of birth defects on "clean" and polluted territories. Endocrine diseases were confirmed to be an important factor of the origin of birth defects, which is important for planning pregnancy on both polluted and "clean" territories.

Teratogen update: radiation and Chernobyl

The 1986 nuclear reactor accident at Chernobyl caused nonuniform radiocontamination of air and land, primarily within regions of the former Soviet Union and Western Europe. Major exposure groups included the reactor workers, villagers evacuated from within 30 km of the accident, the "liquidators" who decontaminated the evacuation zone afterward, those in radiocontaminated villages not evacuated, and "others" not in the latter categories. The possibility of being exposed to radiation caused considerable anxiety, especially among pregnant women. Were teratogenic levels of radiation (> or = 0.1 Gy) exposure attained? To date there is no consistent proof that this level of radiation exposure was received. Nevertheless, thousands of induced abortions were perf ormed. Radioiodine (I-131) caused thyroid cancer in young children in portions of Belarus, the Ukraine, and Russia. It is not known but very possible that I-131 fetal thyroid exposure contributed to this observation. The relationship between mental retardation and radiation exposure has not been confirmed. Leukemia and other cancers, while predicted for the liquidators (mainly males), has not been found in the other exposure groups at this time. Investigations of aborted fetuses and newborns in Belarus showed an increase in the frequency of both congenital and fetal abnormalities in high and low Cs-137 contaminated regions. This study is unreliable due to detection and selection biases. Accident and environmental factors unrelated to radiation doses may have contributed to these observations. Occasional positive teratogenic studies in less contaminated regions of Westem Europe are suspect because of the low radiation doses received. There is no substantive proof regarding radiation-induced teratogenic effects from the Chernobyl accident.

Chronicled report on the period from May 1 to September 27, 1989. Discussion of risk factors

The Institute of Mother and Child was invited in 1988 by professor J. Nauman to his Chernobyl program, so as to inspect children born after Chernobyl accident, particularly these born in first days following the accident dated 26 april 1986. The central part of Poland is covered with screening for congenital PKU and hypothyroidism therefore all children had estimated TSH-spot levels between 3rd and 5th day of life. So as to control the present state of general health and thyroid state in the study group a questionnaire with a letter to parents explaining the aim of the inquiry was sent to the parents (see addenda). About 14000 letters were send from which around 12000 responses were returned to the Institute. From informations received this way we draw the preliminary conclusion that no significant damage in health of these children or their siblings can be found. About 20% of the mothers admitted taking the Lugol solution in a last day of pregnancy. However it should be taken into account that these data were collected 2 years after the accident and are not fully reliable. In the period 1989-1990 a group of 1912 children (938 boys and 974 girls) was called to the Department of Endocrinology of the Institute and inspected. The age was from 2.9 to 4.2 years. All children had screening TSH-spot test result negative (below 30 microIU/ml). General health state The general health state of the children inspected was good. Only 33 of them (1.7%) had various congenital malformations what is not different from general population of polish children. Mental development was in 1897 cases normal, in 15 cases IQ was decreased and the score varied from 75 to 80 according the Brunet-Lezine scale. Average physical development was normal. Body height evaluated in standard deviation score (SDS) was as follows: SDS = 0.0 in 359; SDS = +0.9 +/- 0.6 in 906 and SDS = -0.5 +/- 0.3 in 647 cases. Thyroid state At 1904 inspected and analytically estimated children the thyroid function was normal. Only in 8 cases (0.8%) a goiter was found with euthyroid state. Analytical data were as follows: total T4 serum level = 111.8 + 43.1 nmol/l (50.4-171.9), ref. value: 50.1-170.0 nmol/l; total T3 serum level = 2.5 +/- 0.4 nmol/l (ref. value 1.9-3.6);

TSH serum level 4.4 +/- 2.6 uIU/ml. Trace amounts of antithyroid membrane antibodies were found at 12 children (0.63%) of the group in serum diluted 1:250.(ABSTRACT TRUNCATED AT 400 WORDS)

Les fentes labiopalatines et l'environnement en Russie

Les 89 re´gions composant la Fe´de´ration de Russie sont peu-ple´es par des groupes ethniques aux caracte´ristiques e´pide´- miologiques spe´cifiques. Les habitants de certaines re´gions industrielles subissent par ailleurs l'influence d'une pollution intense aux conse´quences me´dicales lourdes. Enfin, plusieurs catastrophes sanitaires ont marque´ la seconde moitie´ du xxe sie`cle. De nombreuses e´tudes re´centes publie´es en langue russe ont analyse´ l'influence de ces contraintes sur la mor- phogene`se faciale et donnent un e´clairage inte´ressant a`l'e´pide´miologie des fentes labiopalatines en Russie.

The genetic sequelae of the Chelyabinsk and Chernobyl radioactive contaminations

Genetic consequences of radioactive fall-outs of the Chelyabinsk plant producing plutonium (1949-1952) and the Chernobyl accident have been analysed. Three powerful radioactive fall-outs caused a population genetic dose of 682,801 cSv per 217,750 persons (the average dose was 2.25 cSv). Individual variations were from 1-2 mSv to 1.2 Sv or more. The population genetic dose from the Chernobyl accident was higher (32 x 10(6) man/cSv), but the individual dose was lower (mainly no more than 1 cSv). Progenic analyses of residents of radiation contaminated areas showed no increase in the incidence of congenital anomalies, spontaneous abortions, developmental microanomalies, and Down syndromes (except Byelorussia). Calculations of genetic consequences for the Ural region demonstrated that only in the most contaminated area (the average gonadal dose was 19.5 cSv); a 4.13% increase of the spontaneous level could be observed. In all other areas it was less than 1%. It is difficult to reveal possible genetic consequences of the Chernobyl accident using the real sample size of the newborns. Even in the areas with fall-outs above 15 Ci/km2, the incidence of congenital anomalies did not exceed 1% of the spontaneous level.

Evaluation of the impact of Chernobyl on the prevalence of congenital anomalies in 16 regions of Europe. EUROCAT Working Group

Background: Surveillance data from population-based congenital anomaly registers in 16 regions of Europe (mainly Western Europe) were analysed to assess the impact of the Chernobyl accident on the prevalence of selected congenital anomalies.

Methods: Three cohorts of pregnancies were defined: those exposed during the first month following Chernobyl (External Exposure Cohort), the first year (Total Exposure Cohort) and the two subsequent years (Control Cohort). Expected numbers of congenital anomalies in these cohorts were calculated from 1980-1985 baseline rates. Registries were grouped into three exposure categories according to first-year exposure estimates.

Results: There was no overall or dose-related increase in prevalence in the two exposed cohorts for Down's Syndrome, neural tube defects, other central nervous system defects or eye defects. There was a statistically significant overall 22% (95% CI: 13-31%) excess of Down's Syndrome in the Control Cohort, with no dose-response relationship.

Conclusions: Chernobyl had no detectable impact on the prevalence of congenital anomalies in Western Europe, suggesting that in retrospect the widespread fear in the population about the possible effects of exposure on the unborn fetus was not justified. An increasing prevalence of Down's Syndrome in the 1980s, probably unrelated to Chernobyl, merits further investigation.

Iodine 131: biokinetics, radiation exposure and risk assessment with reference to the reactor accident at Chernobyl

Following the reactor accident at Chernobyl, this paper describes the biokinetics of radioiodine in man and discusses the radiation exposure resulting from intake of 131I. The risk of radiation-induced thyroid carcinomas and of congenital abnormalities is evaluated. Assuming a linear dose/risk relationship, one can calculate an increase in mortality from thyroid carcinomas amongst children in southern Germany of 100 to 101 per million children. For adults in southern Germany, and for the rest of the population in Germany, the figure is considerably lower. Gonadal dose from the 131I released is so small, compared with the annual natural radiation exposure, that it is not appropriate to discuss genetic effects.

Base de datos	**PUBMED**
Algoritmo	((Chernobyl) AND (Effect, Radiation OR stochastic model)) AND (Cleft lip palate OR malformations)

Radiation Exposure In Pregnancy

Choosing the most appropriate imaging modality for pregnancy patients is a common clinical question encountered daily. The general principle for imaging during pregnancy is similar to imaging for the general population, with the goal of radiation exposure being as low as reasonably achievable (ALARA). What is unique during pregnancy is that fetus radiation exposure is an essential factor in deciding optimal imaging studies. Understanding of consequences of radiation exposure on a fetus, degrees of fetal radiation exposure by each imaging modality, and techniques on reducing fetal radiation exposure is vital in choosing the best diagnostic imaging modality. While it is crucial to minimize fetal radiation exposure as much as possible, it is essential to remember that diagnostic studies should not be avoided for fear of radiation exposure, especially when these studies can dramatically change patient management. This activity will discuss the consequences of radiation exposure on a fetus, degrees of radiation exposure by each modality, and techniques of reducing fetal radiation exposure. Solid understanding of how each imaging modality contributes to fetal radiation dose will significantly help in choosing the most appropriate imaging study that provides

the best diagnostic information at the lowest level of radiation exposure. The consequence of radiation exposure in fetuses is mostly based on observations rather than based on scientific research. Ethical issues prohibit researching on the fetus. Therefore, most of the data on the impact of radiation on the fetus derives from observations of patients who suffered Japan's Hiroshima bombing and the Chernobyl nuclear power plant disaster. Based on the observations made from the victims of the high level of radiation exposure, the consequences of radiation exposure can categorize into four broad groups, including pregnancy loss, malformation, developmental delay or retardation, and carcinogenesis. Pregnancy loss most often happens when radiation exposure happens during early gestation (less than two weeks). Malformations of body parts and developmental delays occur during the organogenesis period (2 weeks to 8 weeks) and are dependent on the radiation dose. Below the threshold level of radiation exposure, there is minimal disruption of organogenesis. Above the threshold, the degree of malformation is related to the dose of the radiation. Lastly, carcinogenesis is considered a stochastic effect. In other words, cancer can develop at any level of radiation exposure. However, the probability of developing cancer increases with the increase in the dose of radiation. In the United States, the background radiation exposure for the whole body per year is estimated to be 3.1 mSv (310 mrem). United States Nuclear Regulation Commission (USNRC) also recommends total fetus exposure during pregnancy to be less than 5.0 mSv (500 mrem). The fetus radiation dose below 50 mGy is considered safe and not cause any harm. According to the Center for Disease Control (CDC), radiation dose between 50 mGy to 100 mGy is regarded inconclusive in terms of impact on the fetus. Doses above 100 mGy, especially doses above 150 mGy, are viewed as the minimum amount of dosage at which negative fetal consequences will occur, based on observation. The majority of the diagnostic studies performed during the pregnancy are below the threshold level. The effect of radiation exposure during pregnancy also depends on the gestational age of the fetus. The embryo/fetus is most susceptible to radiation during organogenesis (2 to 7 weeks gestational age) and in the first trimester. The fetus is more resistant to the radiation during the second and third trimester. Dose between 0.05 to 0.5 Gy is generally considered safe for the fetus during the second and third trimester while it is considered potentially harmful during the 1st-trimester fetus. Even though the fetus is more resistant to the radiation during the second and third trimester, a high dose of radiation (greater than 0.5 Gy or 50 rad) may result in adverse effects including miscarriage, growth reduction, IQ reduction, and severe mental retardation. Therefore, clinicians and radiologists should counsel the pregnant patient regardless of the gestational age. Occupational radiation exposure for a pregnant employee should be monitored to make sure the total amount of radiation exposure is under the regulatory limit. According to the National Council of Radiation Protection and Measurement (NCRP), the total dose equivalent to the embryo/fetus should not exceed 500 mRem during the length of the pregnancy. It should not exceed 50mRem in any month during pregnancy. The practice decision on selecting the most appropriate imaging modality for pregnancy should have their basis in the expert opinions of the treating clinician. Nonetheless, the American College of Radiology does provide recommendations on the appropriateness of imaging modalities in accessing common clinical conditions. Each imaging modality is categories into usually appropriate, may be appropriate, and usually not appropriate. For instance, for a pregnant patient presenting with right lower abdominal pain concerning for appendicitis, ultrasound and MRI are usually appropriate imaging modality. CT abdomen and pelvis with or without contrast is categorized as may be appropriate. Abdominal radiograph, Tc-99m WBC scan, and fluoroscopy contrast enema are considered usually

not appropriate. The American College of Radiology appropriateness criteria provides the current practice policies and guidelines in the US regarding imaging in pregnant patients.

Cleft lip and cleft palate birth rate in Bavaria before and after the Chernobyl nuclear power plant accident

Background: Cleft lip and palates (CLP) occur with a frequency of between 1 and 2 cases in 1000 live births and thus belong to the most frequent congenital anomalies. In the former German Democratic Republic (GDR), records covering 1967-1989 for CLP newborns show a 9.4% increase of the prevalence of CLP from 1987 to 1989, possibly due to Chernobyl. DATA AND STATISTICAL METHOD: In Bavaria, all congenital malformations in children's hospitals have been recorded from 1984 to 1991. Among these data, 1324 cases with CLP were found. A spatial-temporal analysis aimed at uncovering a possible association of the CLP occurrence with the Chernobyl fallout on a district level, as well as a synoptic analysis of the GDR and Bavarian data, were carried out.

Results: In Bavaria, from October 1986 to December 1990, the CLP frequency increased by 9.5% (p=0.10) relative to the trend as computed from the remaining years. The association of CLP rates with fallout on a district level is reflected by a significant relative risk (RR) per kBq/m(2) of RR=1.008 (p=0.03). A synoptic analysis of the Bavarian data and the GDR data restricted to the overlapping time window from 1984 to 1989 discloses a simultaneous significant jump of the CLP prevalence by 8.6% (p=0.02) after 1986.

Conclusion: The presumption of a long-term increase of CLP after exposure to Chernobyl fallout is corroborated by the analysis of the Bavarian congenital malformation data

Before and after Chernobyl Accident (Memoirs, Researches Hypotheses

In the first part of the article the results of studies performed in the 1970-1980s on the progeny of irradiated animals (drosophila, mouse, rat) are presented. It was found that except severe disorders in this progeny named non target genetic radiation effects were observed (genome instability, increased cancer risk, impaired fitness) which were similar to the late somatic radiation effects. The hypothesis on the likeness of pathogenic nature of somatic and genetic effects of ionizing radiation was proposed. Comparison of effects of parental irradiation in humans and animals gave reason to propose that the frequency of severe disorders observed in the progeny (stillbirth, birth defects etc.) depends on the reproductive potential of a species. In the second part of the article the reminiscences on the author's work in Chernobyl in 1987 are presented. The last part is devoted to description of the main results, obtained in the post Chernobyl period in the frames of various national and international projects.

De novo congenital malformation frequencies in children from the Bryansk region following the Chernobyl disaster (2000-2017)

Background: Ionizing radiation and chemical pollution can disrupt normal embryonic development and lead to congenital malformations and fetal death. We used official government statistical data

for 2000-2017 to test the hypothesis that radioactive and chemical pollutants influenced the frequency of de novo congenital malformations in newborns of the Bryansk region of southwest Russia.

Methods: A variety of statistical approaches were used to assess congenital malformation frequencies including the Shapiro-Wilk test, White's homoscedasticity test, Wilcoxon T-test, Spearman's rank correlation test, and the inversely proportional regression.

Results: We found that the frequency of polydactyly, multiple congenital malformations, and the frequency of de novo congenital malformations in newborns were significantly higher ($p = 0.001$-0.054) in regions with elevated radioactive, chemical and combined contamination. Polydactyly, multiple congenital malformations, and the sum of all congenital malformations were 4.7-7.4 times, 2.5-6.8 times, and 3.5-4.6 times higher in contaminated regions in comparison with the control group. The combination of both radioactive and chemical pollutants led to significantly higher frequencies of multiple congenital malformations when compared to regions with only one pollutant (radiation alone: 2.2 times, $p = 0.034$; chemical pollutants alone: 1.9 times, $p = 0.008$) implying that the effects of these stressors were at minimum additive. Although there was a trend for decreasing frequencies of multiple congenital malformations during the 2000-2017 period in areas of combined pollution, the opposite was true for regions with radioactive or chemical pollutants alone. However, overall, our models suggest that the frequency of multiple congenital malformations in areas of combined pollution will significantly ($p = 0.027$) exceed the frequencies observed for regions containing radioactive or chemical pollutants alone by 39.6% and 45.7% respectively, by 2018-2023.

Conclusion: These findings suggest additive and potentially synergistic effects of radioactive and chemical pollutants on the frequencies of multiple congenital malformations in the Bryansk region of southwestern Russia.

Karyopathological traits of thyrocytes and exposure to radioiodines in Belarusian children and adolescents following the accident at the Chernobyl nuclear power plant

The Belarus-American (BelAm) thyroid study cohort consists of persons who were 0-18 years of age at the time of exposure to radioactive iodine fallout from the 1986 Chernobyl nuclear power plant accident and who have undergone serial thyroid screenings with referral for fine-needle aspiration biopsy (FNAB) using standardized criteria. We investigated thyrocyte nuclear abnormalities in cytological samples from FNABs in 75 BelAm subjects with single and multiple thyroid nodules and 47 nodular goiter patients from Leningrad, Russia, unexposed to Chernobyl fallout. Nuclear abnormalities examined included internuclear chromosome bridges and derivative nuclei with broken bridges (i.e., "tailed" nuclei), which are formed from dicentric and ring chromosomes and thus may be cellular markers of radiation exposure. Among subjects with single-nodular goiter, thyrocytes with bridges were present in 86.8% of the exposed BelAm cohort compared with 27.0% of unexposed controls. The average frequency of thyrocytes with bridges and with tailed nuclei was

also significantly higher in the BelAm subjects than in controls. Among subjects with multinodular goiters, thyrocytes with bridges were present in 75.7% of exposed BelAm patients compared with 16.7% of unexposed controls; thyrocytes with tailed nuclei were observed in all of the BelAm subjects but in only 40% of controls, and the mean frequencies of bridges and tailed nuclei were significantly higher in the exposed group. Unusually, long bridges were detected in 29% of BelAm patients with single-nodular goiters and 35% of those with multinodular goiters, while no such abnormalities were observed among patients from the Leningrad region. In the exposed subjects from BelAm, we also found positive correlations between their estimated dose of Iodine-131 from Chernobyl fallout and the frequency of tailed nuclei ($p = 0.008$) and bridges ($p = 0.09$). Further study is needed to confirm that these phenomena represent consequences of radiation exposure in the human organism.

Changes in health status of child population of Ukraine after Chernobyl catastrophe

Introduction: The article is concerned with problems of morbidity of children and infant mortality during the latest 30th years after Chernobyl catastrophe. The 30th anniversary of the Chornobyl disaster is a stage that determines the analysis of its consequences, the assessment of the effects of radiation, the impact of the accident factors on the health of the population of the most affected countries and on global processes.

The aim: To study the condition of child population of regions of Ukraine, which were contaminated by radionuclides in the result of Chernobyl catastrophe.

Material and methods: Statistic assessment and epidemiological analysis were used to analyze materials of the investigations.

Conclusions: Results of comparative analysis demonstrate the stabile increase of morbidity level as residents of regions of TRC. Abnormalities of respiratory system present the first group of the morbidity among children. The morbidity level of blood and blood forming diseases, tumors formation, diseases of endocrine system, digestive disorders, metabolism disorders significantly increases. The level of child population morbidity after Chernobyl catastrophe increases in 3.2 times. Respiratory diseases are involved in the first place in this structure.Introduction: The article is concerned with problems of morbidity of children and infant mortality during the latest 30th years after Chernobyl catastrophe. The 30th anniversary of the Chornobyl disaster is a stage that determines the analysis of its consequences, the assessment of the effects of radiation, the impact of the accident factors on the health of the population of the most affected countries and on global processes.

The aim: To study the condition of child population of regions of Ukraine, which were contaminated by radionuclides in the result of Chernobyl catastrophe.

Material and methods: Statistic assessment and epidemiological analysis were used to analyze materials of the investigations.

Conclusions: Results of comparative analysis demonstrate the stabile increase of morbidity level as residents of regions of TRC. Abnormalities of respiratory system present the first group of the morbidity among children. The morbidity level of blood and blood forming diseases, tumors formation, diseases of endocrine system, digestive disorders, metabolism disorders significantly increases. The level of child population morbidity after Chernobyl catastrophe increases in 3.2 times. Respiratory diseases are involved in the first place in this structure.

Chronic radiation exposure in the Rivne-Polissia region of Ukraine: implications for birth defects

Objectives: The health effects of chronic low-dose radiation exposure remains a controversial question. Monitoring after the Chernobyl nuclear accident in Ukraine suggested that chronic low-dose radiation exposure was not linked to cancer mortality among the general population. However, elevated rates of birth defects in contaminated compared to uncontaminated regions suggest that exposure to radiation in utero might impact development and that chronic radiation exposure might represent an underestimated risk to human health.

Methods: We sought to determine current radiation exposure routes in Rivne-Polissia, a region of Ukraine contaminated by the Chernobyl accident. This represents a first step toward comprehensive studies of the effects of chronic radiation exposure on human health. We designed and administered a dietary and activity survey to 344 women in Polissia. We assessed types and sources of food consumed, types of outdoor activities, and alcohol intake.

Results: Alcohol intake was low and alone does not account for the observed high rates of birth defects. Wild foods, especially mushrooms and berries, and locally produced foods, especially milk related, were major radiation exposure routes. Additionally, women were exposed to radiation through inhalation while burning grasses and potato vines in fields, and wood for cooking and heating.

Conclusions: Twenty four years after the Chernobyl accident, women continue to be chronically exposed to low-dose radiation at levels exceeding current recommendations. This might contribute (especially synergistically with alcohol consumption and micronutrient deficiencies) to higher prevalence of birth defects in areas of Ukraine with high levels of radiation contamination compared to uncontaminated areas.

Facial cleft birth rate in former East Germany before and after the reactor accident in Chernobyl

Cleft lip palates (CLP) are caused by a variety of factors. Ionizing radiation is only one of these factors. The meltdown of the nuclear reactor at Chernobyl on April 26, 1986, and the subsequent radioactive fallout did not cause any acute radiation sickness in Germany. Nevertheless, in West Berlin a significant increase of trisomy-21 cases was reported in births 9 months after the Chernobyl reactor accident. In our study we analyzed the influence of the radioactive fallout after the Chernobyl disaster on the rate and regional distribution of CLP newborns in the former German Democratic Republic (GDR). In contrast to the Federal Republic of Germany an ongoing malformation register for CLP newborns had existed in the former GDR since 4 July 1967. Environmental data were collected from national and international environmental authorities and atomic energy agencies. Population statistics were taken from the statistical year-book of the former GDR. During a 10-year period from 1980 to 1989, the average number of CLP newborns in the GDR was 1.88 per 1,000 live births. A significant prevalence increase was recorded in 1983, 1987 und 1988. In comparison to the mean rate in the period from 1980 until 1986, 1987 demonstrated an increase of 9.4%. Regional prevalence increases were seen in the three northern districts of Schwerin, Rostock and Neubrandenburg, where the radioactivity measurements in general showed higher levels of the radionuclides caesium-137 und strontium-90 than in other districts. Owing to the comprehensive malformation register for CLP patients in the GDR, this is the first study for Germany, analyzing the CLP rate before and after the fallout in Chernobyl. The results support the allegation of the influence of radiation-induced increase of CLP newborns after the Chernobyl reactor accident.

The evidence of radiation effects in embryos and fetuses exposed to Chernobyl fallout and the question of dose response

Current legal frameworks for radiation exposure limits are based on the risk models of the International Commission on Radiological Protection (ICRP). In Publication 90 (2003), ICRP presents a safe (threshold) dose range of up to 100 mSv for radiogenic effects resulting from in utero exposure and bases this conclusion on the findings in Hiroshima and Nagasaki. However, a variety of observations of congenital malformations, fetal loss, stillbirths and infant deaths, as well as of Down's syndrome and other health defects in children after the Chernobyl accident exposures suggest that the A-bomb survivor data are incomplete. The Chernobyl findings are generally marginalized or even denied because of the low values of the estimated human exposures and the inconsistency of the results with the accepted risk models. One explanation for the observations is that physical dosimetric models have underestimated the effective exposure. This possibility is supported by biological dosimetry in the contaminated regions. The assumptions about effects after in utero exposure by incorporated radionuclides need to be revised.

Malformations in a chornobyl-impacted region

Objective: One of the populations most exposed to chronic low-dose radiation from Chornobyl (Chernobyl in Russian) lives in Polissia, the region representing the northern half of Rivne Province (Oblast) in Ukraine. Here the patterns and population rates of malformations are reported and possible etiologic factors and regional contrasts are explored.

Patients and methods: Malformations, as defined by international standards, noted among all 96 438 births in Rivne between 2000 and 2006, were analyzed statistically. Contrasts of rates in Polissia compared with the rest of Rivne also were investigated.

Results: The overall rate of neural tube defects in Rivne is among the highest in Europe (22.2 per 10,000 live births). The rates of conjoined twins and teratomas also seem to be elevated. In Polissia, the overall rates of neural tube defects are even higher (27.0 vs 18.3, respectively; odds ratio: 1.46 [95% confidence interval: 1.13-1.93]), and the rates of microcephaly and microphthalmia may also be elevated.

Conclusions: The malformation patterns observed suggest early disruptions of blastogenesis, manifesting as alterations of body axes, twinning, duplications, laterality, and midline formation. The results are sufficiently compelling to justify continuing and expanding this investigation of malformations in chronic low-dose radiation-impacted regions of Ukraine.

Incidence of congenital anomalies in 2 communities in Croatia before and after the Chernobyl nuclear accident

The Institute for Medical Protection of Mothers and Children, being regional centre of European registry of congenital malformations (EUROCAT) since 1982, registers congenital anomalies in municipals of Varazdin and Rijeka. Following the nuclear disaster of Chernobyl, there were numerous articles published mainly in daily newspapers, pointing to the increased number of malformations, particularly to Down's syndrome, due to additional irradiation imposed on population. Through this study we wanted to find out whether in Varazdin and Rijeka, following the Chernobyl's accident, there has been any increase of congenital anomalies and whether our regional and EUROCAT registry have been adequate to find out genetic effects of small doses of ionizing radiation. The total incidence of registered congenital anomalies in Varazdin and Rijeka in previous four-year period, amounted to 12.97%, while following Chernobyl, it amounted to 12.7%. Not even nine marker malformations, including Down's syndrome, show any statistically significant increased number of malformations, a year after this nuclear accident. In 18 EUROCAT registries, on almost half a million of newly born children and foetuses, conceived before and after May 1, 1986, the frequency of Down's syndrome and congenital malformations of central nervous system and eyes has been compared. There have been no important differences between two compared groups, and the rate of Down's syndrome was 1.26% before, and 0.91% after the accident. Anticipated stochastic genetic effects of measured and estimated additional doses of radiation imposed to our and Western European populations are too small to be found out neither by regional nor by EUROCAT registries.

Congenital malformations among newborns and developmental abnormalities among human embryos in Belarus after Chernobyl accident

Evaluation of the effects of radioactive contamination on human populations is important for an understanding of the present and future risk for human health, including the genetic risk. This review

centers on the results of population monitoring of developmental anomalies among human embryos and congenital malformations among newborn in the Republic of Belarus before and after Chemobyl accident. The data revealed that the incidences of developmental anomalies and congenital malformation from the mostly radionuclide-contaminated rural regions of Belarus reliably exceed the indices in control areas.

Birth defects in Norway by levels of external and food-based exposure to radiation from Chernobyl

In Norway, external doses of radiation resulting from fallout from the Chernobyl nuclear accident were estimated from detailed measurements, including soil deposition patterns. Internal doses were estimated from measurements of radioactive cesium in meat and milk supplies. The doses were calculated as average monthly doses for each of 454 municipalities during 36 consecutive months after the accident in spring 1986. Prospectively collected data on all newborns listed in the Medical Birth Registry of Norway who were conceived in the period May 1983-April 1989 were used to assess possible dose-response relations between estimated external and food-based exposures and congenital malformations and some other conditions. A positive association was observed between total radiation dose (external plus food-based) and hydrocephaly, while a negative association was observed for Down's syndrome. However, an important conclusion of the study was that no associations were found for conditions previously reported to be associated with radiation, i.e., small head circumference, congenital cataracts, anencephaly, spina bifida, and low birth weight. Potential sources of bias, including exposure misclassification and incomplete ascertainment of cases, are discussed.

Changes in registered congenital anomalies in the Republic of Belarus after the Chernobyl accident

A descriptive analysis of birth defects and malformations was performed to assess whether the rates of these defects correlate with the geographic areas of Belarus that received different levels of 137Cs contamination resulting from the Chernobyl catastrophe. Since this accident in 1986, the frequency of both congenital and fetal abnormalities in the Republic of Belarus has apparently increased. This increase is most prominent in areas with at least 555 9Bq/m2 radioactive contamination, although it has not been possible to correlate the individual dose received by a pregnant woman with the incidence of congenital malformations. The types of anomalies that were most increased in frequency were multiple congenital malformations, polydactyly, and reduction limb defects. These malformations are commonly associated with dominant new mutations. Chromosomal disorders such as occur in Down syndrome were not increased in frequency, nor could teratogenic effects be attributed to exposure to ionizing radiation. Preventive measures have apparently reduced the number of births with congenital abnormalities but have had no apparent effect on the frequency of fetal defects. Results of our analysis are consistent with the hypothesis that ionizing radiation released during the Chernobyl accident may have placed fetuses and neonates at risk for congenital malformations. Epidemiological studies are now required to determine whether a mother's radiation dose correlates with congenital malformations in her children.

Congenital malformations among offspring of the liquidators of the consequences from Chernobyl accident

The frequency and the structure of congenital malformations at children of the liquidators of the consequences from Chernobyl accident, undergone to an external scale gamma-irradiation in dozes up to 25 cGy. In total is surveyed 2379 newborn at which is revealed 318 intrauterine development defects. The received results are compared to the earlier published data on birth of congenital malformations in families of the fathers who have undergone to an irradiation in connection with professional activity at the enterprises of a nuclear industry, with emergency irradiation, with irradiation as a result of explosions of nuclear bombs in Japan, and are discussed from positions of the basic rules (situations) of radiating genetics. Total frequency, the frequency of forms 21 of inherent defects of development, taken into account in the International register of congenital malformations and frequency 9 forms heaviest of congenital intrauterine development defects with the high contribution mutation components at children of the liquidators authentically is higher than on the average on Russian Federation. The dependence of the frequency congenital malformations at children from dozes of an irradiation of the fathers--liquidators is revealed. The curve of dependence of the frequency of congenital malformations from time, past after work up to copulation carries arched character with peak of rise of frequency of congenital malformations in 2-3 years and decrease in 6-7 years.

The Chernobyl accident, congenital anomalies and other reproductive outcomes

Studies of the association between the Chernobyl accident in April 1986 and reproductive outcome, with particular reference to congenital anomalies, are reviewed. All of the studies so far have been based on the detection of a change in frequency over time. An increased frequency of trisomy 21 in the former West Berlin in January 1987, and increases in the frequency of neural tube defects in several small hospital-based series in Turkey, are not confirmed in larger and more representative series in Europe. No clear changes in the prevalence at birth of anomalies which might be associated with the accident are apparent in Byelorussia or the Ukraine, the republics with the highest exposure to fallout. However, these data are difficult to interpret as the methods of acquisition have not been described and they have not yet been reported in full. Thus, there is no consistent evidence of a detrimental physical effect of the Chernobyl accident on congenital anomalies. This is also the case for other measured outcomes of pregnancy. There is evidence of indirect effects--an increase in induced abortions substantial enough to show as a reduction in total births, due to anxieties created. Data are not available on the reproductive outcomes of women pregnant at the time of the accident who were evacuated from the 30 km zone of immediate contamination, of workers in the plant at the time of the accident or of decontamination workers. Moreover, no data are available from several of the other countries closest to the Chernobyl area.

Pregnancy outcome in Finland after the Chernobyl accident

The explosion at the Chernobyl nuclear power plant caused radioactive fallout in Finland in April-May 1986. The fallout was unevenly distributed geographically, and, accordingly, the country was divided into 3 fallout zones. Whole-body radioactivity measurements of randomly chosen persons showed that the regional differences prevailed throughout the following 2 years. Data for legal abortions, registered congenital malformations as well as preterm births and stillbirths of malformed children were collected. The corresponding expected figures were obtained from

statistics from 1984 and 1985. No differences in the expected/observed rates of the above parameters were detected.

PIP: The effects of the 1986 Chernobyl accident on Finland are reported. Legal abortions, registered congenital malformations, preterm births, and stillbirths showed no differences in observed vs. expected rates after the accident. The limitations are that the population base is small, the detection system is incomplete, no reliable data are available on early abortions, and germinal mutations were not presently analyzed. Measurement of radiocesium (Cs 134 and 137) was accomplished by the Research Institute for Social Security with a stratified random sample of 380 people. 5 fallout zones differentiated groups, which were then collapsed into 3 groups. Regional differences in levels persisted into 1988. The Finnish Register of Congenital Malformations provided the compulsory data on congenital malformations. The 3 groups (children born before the accident in 1984-85, in the latter half of 1986, and in 1987) were analyzed in the 3 zones during 2 study periods (August-December 1986 and January-December 1987). Monthly analysis of induced abortions showed no increase following the accident. There was a slight decrease in births between January and March 1987, which is believed to be related to anxiety reinforced by public advice. There were no differences between expected and observed congenital defects in the 2 study periods. Preterm and stillbirths followed a similar pattern. The analysis showed no association between the temporal and spatial variations in radioactivity and variable incidence of congenital malformations.

Chernobyl's public health consequences

Problems complicating a full assessment of the effects from Chernobyl included official secrecy and falsification of medical records by the USSR for the first 3.5 years after the catastrophe and the lack of reliable medical statistics in Ukraine, Belarus, and Russia. Official data concerning the thousands of cleanup workers (Chernobyl liquidators) who worked to control the emissions are especially difficult to reconstruct. Using criteria demanded by the International Atomic Energy Agency (IAEA), the World Health Organization (WHO), and the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) resulted in marked underestimates of the number of fatalities and the extent and degree of sickness among those exposed to radioactive fallout from Chernobyl. Data on exposures were absent or grossly inadequate, while mounting indications of adverse effects became more and more apparent. Using objective information collected by scientists in the affected areas--comparisons of morbidity and mortality in territories characterized by identical physiography, demography, and economy, which differed only in the levels and spectra of radioactive contamination--revealed significant abnormalities associated with irradiation, unrelated to age or sex (e.g., stable chromosomal aberrations), as well as other genetic and nongenetic pathologies.

Morbidity in a large cohort study of children born to mothers exposed to radiation from Chernobyl

Reproductive health was reviewed in four oblasts of the Republic of Belarus that were either heavily exposed (Mogilev and Gomel) or lightly exposed (Brest and Vitebsk) to ionizing radiation after the meltdown of a nuclear reactor in Chernobyl. A retrospective analysis was conducted on pregnancies occurring between January 1, 1982, and December 31, 1990, and a comparison of results was made

between pregnancy outcomes prior to and after the meltdown for individuals residing in heavily exposed and lightly exposed oblasts. Pregnant women who resided in heavily exposed oblasts appeared to be at risk for development of toxemia, renal insufficiency and anemia. Neonates born in heavily contaminated areas were apparently at risk for development of anemia and congenital malformations and perinatal death. In addition, a cohort of 757 neonates, 0-18 months old, with a normal physical examination, was identified for laboratory analysis of hematological, immunological, endocrinological and nutritional status. Decreased levels of copper and zinc were documented in erythrocytes from neonates from heavily contaminated oblasts, findings that may be related more to inadequate nutrition than to radiation exposure. Increased absolute "null" lymphocyte number and diminished absolute T lymphocyte number with a reduction in the "helper" (i.e., T4) subclass of T cells were evident in neonates born-in heavily exposed oblasts. Geographic differences in reproductive health and immune status are apparent in Belarus that may be related to radiation exposure. Additional studies are required to exclude confounding variables and possible selection bias.

4 years after Chernobyl: medical repercussions

The nuclear accident at Chernobyl accounted for an acute radiation syndrome in 237 persons on the site. Triage was the initial problem and was carried out according to clinical and biological criteria; evaluating the doses received was based on these criteria. Thirty one persons died and only 1 survived a dose higher than 6 Gy. Skin radiation burns which were due to inadequate decontamination, greatly worsened prognosis. The results of 13 bone marrow transplantations were disappointing, with only 2 survivors. Some time after the accident, these severely irradiated patients are mainly suffering from psychosomatic disorders, in the USSR, some areas have been significantly contaminated and several measures were taken to mitigate the impact on population: evacuating 135,000 persons, distributing prophylactic iodine, establishing standards and controls on foodstuff. Radiation phobia syndrome which developed in many persons, is the only sanitary effect noticed up to now. Finally, in Europe, there was only an increase in induced abortions and this was totally unwarranted. If we consider the risk of radiation induced cancer, an effect might not be demonstrated.

Fallout from the Chernobyl nuclear disaster and congenital malformations in Europe

Investigators estimate that the population exposure that resulted from the Chernobyl fallout is in the range of natural background radiation for most European countries. Given current radiobiologic knowledge, health effects-if any-would not be measurable with epidemiologic tools. In several independent reports, however, researchers have described isolated peaks in the prevalence of congenital malformations in the cohort conceived immediately after onset of the fallout. The consistency of the time pattern and the specific types of malformation raise concern about their significance. In this study, the author summarizes findings from Turkey, Belarus, Croatia, Finland, Germany, and other countries, and implications for radiation protection and public health issues are discussed.

Epidemiological survey of the medical consequences of the Chernobyl accident in Ukraine

The characteristics of the contamination resulting from the Chernobyl accident are defined, as a basis for epidemiological investigations. Due to loss of integrity of the nuclear fuel and thermal buoyancy from fire and nuclear heating, a large quantity of radioisotopes were released over a period of up to 16 days. The areas affected were very large, 37 million hectares in Ukraine alone. About 5 million persons were affected in one way or another, over 2 million of them in Ukraine. For registration and follow-up of health consequences from the accident, 4 main groups were distinguished, namely: (1) the participants in the containment of the accident and its cleanup ("liquidators"); (2) evacuees; (3) residents of contaminated areas; and (4) children born to parents with significant radiation exposure. Registration and epidemiological follow-up in the former USSR and the three republics afterwards are presented with an emphasis on Ukraine. Considering the long incubation times for some of the expected illnesses and relatively low average doses, the difficulties of confirming significant effects become evident. For example leucosis morbidity among cleanup personnel within a 30 km zone around the accident was 3.4 per 100,000 before the accident and 7 per 100,000 afterwards. The question of the statistical significance of such numbers is discussed by the authors, in the context of confounding factors. For some of the observed effects it has already been established that stress and anxiety caused by the accident and living conditions in the affected areas are the principal cause rather than radiation. According to the authors, more detailed retrospective and prospective epidemiological studies are needed in the future, in order to clarify the causes of observed health effects.

Radiation effects on the population of Belarus after the Chernobyl accident and the prediction of stochastic effects

Evaluation of conditions of exposure during the post-accident period makes it possible to identify two periods in the radiation exposure of Belarus's population. As a result of our investigations we obtained data about doses for four different categories in the exposed population: people who lived in the contaminated territories without evacuation and relocation; evacuated people: cleanup workers ("liquidators"); and people who were exposed in childhood, especially for thyroid exposure. The total doses for these categories in different time periods were analysed. Evaluation of doses received by the Belarusian population due to the Chernobyl accident shows no evidence of doses, that could lead to the deterministic consequences of radiation exposure. For all exposed groups we made predictions about different types of stochastic consequences of exposure.

The congenital anomalies registry in Belarus: a tool for assessing the public health impact of the Chernobyl accident

A national population-based malformation registry (BNR) has been in operation since 1979 in Belarus, one of the countries most heavily exposed to the contamination from the Chernobyl accident of 26 April 1986. We describe its methodology and its compliance with established criteria, evaluate the completeness of its reporting, and analyze the data collected in four administrative regions with contrasting contamination levels from 1983 through 1999. Nine easily diagnosed malformations have been monitored since 1983. Reporting completeness exceeds 85% for all periods and all regions. In all periods, the prevalence at birth of these malformations was lower in the most contaminated regions and showed a similar positive time trend in areas of low and high contamination. We conclude that the BNR is a reliable tool for studying the possible effects on

congenital malformations caused by the Chernobyl accident. Although the trend we observed may be explained by better ascertainment and prenatal diagnosis, a real increase cannot be ruled out.

Health state and physical development of children prenatally exposed to radiation as a result of Chernobyl accident

1144 children which had been exposed to radiation at the stage of their intrauterine life have been observed. Assessment of their health state and physical development has been carried out. Radiation doses load on thyroid gland of fetuses varied from 0.01 till 3.34 Gr, whole-body irradiation doses varied from 10.0 till 376.0 mZb. The level of health state of children exposed during their intrauterine life to radiation was lower at all stages of postnatal ontogenesis than that one of children of the control group. A presence of a definite correlation ratio between whole-body irradiation doses of fetuses and development of chronical somatic pathology in children was established during the study. It was noted that frequency of abnormalities of physical development and chronical somathic pathology increased after a thyroid gland of the fetuses had been exposed to radiation dosed from 0.36 to 0.75 Gr.

Birth prevalence of congenital malformations in Bavaria, Germany, after the Chernobyl accident

This study considers whether or not exposure to radioactive fallout from the Chernobyl accident led to an increased prevalence of congenital malformations in infants born in Bavaria, the German state with the highest levels of contamination after the accident. The odds ratios for major malformations after the accident relative to before were used as indicators for adverse health effects. Since measurements of caesium in soil showed that contamination was considerably higher in Southern Bavaria than in Northern Bavaria, the odds ratios were calculated for both regions separately. Analysis did not show a significant increase in any of the odds ratios of the selected malformations in Southern Bavaria as compared to Northern Bavaria. Consequently, this study provides no evidence that radiation from Chernobyl caused an increase in the birth prevalence of major congenital malformations.

Selective monitoring for a Chernobyl effect on pregnancy outcome in Kiev, 1969-1989

The aim of this investigation was to determine the frequency of adverse pregnancy outcomes in Kiev during the period surrounding the Chernobyl accident on April 26, 1986. Additional effective equivalent doses resulting from the catastrophic irradiation in 1986-1991 was 8.04 mSv for Kiev inhabitants. We retrospectively analyzed the archives of the two largest obstetric hospitals between 1969 and 1990. Spontaneous miscarriages, congenital anomalies, and perinatal mortality varied during the two decades without any pronounced changes in any direction. Additional long-term follow-up is needed to determine mutagenic or carcinogenic effects.

Frequency of congenital abnormalities in Hungary after the Chernobyl nuclear power accident

Introduction: The only positive result of earlier Hungarian teratological investigations on consequences of Chernobyl nuclear power station accident was the description of increased prevalence of birth with less than 2500 g body weight. It was attributed to the concern of the pregnant women, not to the direct effect of ionising radiation.

Aim: The present study aimed to refine the earlier results by application of sensitive epidemiological techniques.

Method: The exposure data observed in the 150 districts of Hungary were correlated with the prevalence of Down syndrome by geographical information system and the monthly detected prevalences were analysed in the function of exposure.

Results: The ecological investigation on geographical inequalities revealed that there is no correlation between the district level exposure and Down syndrome prevalence. The time trend analysis on monthly data showed no exposure-related elevation of Down-syndrome occurrence.

Conclusion: The results supported the earlier conclusions of the studies that the Chernobyl accident related exposure did not elicited detectable increase of Down syndrome.

Incidence of developmental defects in human embryos in the territory of Byelarus after the accident at the Chernobyl nuclear power station

The incidence of developmental abnormalities (DA) among 5 to 12-week human embryos collected in Minsk during abortions before the Chernobyl' accident was compared to that in Minsk, Mogilev, and southeastern districts of Gomel' and Mogilev regions before and after the accident. The incidence of DA among human embryos from the most radionuclide-contaminated rural regions of Byelarus exceeds that of the control group and of the urban population after the Chernobyl' accident by a factor of 1.5-2. The mutagenic effect of irradiation is the most probable cause of the increased DA frequency. These data suggest that recording of DA in embryos obtained by medical abortions is a new promising approach to the monitoring of genetic consequences of irradiation in human populations.

Health effects resulting from the Chernobyl accident

This article reviews the health effects of the Chernobyl accident. The clearest effect to be seen to date is the dramatic increase in thyroid cancer in children. The evidence for increased leukaemia is less clear, but there are indications of increased leukaemia incidence in Russian clean-up workers. There is also evidence of increases in breast cancer, cataract and cardiovascular disease. However, to date the largest public health problem caused by the accident is the mental health impact.

The incidence of congenital developmental defects among the newborn infants of Rivne Province

A study was made of frequency of developmental defects among newborn babies in Rivne Province and two its regions (the northern territories relatively free from contamination and those affected by radioactive contamination) that are under control because of the Chernobyl accident. Variations in the frequency of developmental defects (DD) over the studied period (1985-1997) in the province averaged 153 to 372.8 per 10,000 newborns, i.e., the parameter increased more than 2.4-fold. In

the controlled regions it averaged 163 to 401.1 per 10,000 neonates (an increase 2.5 as much). A linear increase in DD prevalence might be related both to effects of adverse environmental factors and improvement in diagnosis and registration of pathological states. Retrospectively, 17 DD forms were registered, which, according to the European Register, were grouped under the heading "old defects", and 16 forms placed in the category "new defects". Comparison of DD prevalence with data of the European Register showed that, on the whole, prevalence of some DD among neonates in Rivne Province over the stated period (1985-1997) corresponds to analogous indices in other regions of Europe.

Base de datos	**PUBMED**
Algoritmo	((Chernobyl) AND (Cleft lip palate OR malformations)) AND (('chernobyl accident'/exp OR 'chernobyl accident') AND 'air pollution' AND 'cleft lip')
Les fentes labiopalatines et l'environnement en Russie Les 89 re´gions composant la Fe´de´ration de Russie sont peu-ple´es par des groupes ethniques aux caracte´ristiques e´pide´- miologiques spe´cifiques. Les habitants de certaines re´gions industrielles subissent par ailleurs l'influence d'une pollution intense aux conse´quences me´dicales lourdes. Enfin, plusieurs catastrophes sanitaires ont marque´ la seconde moitie´ du xxe sie`cle. De nombreuses e´tudes re´centes publie´es en langue russe ont analyse´ l'influence de ces contraintes sur la mor- phogene`se faciale et donnent un e´clairage inte´ressant a`l'e´pide´miologie des fentes labiopalatines en Russie.	

Base de datos	**PUBMED**
Algoritmo	('chernobyl accident'/exp OR 'chernobyl accident') AND 'air pollution' AND 'cleft lip'
Les fentes labiopalatines et l'environnement en Russie Les 89 re´gions composant la Fe´de´ration de Russie sont peu-ple´es par des groupes ethniques aux caracte´ristiques e´pide´- miologiques spe´cifiques. Les habitants de certaines re´gions industrielles subissent par ailleurs l'influence d'une pollution intense aux conse´quences me´dicales lourdes. Enfin, plusieurs catastrophes sanitaires ont marque´ la seconde moitie´ du xxe sie`cle. De nombreuses e´tudes re´centes publie´es en langue russe ont analyse´ l'influence de ces contraintes sur la mor- phogene`se faciale et donnent un e´clairage inte´ressant a`l'e´pide´miologie des fentes labiopalatines en Russie.	

Base de datos	PUBMED
Algoritmo	('chernobyl accident'/exp OR 'chernobyl accident') AND 'air pollution'

Pregnancy and labor in women in the region of the accident at the Chernobyl Atomic Electric Power Station

The authors analyze the tentative results of a multiprofile study, including a review of labor histories, examinations of pregnant women and parturients, measurements of fetoplacental hormones, study of the immunity status and microbiocenosis of the mothers and newborns, living in the first (up to 15 Ci/km2) and second (15 to 40 Ci/km2) zones of radioactive contamination. The detected shifts of a compensatory nature were found mostly in women living in the first zone. The disorders found in the women living in the second zone evidenced a decrease of the defense potential of the body, this necessitating nonspecific and correcting therapy during pregnancy, in labor and the postpartum period

On protecting the inexperienced reader from Chernobyl myths

The health and environmental consequences of the Chernobyl accident continue to attract the attention of experts, decision-makers and the general public, and now these consequences have been given added relevance by the similar accident in 2011 at the Fukushima-1 nuclear power plant (NPP) in Japan. Expert analysis of radiation levels and effects has been conducted by international bodies--UNSCEAR in 2008 and the Chernobyl Forum during 2003-5. At the same time, three Russian and Belarusian scientists, Yablokov, Nesterenko and Nesterenko (2009 Chernobyl. Consequences of the Catastrophe for People and the Environment (New York: Annals of the New York Academy of Sciences)) published both in Russian and English a substantial review of the consequences of Chernobyl based mostly on Russian-language papers. In this book, they suggested a departure from analytical epidemiological studies in favour of ecological ones. This erroneous approach resulted in the overestimation of the number of accident victims by more than 800 000 deaths during 1987-2004. This paper investigates the mistakes in methodology made by Yablokov et al and concludes that these errors led to a clear exaggeration of radiation-induced health effects. Should similar mistakes be made following the 2011 accident at Fukushima-1 NPP this could lead quite unnecessarily to a panic reaction by the public about possible health effects and to erroneous decisions by the authorities in Japan.

Genomic instability in chidren born after the Chernobyl nuclear accident (in vivo and in vitro studies)

Analysis of peripheral blood lymphocytes in children born after the accident at the Chernobyl Nuclear Power Plant in the period from 1987 to 2004 (permanent residents of territories contaminated with radionuclides, n = 92; and children of irradiated fathers-liquidators, n = 88)) revealed increased levels of aberrant cells (ACs) and aberrations of the chromosomal type as compared to the control ($P < 0.05$). In three subgroups of children with different initial AC frequencies (children with high AC frequencies, > or = 3%; children with medium AC frequencies, 2%; and children with low AC frequencies, > or = 1%), the levels of aberrations of the chromosomal type are increased as compared to the control ($P < 0.05$). The levels of aberrant cells and chromosome aberrations (CAs) in the subgroup of children with > or = 3% frequencies significantly differ from those in the subgroup of children with > or = 1% AC frequencies. No dependence of the AC and CA frequencies on the year of birth after the Chernobyl accident was revealed. After fractional and single gamma-irradiation (137Cs) of blood in vitro in the 10-30 cGy dose range, the average CA frequencies in the first and second mitoses increased in a similar way depending on the initial AC frequencies in the children and parents. All these results suggest an individual character of genomic instability induced by low radiation doses and its transgenerational phenomenon in the organisms of children.

Czech Republic 20 years after Chernobyl accident

The territory of the Czech Republic was contaminated as a result of the breakdown in the Chernobyl nuclear power plant in 1986. The Czech population received low doses of ionising radiation which, though it could not cause a deterministic impact, could have had stochastic effects expressed in the years following the accident. Twenty years after the accident is a long enough time to assess its stochastic effects, primarily tumours and genetic impairment. The moderate amount of radioactive fallout received by the Czech population in 1986 increased thyroid cancer in the following years; on the other hand, no obvious genetic impact was found.

The Chernobyl accident--radionuclide fallout in S.W. England

Initial fallout data from the nuclear reactor accident at Chernobyl is presented for the Plymouth region of Devon S.W. England which received low levels of radioactivity. During the period of maximum fallout the overall gross gamma activity for the Plymouth area was approximately 10% higher than levels recorded prior to the Chernobyl accident. The increase in levels of radioactivity were within the variability of natural background found in local houses.

The dose dependence of the induction of chromosome aberrations in those who worked in the cleanup of the Chernobyl accident

The method of biological dosimetry based on registration of frequency of chromosome aberrations in peripheral lymphocytes was proven to be a valuable technique for estimation of large absorbed doses. In the case of low absorbed doses or low dose rate the suitability of this method is restricted because of deficiency of suitable dose-response curve for yield of chromosome aberrations. In this work chromosome aberration rate was estimated in 31 ameliorators of the Chernobyl accident with the known data of physical dosimetry in the range of 12-30 cGy. Linear dependence of induction of chromosome aberrations was found in this dose range. The coefficients for induction of dicentrics and all unstable aberrations of chromosome type was found to be 1.4 +/- 0.4 and 7.2 +/- 1.2 per 100 cells per 1 Gy, respectively.

The health status of children up to 14 years old living in an area of long-term post-accident exposure to low doses of ionizing radiation

An assessment is submitted of morbidity rates and physical development of children aged under 14, residing in the territories being monitored after the Chernobyl Power Plant accident. A high level of disharmony in physical development of the children examined was recordable, as was an excess in morbidity of both general and separate classes of disease entities among the pediatric population having been victims of the Chernobyl accident, as compared to that in relatively "clean" areas and in Ukraine as a whole.

A preliminary analysis of oral morbidity in the children of Byelarus after the accident at the Chernobyl Atomic Electric Power Station

Presents the data of analysis of medical files of therapeutic institutions, of questionnaires distributed among dentists, and the results of examinations of 883 children aged 3 to 6, living in 19 towns of Byelorussia. The incidence and clinical picture of a number of dental diseases were found changed in the children living in the regions contaminated with radionuclides, as well as the general well-being of these children.

Base de datos	**PUBMED**
Algoritmo	('chernobyl accident'/exp OR 'chernobyl accident') AND 'stochastic model'

Mechanistic basis for nonlinear dose-response relationships for low-dose radiation-induced stochastic effects

The linear nonthreshold (LNT) model plays a central role in low-dose radiation risk assessment for humans. With the LNT model, any radiation exposure is assumed to increase one's risk of cancer. Based on the LNT model, others have predicted tens of thousands of deaths related to environmental exposure to radioactive material from nuclear accidents (e.g., Chernobyl) and fallout from nuclear weapons testing. Here, we introduce a mechanism-based model for low-dose, radiation-induced, stochastic effects (genomic instability, apoptosis, mutations, neoplastic transformation) that leads to a LNT relationship between the risk for neoplastic transformation and dose only in special cases. It is shown that nonlinear dose-response relationships for risk of stochastic effects (problematic nonlethal mutations, neoplastic transformation) should be expected based on known biological mechanisms. Further, for low-dose, low-dose rate, low-LET radiation, large thresholds may exist for cancer induction. We summarize previously published data demonstrating large thresholds for cancer induction. We also provide evidence for low-dose-radiation-induced, protection (assumed via apoptosis) from neoplastic transformation. We speculate based on work of others (Chung 2002) that such protection may also be induced to operate on existing cancer cells and may be amplified by apoptosis-inducing agents such as dietary isothiocyanates.

Modelling the Chernobyl radioactive fallout (II): A multifractal approach in some European countries

This paper deals with the 137Cs cumulative soil deposition measured in some European Countries after the Chernobyl accident. We devised a multifractal model to aid in describing the spatial distribution of radioactivity. The model is based the Fractal Sum of Pulses theory, involving additive stochastic processes. We use, as input source of information, the available data of radioactive deposition measured in some European Countries. The results look promising, since realistic scenarios of environmental pollution are produced.

Base de datos	**Embase**
Algoritmo	('chernobyl accident'/exp OR 'chernobyl accident') AND 'stochastic model'

Stochastic model for the fluctuations of the atmospheric concentration of radionuclides and its application to uncertainty evaluation We propose a new model of the atmospheric concentration of a radionuclide with the inclusion of fluctuations of the concentration. The model is a stochastic differential equation and we derive the analytic solution of the equation. The solution agrees very well with the Chernobyl Cs-137 data. The advantage of the model is that the uncertainty in radiation exposure risk, with regard to the concentration fluctuations, can be quantitatively estimated. We show the range of fluctuations of ±. σ, ±2. σ, ±3. σ in the 10-year measurement of the atmospheric concentration in Chernobyl and confirmed the validity of the model
Chernobyl experience in field of retrospective dosimetry: Reconstruction of doses to the population and liquidators involved in the accident Evacuees from the 30 km zone and liquidators are likely to have received the highest Chernobyl exposures. Doses to the majority of them remained unknown, calling for dose reconstruction. This need prompted development of new techniques of retrospective dosimetry. Application of state-of-art stochastic dosimetric models and determination of site-specific location factors allowed the determination of individual doses and uncertainty ranges for a significant part of the evacuated population. A number of approaches were used to recover existing gaps in dosimetric information related to liquidators. EPR dosimetry with teeth is useful for high precision retrospective dosimetry of liquidators; now teeth from liquidators are being collected systematically in Ukraine. Analytical dose reconstruction was conducted for about 2000 Chernobyl workers. Reconstruction of doses to the rest of the liquidators requires application of a different methodology based on analysis of regularities of exposure and assignment of dose intervals according to attributes of the liquidators.
Statistical analysis of radioactive contamination levels in settlements of the Chernobyl middle zone A statistical analysis of the measurements of 137Cs activity density carried out in 1990-1991 in 30 settlements of the mesozone (and partially in the nearest zone) of the Chernobyl nuclear power plant is presented. It is shown that the mean activity density of radionuclides is close to 14 Bq cm-2 for the inspected settlements of Byelorussia which is significantly less than that for the inspected settlements of the nearest zone (48 Bq cm-2). The analysis shows that there is a near linear correlation between rms deviation of activity density and its mean value. It is also shown that the correlation radius of the data is comparable with the spatial step of the measurements and that the activity density distribution is reasonably described in terms of a normal distribution.

Base de datos	**Embase**
Algoritmo	('chernobyl accident'/exp OR 'chernobyl accident') AND 'air pollution'

Birth defects on Chernobyl radionuclide polluted territories

147318 pregnancy outcomes were analyzed in Zhytomyrska Oblast during 2000-2010; the descriptive analysis was performed. The frequency of birth defects was estimated among newborns, still-born babies and abortions due to genetic disorders of a fetus on "clean" and polluted territories. There was an increase of all birth defects on the polluted territories; among newborns it was (26.10 ± 0.80) per thousand and (24.23 ± 0.47) per thousand, $p < 0.05$; among newborns and still-born babies it was (26.54 ± 0.81) per thousand and (24.78 ± 0.48) per thousand, $p < 0.06$. The increase in the birth defects of the nervous system was detected: among newborns it was (1.09 ± 0.17) per thousand and (0.75 ± 0.08) per thousand, $p < 0.05$; among newborns and still-born babies it was (1.22 ± 0.18) per thousand and (0.81 ± 0.09) per thousand, p. < 0.05; among newborns, still-born babies and genetically caused abortions it was 2.76 ± 0.26) per thousand and (2.34 ? 0.15) per thousand, $p = 0.165$. X2 criteria confirmed the difference between the frequency of birth defects on "clean" and polluted territories. Estimation by Bayes did not confirm the hypothesis about the difference between the frequency of birth defects on "clean" and polluted territories. Endocrine diseases were confirmed to be an important factor of the origin of birth defects, which is important for planning pregnancy on both polluted and "clean" territories.

Geographical trends in 137Cs fallout from the chernobyl accident and leaching from natural surface soil in Norway

In order to follow the turnover of ^{137}Cs in natural soils and estimate future trends in exposure of livestock, samples of natural surface soils were collected at 0-3cm depth at 464 sites in 1995 and 463 sites in 2005 covering the country. In both cases the geographical pattern observed was similar to the original distribution from 1986, but the decline of ^{137}Cs activity in the surface soil was not the same everywhere. In 1995 the ^{137}Cs reduction since 1986 was found to be considerably greater in coastal areas than farther inland. The main reason for this appears to be the much greater deposition of marine cations such as Mg^{2+} and Na^{+} in the coastal areas, replacing Cs ions fixed on soil particle surfaces. This cation exchange appeared to be particularly strong near the southern coast where deposition of NH4+ from transboundary air pollution is evident in addition to the marine cations. During 1995-2005 the ^{137}Cs decline in the surface soil was more uniform over the country than in the preceding 10-year period but still significantly higher in coastal areas than inland. Differences in precipitation chemistry may have influenced the uptake of ^{137}Cs in terrestrial food chains.

Chernobyl and reproductive health of a female rural population (an epidemiological study)

OBJECTIVE: To study the combined effect of radioactive and chemical factors on the reproductive health of a female rural population residing and working on territories contaminated after the Chornobyl accident.
MATERIALS AND METHODS: The sociological questioning and gynecological examination of 1850 women have been made including the evaluation of 29520 medical reports of deliveries, 19502 medical reports of newborns, 1694 medical reports of women with spontaneous abortions as well as the state of menstrual function in 480 girls-adolescents residing on the contaminated territories. The radioactive contamination of the studied territories as well as the total effective dose of radiation for the population was evaluated by the results of the general dosimetric dose established for settlements of Ukraine. Factors of the work environment (noise, microclimate, dust, bacterial air pollution, work intensity and strain) were studied by the common hygienic methods and assessed by the criteria of the "Hygienic Classification of Work..." # 4137-86. The residues of pesticides, their

isomers and products of transformation in biological fluids (blood, breast milk, cord blood) were assayed by gas-liquid chromatography method and electron capture detector with the device "Kristallux 4000" and the model M-3700. Correlative, regression, and discriminative analyses were used for mathematical processing of the data.
RESULTS: It is proved that the reproductive health of rural women has become significantly worse after the Chornobyl accident, the most expressed disorders are seen in young women aged under 30. Worsening of reproductive health is found being the result of a combined effect of factors of radioactive and nonradioactive nature, specific for territories of residence, occupational activity and style of life. In particular, the effect of pesticides at the background of the radioactive contamination is likely to be an additional risk factor of disorders of the reproductive health of women. According to the biomonitoring data the content of organochlorine pesticides in biological fluids of women with reproductive health disorders was significantly higher ($p<0.05$) vs. with healthy ones. It is established that women of the childbearing age residing on territories with the density of contamination of more than 5 Ci/km and with rates of pesticide load over 5 kg/ha should be referred to a high risk group of the reproductive health disorders.
CONCLUSION: The perspectives of epidemiological studies on the reproductive health are related on the use of the combination of many-aspect healthcare and biological approaches. It is equally important to assess adequately the factors of environment and work-related conditions, and their combined effect with dwelling load.

The effect of Chernobyl accident on the development of malignant diseases--situation after 20 years

The accident that occurred at the Chernobyl Nuclear Power Plant in 1986, released large quantities of radionuclides--among them radioiodine--into the atmosphere, thereby raising public concerns about its influence on thyroid structure and function, especially the development of malignancy. There were even reports about 700 deaths due to thyroid carcinoma in Russian Federation, Ukraine and Belarus, resulting from the accident. In this review we discussed the incidence of thyroid cancer in different parts of the world, especially in heavily contaminated countries, as Ukraine and Belarus, and the possible link between radioisotope activity in the thyroid and the development of malignancy. The study carried out in Minsk showed 40-fold increase of the incidence of thyroid cancer in the years 1986-1994, in comparison to the period 1977-1985. An increase of the incidence of thyroid cancer has generally been observed in many countries after the Chernobyl accident. We focused on the factors that may have an influence on this phenomenon, especially diagnostic tests, health care, social and environmental factors, like iodine level in water and soil. The results of molecular biology studies, e.g. RET translocation in carcinoma type RET/PTC1 in elderly and RET/PTC3 in children, and expression Ax1 and Gas6 in children were reviewed as well. We also mentioned other thyroid diseases, like nodular goitre, cysts, the disturbance of thyroid function and autoimmunity, possibly linked to the radiation after Chernobyl accident. Data obtained from the regions near Chernobyl showed no increased risk of other types of malignancy (leukaemia, Hodgkin's and non Hodgkin's lymphoma) in 1986-1996. In this article the epidemiology of thyroid diseases in Poland was also reviewed.

Plutonium isotopes in ground-level air in Northern Germany since 1990

The activity concentrations, ratios and seasonal fluctuations of plutonium isotopes in ground-level air in Northern Germany are reported for the years 1990 to 1997. The 239+240Pu activity concentrations (a) measured on quarterly samples lie in a range 0.4 nBq/m3<a<4 nBq/m3, the 238Pu activity concentrations are lesser by up to a factor of 0.1 (0.1 nBq/m3<a<0.8 nBq/m3). The total activity concentration shows a typical seasonal fluctuation in the time period under review. In a few quarterly samples the activity ratio of a(238Pu)/a(239+240Pu) is significantly increased.

Aerosol migration near Chernobyl: Long-term data and modeling

Airborne particles from a polluted area can pose a long-term health hazard to residents nearby. However, the long-term prediction of aerosol migration has never been successful. We show in the present paper that a recently proposed model successfully reproduces data of the aerosol concentration measured near Chernobyl over a decade. The time dependence of the resuspension factor is also reproduced very well. In fitting our theoretical formula to the data, we obtain values of the fitting parameters that provide important information on the emission quantity and removal processes of nuclides from the accident. We show that 2200 days of measurement after the accident should be enough to predict the concentration in the air 10 years later.

Effect of the Chernobyl accident on the gamma radiation level in the Belgrade region

This article presents the results of measurements of the gamma radiation level during and after the Chernobyl accident at the reference point located near Belgrade, Yugoslavia. The measurements started a day before the arrival of the plume of contaminated air from Chernobyl, were carried out during the active phase of the accident, and continued afterward up to the present day. Those measurements enabled authorities to (1) register the arrival of the central part of the contaminated plume over Belgrade on May 1, 1986, at 10:30 a.m. local time; (2) monitor the passing of the plume; (3) record the beginning of substantial deposition of radioactive materials caused by heavy fallout in the afternoon of the same day; and finally, (4) record the moment the maximum deposition level (i.e., gamma radiation level) was reached the next day. The results of the measurements in postaccident conditions indicated the decrease of the gamma radiation level because of radioactive decay of deposited gamma emitters and the influence of various environmental factors. The measurements were carried out by a high-pressure argon ionization chamber. Presented data may be used for testing of atmospheric dispersion and deposition models and also for predicting the behavior of deposited gamma emitters in the environment over a long time period after a nuclear accident.

(239(240)238)Pu, 90Sr, 103Ru and 137Cs concentrations in surface air in Austria due to dispersion of Chernobyl releases over Europe

After the reactor accident at Chernobyl on 26 April 1986, Austria, situated in the central part of Europe, was one of the most stricken countries. Radionuclide concentrations in surface air have been measured at five different sampling stations, viz. in Vienna, Linz, Salzburg, Bregenz and Klagenfurt, during the period 28 April-9 May 1986. In addition to the results of the γ-spectroscopic measurements of 103Ru and 137Cs, data for (239(240),238)Pu and 90Sr determined by radiochemical analyses of the same air filters are presented. These results show that in Austria generally most of the 137Cs and 103Ru contamination occurred before 2 May, whilst most of the 90Sr and (239(240))Pu contamination took place between 2-5 May. Initially 103Ru/137Cs ratios of ~2 could be observed, which later decreased to 0.3-0.6 and increased again after 2 May, up to as high as 5. The ratios of 90Sr/137Cs remained between 0.004 and 0.017, those of (239(240)) Pu/137Cs between 1.3 x 10-6 and 2 x 10-5.

Base de datos	**Embase**
Algoritmo	('chernobyl accident'/exp OR 'chernobyl accident') AND prevalence AND 'cleft lip'
The congenital anomalies registry in Belarus: A tool for assessing the public health impact of the Chernobyl accident A national population-based malformation registry (BNR) has been in operation since 1979 in Belarus, one of the countries most heavily exposed to the contamination from the Chernobyl accident of 26 April 1986. We describe its methodology and its compliance with established criteria, evaluate the completeness of its reporting, and analyze the data collected in four administrative regions with contrasting contamination levels from 1983 through 1999. Nine easily diagnosed malformations have been monitored since 1983. Reporting completeness exceeds 85% for all periods and all regions. In all periods, the prevalence at birth of these malformations was lower in the most contaminated regions and showed a similar positive time trend in areas of low and high contamination. We conclude that the BNR is a reliable tool for studying the possible effects on congenital malformations caused by the Chernobyl accident. Although the trend we observed may be explained by better ascertainment and prenatal diagnosis, a real increase cannot be ruled out.	

Base de datos	**Embase**
Algoritmo	((Chernobyl) AND (Cleft lip palate OR malformations)) AND (('chernobyl accident'/exp OR 'chernobyl accident') AND 'air pollution' AND 'cleft lip')
	(Chernobyl) AND (Cleft lip palate OR malformations)) AND (Air PollutaAir Pollutants, Radioactive OR Air pollutionnts, Radioactive OR Air pollution)
Les fentes labiopalatines et l'environnement en Russie Les 89 re´gions composant la Fe´de´ration de Russie sont peu-ple´es par des groupes ethniques aux caracte´ristiques e´pide´- miologiques spe´cifiques. Les habitants de certaines re´gions industrielles subissent par ailleurs l'influence d'une pollution intense aux conse´quences me´dicales lourdes. Enfin, plusieurs catastrophes sanitaires ont marque´ la seconde moitie´ du xxe sie`cle. De nombreuses e´tudes re´centes publie´es en langue russe ont analyse´ l'influence de ces contraintes	

sur la mor- phogene`se faciale et donnent un e´clairage inte´ressant a`l'e´pide´miologie des fentes labiopalatines en Russie.

- **Hiroshima**

Base de datos	**Pubmed**
Algoritmo	((Effect, Radiation OR stochastic model) AND (Hiroshima)) AND (Air Pollutants, Radioactive OR Air pollution)

Rediscovery of an old article reporting that the area around the epicenter in Hiroshima was heavily contaminated with residual radiation, indicating that exposure doses of A-bomb survivors were largely underestimated

The A-bomb blast released a huge amount of energy: thermal radiation (35%), blast energy (50%), and nuclear radiation (15%). Of the 15%, 5% was initial radiation released within 30 s and 10% was residual radiation, the majority of which was fallout. Exposure doses of hibakusha (A-bomb survivors) were estimated solely on the basis of the initial radiation. The effects of the residual radiation on hibakusha have been considered controversial; some groups assert that the residual radiation was negligible, but others refute that assertion. I recently discovered a six-decade-old article written in Japanese by a medical doctor, Gensaku Obo, from Hiroshima City. This article clearly indicates that the area around the epicenter in Hiroshima was heavily contaminated with residual radiation. It reports that non-hibakusha who entered Hiroshima soon after the blast suffered from severe acute radiation sickness, including burns, external injuries, fever, diarrhea, skin bleeding, sore throat and loss of hair-as if they were real hibakusha. This means that (i) some of those who entered Hiroshima in the early days after the blast could be regarded as indirect hibakusha; (ii) 'in-the-city-control' people in the Life Span Study (LSS) must have been irradiated more or less from residual radiation and could not function properly as the negative control; (iii) exposure doses of hibakusha were largely underestimated; and (iv) cancer risk in the LSS was largely overestimated. Obo's article is very important to understand the health effects of A-bombs so that the essence of it is translated from Japanese to English with the permission of the publisher.

Ionizing radiation: future etiologic research and preventive strategies

Estimates of cancer risks following exposure to ionizing radiation traditionally have been based on the experience of populations exposed to substantial (and known) doses delivered over short periods of time. Examples include survivors of the atomic bombings at Hiroshima and Nagasaki, and persons treated with radiation for benign or malignant disease. Continued follow-up of these populations is important to determine the long-term effects of exposure in childhood, to characterize temporal patterns of excess risk for different types of cancer, and to understand better the interactions between radiation and other host and environmental factors. Most population

exposure to radiation occurs at very low dose rates. For low linear energy transfer (LET) radiations, it often has been assumed that cancer risks per unit dose are lower following protracted exposure than following acute exposure. Studies of nuclear workers chronically exposed over a working lifetime provide data that can be used to test this hypothesis, and preliminary indications are that the risks per unit dose for most cancers other than leukemia are similar to those for acute exposure. However, these results are subject to considerable uncertainty, and further information on this question is needed. Residential radon is the major source of population exposure to high-LET radiation. Current estimates of the risk of lung cancer due to residential exposure to radon and radon daughters are based on the experience of miners exposed to much higher concentrations. Data indicate that lung cancer risk among miners is inversely associated with exposure rate, and also is influenced by the presence of other lung carcinogens such as arsenic in the mine environment. Further study of populations of radon-exposed miners would be informative, particularly those exposed at below-average levels. More direct evidence on the effects of residential exposure to radon also is desirable but might be difficult to come by, as risks associated with radon levels found in most homes might be too low to be quantified accurately in epidemiological studies.

Health impacts of large releases of radionuclides. Late somatic health effects

This chapter reviews the risks of radiation-induced cancer for the dose range likely to occur after releases of radionuclides into the environment. Epidemiological evidence from exposed workers and the atomic bomb survivors of Hiroshima and Nagasaki is surveyed. Influences on such risk functions of individual related quantities (e.g. age, sex, nationality, time since exposure and organs exposed) and of radiation modality-related quantities (e.g. dose, dose rate and radiation quality) are also briefly discussed.

Radon concentrations in residential housing in Hiroshima and Nagasaki

A measurement of indoor radon (222Rn) concentrations in Hiroshima and Nagasaki was carried out to assess the variability of exposure expected among atomic bomb survivors. Two hundred dwellings, mostly belonging to members of the fixed cohort of atomic bomb survivors under study by the Radiation Effects Research Foundations, were selected for this measurement. The geometric mean values of the radon concentrations for 100 dwellings in Hiroshima and 99 dwellings in Nagasaki measured by Track-Etch Type SF detectors were 56.8 Bq m-3 and 28.5 Bq m-3, respectively. No statistically significant difference was observed between lung cancer mortalities in the low-dose range in the two cities. However, apparent values of the mortality rate for low dose range in Hiroshima are consistently greater than those in Nagasaki. The exposure to radon and its progeny and the atomic bomb radiation effect might have some cooperative effects on the lung cancer incidence.

Base de datos	**Pubmed**

Algoritmo	"((Effect, Radiation OR stochastic model) AND (Hiroshima)) AND (Cleft lip palate OR malformations)"

Hiroshima/Nagasaki survivors and their offspring: results of longterm epidemiological studies

After the atomic bombing of Hiroshima and Nagasaki, long-term epidemiological studies were undertaken on the irradiated survivors and their offspring, and are still underway. These thorough studies involving tens of thousands of persons and published in hundreds of papers have shown a moderate increase in cancer incidence for irradiated survivors, with limited impact on their life span (loss of one year at most). In studies on the offspring of these survivors, no statistically significant deleterious effect on malformation frequency, incidence of mutations or mortality from cancer and other diseases has been seen so far. These data are actually the basis for current radiation safety levels; they show that health risks from radiation are limited, but they are not applicable to complex situations such as nuclear power station accidents that involve diverse types of radiation as well as contamination by radioactive materials

The Hiroshima/Nagasaki Survivor Studies: Discrepancies Between Results and General Perception

The explosion of atom bombs over the cities of Hiroshima and Nagasaki in August 1945 resulted in very high casualties, both immediate and delayed but also left a large number of survivors who had been exposed to radiation, at levels that could be fairly precisely ascertained. Extensive follow-up of a large cohort of survivors (120,000) and of their offspring (77,000) was initiated in 1947 and continues to this day. In essence, survivors having received 1 Gy irradiation (~1000 mSV) have a significantly elevated rate of cancer (42% increase) but a limited decrease of longevity (~1 year), while their offspring show no increased frequency of abnormalities and, so far, no detectable elevation of the mutation rate. Current acceptable exposure levels for the general population and for workers in the nuclear industry have largely been derived from these studies, which have been reported in more than 100 publications. Yet the general public, and indeed most scientists, are unaware of these data: it is widely believed that irradiated survivors suffered a very high cancer burden and dramatically shortened life span, and that their progeny were affected by elevated mutation rates and frequent abnormalities. In this article, I summarize the results and discuss possible reasons for this very striking discrepancy between the facts and general beliefs about this situation.

Radiation effects on human heredity

In experimental organisms such as fruit flies and mice, increased frequencies in germ cell mutations have been detected following exposure to ionizing radiation. In contrast, there has been no clear evidence for radiation-induced germ cell mutations in humans that lead to birth defects, chromosome aberrations, Mendelian disorders, etc. This situation exists partly because no sensitive and practical genetic marker is available for human studies and also because the number of people exposed to large doses of radiation and subsequently having offspring was small until childhood cancer survivors became an important study population. In addition, the genome of apparently normal individuals seems to contain large numbers of alterations, including dozens to hundreds of nonfunctional alleles. With the number of mutational events in protein-coding genes estimated as

less than one per genome after 1 gray (Gy) exposure, it is unsurprising that genetic effects from radiation have not yet been detected conclusively in humans.

Effects and consequences of prenatal irradiation

After a brief introduction about the historic development of risk estimates and maximum permissible doses of ionizing radiation, the risks of prenatal irradiation are discussed. Experimental data mainly obtained with mice indicate that the most important risk exists during the period of organogenesis and concerns the induction of malformations. Although in man this period lies between about 10 and 80 days after fertilization for most organs, the main development of the brain occurs later, namely between the 8th and 15th week after conception. Data from Japanese victims of the atomic bomb explosions above Hiroshima and Nagasaki indicate that during development the brain is the most sensitive organ to irradiation and maximal sensitivity is found between the 8th and 15th week after fertilization. A dose of one Gray received during this period induces a severe mental retardation in about 45% of the newborns. The dose response relationship is not significantly different from a linear one without a threshold dose. Studies of intelligence and school performance have shown that 1 Gray received during the 8th-15th week causes a shift of the average intelligence of about 30 points. Irradiation before the 8th week and after the 25th week had no effect on intelligence or mental retardation. During the 16th and 25th week sensitivity was about one fourth of that during the 8th-15th week. Although the irradiation of the embryo and fetus should be avoided as much as possible, the new data have led to an abandonment of the so-called 10-day rule. Generally an accidental irradiation of the embryo or fetus of less than 5 cGy is not considered as a medical indication for abortion. Retrospective studies showed that mothers from children who died from leukemia or other childhood tumors, had been subjected to a diagnostic irradiation of the pelvis or lower abdomen more frequently than mothers from children that did not develop a tumor. It has been estimated that prenatal sensitivity for induction of leukemia and tumors is higher than sensitivity after birth. However, it is still in discussion, whether the relationship between prenatal irradiation and a higher incidence of tumors is of a causal nature.

Genetic effects of radiation in atomic-bomb survivors and their children: past, present and future

Genetic studies in the offspring of atomic bomb survivors have been conducted since 1948 at the Atomic Bomb Casualty Commission and its successor, the Radiation Effects Research Foundation, in Hiroshima and Nagasaki. Past studies include analysis of birth defects (untoward pregnancy outcome; namely, malformation, stillbirth, and perinatal death), chromosome aberrations, alterations of plasma and erythrocyte proteins as well as epidemiologic study on mortality (any cause) and cancer incidence (the latter study is still ongoing). There is, thus far, no indication of genetic effects in the offspring of survivors. Recently, the development of molecular biological techniques and human genome sequence databases made it possible to analyze DNA from parents and their offspring (trio-analysis). In addition, a clinical program is underway to establish the frequency of adult-onset multi-factorial diseases (diabetes mellitus, high blood pressure, and cardiovascular disease etc) in the offspring. The complementary kinds of data that will emerge from this three-pronged approach (clinical, epidemiologic, and molecular aspects) promise to shed light on health effects in the offspring of radiation-exposed people.

Risk calculations for hereditary effects of ionizing radiation in humans

A prediction of the extent to which an additional dose of ionizing radiation increases the natural germ cell mutation rate, and how much such an increase will affect the health status of future human populations is part of the service that human geneticists are expected to offer to human society. However, more detailed scrutiny of the difficulties involved reveals an extremely complex set of problems. A large number of questions arises before such a prediction can be given with confidence; many such questions cannot be answered at our present state of knowledge. However, such predictions have recently been attempted. The 1988 report of the United Nations Scientific Committee for the Effects of Atomic Radiation and the fifth report of the Committee on Biological Effects of Ionizing Radiation of the US National Research Council have presented a discussion of the human genetics problems involved. Empirical data from studies on children of highly radiation-exposed parents, e.g. parents exposed to the atomic bombs of Hiroshima and Nagasaki, or parents belonging to populations living on soil with high background radiation, have been mentioned in this context. Whereas precise predictions are impossible as yet because of deficiencies in our knowledge of medical genetics at various levels, the bulk of the existing evidence points to only small effects of low or moderate radiation doses, effects that will probably be buried in the "background noise" of changing patterns of human morbidity and mortality.

Radiation risk of individual multifactorial diseases in offspring of the atomic-bomb survivors: a clinical health study

There is no convincing evidence regarding radiation-induced heritable risks of adult-onset multifactorial diseases in humans, although it is important from the standpoint of protection and management of populations exposed to radiation. The objective of the present study was to examine whether parental exposure to atomic-bomb (A-bomb) radiation led to an increased risk of common polygenic, multifactorial diseases-hypertension, hypercholesterolaemia, diabetes mellitus, angina pectoris, myocardial infarction or stroke-in the first-generation (F1) offspring of A-bomb survivors. A total of 11,951 F1 offspring of survivors in Hiroshima or Nagasaki, conceived after the bombing, underwent health examinations to assess disease prevalence. We found no evidence that paternal or maternal A-bomb radiation dose, or the sum of their doses, was associated with an increased risk of any multifactorial diseases in either male or female offspring. None of the 18 radiation dose-response slopes, adjusted for other risk factors for the diseases, was statistically significantly elevated. However, the study population is still in mid-life (mean age 48.6 years), and will express much of its multifactorial disease incidence in the future, so ongoing longitudinal follow-up will provide increasingly informative risk estimates regarding hereditary genetic effects for incidence of adult-onset multifactorial disease.

The children of atomic bomb survivors: a synopsis

When the atomic bombing of Hiroshima and Nagasaki occurred in the summer of 1945, most members of the public presumed that many of the children conceived by the survivors would be grossly deformed or seriously damaged in other ways as a consequence of radiation-induced mutations. Although the experimental data then available, largely limited to studies of Drosophila melanogaster, the common fruit fly, did not support this perception, the limitations of the data and the depth of public concern warranted a careful follow-up of the children born to the survivors. To

this end a surveillance was begun in 1947 of all pregnancy outcomes after 20 weeks of gestation in these two cities. Over the half century subsequent to the initiation of this surveillance, some 80-odd thousand pregnancy outcomes have been studied and a variety of potential indicators of mutational damage measured. This report summarises the findings of these studies and offers an estimate of the genetic risk based on these findings.

Congenital malformations, stillbirths, and early mortality among the children of atomic bomb survivors: a reanalysis

Of all the data sets pertinent to the estimation of the genetic risks to humans following exposure to ionizing radiation, potentially the most informative is that composed of the cohort of children born to atomic bomb survivors. We present here an analysis of the relationship between parental exposure history and untoward pregnancy outcomes within this cohort, using to the fullest extent possible the recently revised estimates of the doses received by their parents, the so-called DS86 doses. Available for study are 70,073 terminations, but DS86 doses have not been or presently cannot be computed on the parents of 14,770. The frequency of untoward pregnancy outcomes, defined as a pregnancy terminating in a child with a major congenital malformation, and/or stillborn, and/or dying in the first 14 days of life, increases with combined (summed) parental dose, albeit not significantly so. Under a standard linear model, when the sample of observations is restricted to those children whose parents have been assigned the newly established DS86 doses (n = 55,303), ignoring concomitant sources of variation and assuming a neutron RBE of 20, the estimated increase per sievert in the predicted frequency of untoward outcomes is 0.00354 (+/- 0.00343). After adjustment for concomitant sources of variation, the estimated increase per sievert in the proportion of such births is 0.00422 (+/- 0.00342) if the neutron RBE is assumed to be 20. A "one-hit" model with appropriate adjustments for extraneous sources of variation results in an almost identical value, namely, 0.00412 (+/- 0.00364). When the sample is extended to include parents lacking the full array of dose parameters necessary to calculate the DS86 dose, but sufficient for an empirical conversion of the previously employed T65DR dose system to its DS86 equivalent, we find under the linear model that the estimated increase per sievert in untoward pregnancy outcomes is some 31% higher than that published previously, 0.00264 (+/- 0.00277), assuming an RBE of 20, after adjustment for extraneous sources of variation. (Since a dose could not be calculated in 367 of the 70,073 outcomes, the n = 69,706). The corresponding value with the one-hit model is 0.00262 (+/- 0.00294).

Health effects of atomic bomb radiation

The health effects of atomic bomb radiation have been studied by the Atomic Bomb Casualty Commission (ABCC) and its successor, the Radiation Effects Research Foundation (RERF) based on a fixed population of atomic bomb survivors in Hiroshima and Nagasaki which had been established in 1950. The results obtained to the present can be classified into the following three categories: (1) The effects for which a strong association with atomic bomb radiation has been found include malignant neoplasms, cataracts, chromosomal aberrations, small head size and mental retardation among the in utero exposed. (2) A weak association has been found in the several sites of cancers, some non-cancer mortalities and immunological abnormalities. (3) No association has been

observed in some types of leukemia, osteosarcoma, accelerated aging, sterility and hereditary effects.

Base de datos	**Embase**
Algoritmo	'hiroshima accident' OR (('accident'/exp OR accident) AND hiroshima AND (effect, AND ('radiation'/exp OR radiation) OR stochastic) AND ('model'/exp OR model))"
Radiation exposure and circulatory disease risk: Hiroshima and Nagasaki atomic bomb survivor data, 1950-2003 Objective: To investigate the degree to which ionising radiation confers risk of mortality from heart disease and stroke. Design: Prospective cohort study with more than 50 years of follow-up. Setting: Atomic bomb survivors in Hiroshima and Nagasaki, Japan. Participants: 86 611 Life Span Study cohort members with individually estimated radiation doses from 0 to >3 Gy (86% received <0.2 Gy). Main outcome measures: Mortality from stroke or heart disease as the underlying cause of death and dose-response relations with atomic bomb radiation. Results: About 9600 participants died of stroke and 8400 died of heart disease between 1950 and 2003. For stroke, the estimated excess relative risk per gray was 9% (95% confidence interval 1% to 17%, P=0.02) on the basis of a linear dose-response model, but an indication of possible upward curvature suggested relatively littl e risk at low doses. For heart disease, the estimated excess relative risk per gray was 14% (6% to 23%, P<0.001); a linear model provided the best fit, suggesting excess risk even at lower doses. However, the dose-response effect over the restricted dose range of 0 to 0.5 Gy was not significant. Prospective data on smoking, alcohol intake, education, occupation, obesity, and diabetes had almost no impact on the radiation risk estimates for either stroke or heart disease, and misdiagnosis of cancers as circulatory diseases could not account for the associations seen. Conclusion: Doses above 0.5 Gy are associated with an elevated risk of both stroke and heart disease, but the degree of risk at lower doses is unclear. Stroke and heart disease together account for about one third as many radiation associated excess deaths as do cancers among atomic bomb survivors.	

Base de datos	**Embase**
Algoritmo	('hiroshima bomb' OR (hiroshima AND ('bomb'/exp OR bomb))) AND (effect, AND radiation OR 'stochastic model') AND (cleft AND lip AND palate OR malformations)
Relationship of five anthropometric measurements at age 18 to radiation dose among atomic bomb survivors exposed in utero	

Five body measurements-standing height, body weight, sitting height, chest circumference and intercristal diameter-of 18-year-old atomic bomb survivors exposed in utero in Hiroshima and Nagasaki were analyzed in relation to DS86 uterine dose. Age in utero was divided into four periods: 0-7, 8-15, 16-25 and ≥26 weeks. This categorization is based upon the study of radiation- induced brain damage. The linear regression analyses for these five variables showed significant decreases with increasing dose. The regression coefficients were -2.65 cm/Gy for standing height, -2.46 kg/Gy for body weight, -0.92 cm/Gy for sitting height, -1.37 cm/Gy for chest circumference and -0.32 cm/Gy for intercristal diameter. The multivariate test statistic for the overall dose effect on five body measurements was significant, but the interaction between dose and gestational period was not significant. Principal-component analysis was applied to the five variables. For the first-component scores, the dose effect was significant, but the interaction between dose and gestational period was not significant. For the second- component scores, the dose effect was significant specifically at 0-7 weeks. The radiation dose effect on the second principal component found at 0-7 weeks of gestation suggests that malformations occur in this period.

Effects and consequences of prenatal irradiation.

After a brief introduction about the historic development of risk estimates and maximum permissible doses of ionizing radiation, the risks of prenatal irradiation are discussed. Experimental data mainly obtained with mice indicate that the most important risk exists during the period of organogenesis and concerns the induction of malformations. Although in man this period lies between about 10 and 80 days after fertilization for most organs, the main development of the brain occurs later, namely between the 8th and 15th week after conception. Data from Japanese victims of the atomic bomb explosions above Hiroshima and Nagasaki indicate that during development the brain is the most sensitive organ to irradiation and maximal sensitivity is found between the 8th and 15th week after fertilization. A dose of one Gray received during this period induces a severe mental retardation in about 45% of the newborns. The dose response relationship is not significantly different from a linear one without a threshold dose. Studies of intelligence and school performance have shown that 1 Gray received during the 8th-15th week causes a shift of the average intelligence of about 30 points. Irradiation before the 8th week and after the 25th week had no effect on intelligence or mental retardation. During the 16th and 25th week sensitivity was about one fourth of that during the 8th-15th week. Although the irradiation of the embryo and fetus should be avoided as much as possible, the new data have led to an abandonment of the so-called 10-day rule. Generally an accidental irradiation of the embryo or fetus of less than 5 cGy is not considered as a medical indication for abortion. Retrospective studies showed that mothers from children who died from leukemia or other childhood tumors, had been subjected to a diagnostic irradiation of the pelvis or lower abdomen more frequently than mothers from children that did not develop a tumor. It has been estimated that prenatal sensitivity for induction of leukemia and tumors is higher than sensitivity after birth. However, it is still in discussion, whether the relationship between prenatal irradiation and a higher incidence of tumors is of a causal nature.

A case-control study of congenital malformations and occupational exposure to low-level ionizing radiation

In a case-control study, the authors investigated the association of parental occupational exposure to low-level external whole-body penetrating ionizing radiation and risk of congenital malformations in their offspring. Cases and controls were ascertained from births in two counties in southeastern Washington State, where the Hanford Site has been a major employer. A unique feature of this study was the linking of quantitative individual measurement of external whole-body penetrating ionizing radiation exposure of employees at the Hanford Site, using personal dosimeters, and the disease

outcome, congenital malformations. The study population included 672 malformation cases and 977 matched controls from births occurring from 1957 through 1980. Twelve specific malformation types were analyzed for evidence of association with employment of the parents at Hanford and with occupational exposure to ionizing radiation. Two defects, congenital dislocation of the hip and tracheoesophageal fistula, showed statistically significant associations with employment of the parents at Hanford, but not with parental radiation exposure. Neural tube defects showed a significant association with parental preconception exposure, on the basis of a small number of cases. Eleven other defects, including Down syndrome, for which an association with radiation was considered most likely, showed no evidence of such an association. When all malformations were analyzed as a group, there was no evidence of an association with employment of the parents at Hanford, but the relation of parental exposure to radiation before conception was in the positive direction (one-tailed p value between 0.05 and 0.10). Given the number of statistical tests conducted, some or all of the observed positive correlations are likely to represent false positive findings. In view of strong contradictory evidence, based on no demonstrated effects in genetic studies of atomic bomb survivors in Hiroshima and Nagasaki, it is unlikely that these correlations result from a cause and effect association with parental radiation exposure.

- **Nagasaki**

Base de datos	**Pubmed**
Algoritmo	((Effect, Radiation OR stochastic model) AND (Nagasaki)) AND (Air Pollutants, Radioactive OR Air pollution)
Health impacts of large releases of radionuclides. Late somatic health effects This chapter reviews the risks of radiation-induced cancer for the dose range likely to occur after releases of radionuclides into the environment. Epidemiological evidence from exposed workers and the atomic bomb survivors of Hiroshima and Nagasaki is surveyed. Influences on such risk functions of individual related quantities (e.g. age, sex, nationality, time since exposure and organs exposed) and of radiation modality-related quantities (e.g. dose, dose rate and radiation quality) are also briefly discussed.	

Base de datos	**Pubmed**
Algoritmo	((Effect, Radiation OR stochastic model) AND (Nagasaki)) AND (Cleft lip palate OR malformations)
Quantification of radiation-induced genetic risk Associated with technical advances of our civilization is a radiation - and chemically-induced increase in the germ cell mutation rate in man. This would result in an increase in the frequency of genetic diseases and would be detrimental to future generations. It is the duty of our generation to keep this risk as low as possible. The estimation of the radiation-induced genetic risk of human	

populations is based on the extrapolation of results from animal experiments. Radiation-induced mutations are stochastic events. The probability of the event depends on the dose; the degree of the damage does not. The different methods to estimate the radiation-induced genetic risk will be discussed. The accuracy of the predicted results will be evaluated by a comparison with the observed incidence of dominant mutations in offspring born to radiation exposed survivors of the Hiroshima and Nagasaki atomic bombings. These methods will be used to predict the genetic damage from the fallout of the reactor accident at Chernobyl. For the exposure dose we used the upper limits of the mean effective life time equivalent dose from the fallout values in the Munich region. According to the direct method for the risk estimation we will expect for each 100 to 500 spontaneous dominant mutations one radiation-induced mutation in the first generation. With the indirect method we estimate a ratio of 100 dominant spontaneous mutations to one radiation-induced dominant mutation. The possibilities and the limitations of the different methods to estimate the genetic risk will be discussed. The discrepancy between the high safety standards for radiation protection and the low level of knowledge for the toxicological evaluation of chemical mutagens will be emphasized.

The longest illness. Effects of nuclear war in children

The destruction of civilization that would follow a nuclear war would render any disaster ever recorded insignificant. Millions of people would perish during the first few hours, and many more would die in the months to come. Survival would exist only in the strictest sense of the word, since societal disorganization, famine, drought, darkness, and nuclear winter would envelope the earth. The comparative frailty of children and their dependence on adults would render them most susceptible to the acute effects of a nuclear holocaust. Furthermore, studies of the Hiroshima and Nagasaki, Japan bombings showed a disproportionate propensity for children to experience leukemias and other cancers years after the bombings. There were also great increases in perinatal deaths and cases of microcephaly and retardation in children exposed in utero to the bombs. In the event that there are future generations after a nuclear war, the issue of heritable genetic effects will become important. Suggestions of permanent genetic damage are emerging from the Hiroshima and Nagasaki studies. By comparison, the genetic effects of modern weaponry will be incalculable.

The present state of atomic bomb survivors, with special reference to biological late-effects of radiation

Atomic bombs were dropped on Hiroshima and Nagasaki in August 1945. Within a few months, the bomb blast, heat and radiation emitted by the atomic explosions led to approximately 114,000 fatalities in Hiroshima and about 70,000 in Nagasaki. The radiation in particular continued to exert effects on the human body over a long period of time, resulting in the development of tumors and functional abnormalities in various organs. This paper briefly outlines the diseases caused by radiation as well as the biological late-effects on the survivors without any specific diseases, and stresses the necessity of our enthusiastic opposition to the use of any kind of nuclear weapons.

Radiation-related mortality among offspring of atomic bomb survivors: a half-century of follow-up

Our objective was to examine whether parental exposure to atomic bomb radiation has led to increased cancer and/or noncancer mortality rates among the offspring. We studied 41,010 subjects born from May 1946 through December 1984 (i.e., conceived between 1 month and 38 years after the bombings) and surviving for at least 1 year. One or both parents were in Hiroshima or Nagasaki at the time of the bombings and childbirth. We analyzed mortality data from 1946 to 1999 using the Japanese family registry system by Cox regression model and examined the effects of paternal and maternal irradiation with adjustment for city, sex, year of birth and parental age at childbirth. During follow-up, 314 cancer deaths and 1,125 noncancer disease deaths occurred. The mean age of living subjects was 45.7 years. Median doses were 143 mSv for 12,722 exposed fathers and 132 mSv for 7,726 exposed mothers. Cancer and noncancer mortality rates were no higher for subjects with exposed parents (5+ mSv or unknown dose) than for reference subjects (0-4 mSv), and mortality did not increase with increasing dose. For subjects with both parents exposed, the adjusted hazard ratios were 1.16 [95% confidence interval (CI) 0.92-1.46] for noncancer and 0.96 (95% CI 0.59-1.55) for cancer. This was true of deaths occurring both before and after 20 years of age. However, because of uncertainty due to the small number of deaths and relatively young ages of subjects, we cannot rule out an increase in disease mortality at this time.

Base de datos	**Embase**
Algoritmo	(effect, AND radiation OR stochastic) AND model AND nagasaki)

Assessing the Relative Biological Effectiveness of Neutrons across Organs of Varying Depth among the Atomic Bomb Survivors

When assessing radiation-related risk among the atomic bomb survivors, choices in modeling approach can have an important impact on the results, which are then used to inform radiation protection standards throughout the world. The atomic bombings of Hiroshima and Nagasaki produced a mixed-field radiation exposure from two sources: neutrons and gamma rays. Neutrons are more densely ionizing and cause greater biological damage per unit absorbed dose, resulting in greater relative biological effectiveness (RBE) than gamma rays. To account for this, a combined weighted dose is typically calculated as the sum of the gamma-ray dose and 10 times the neutron dose in the Radiation Effects Research Foundation's reports of mortality, solid cancer incidence and other outcomes. In addition, the colon, which is often chosen as the whole-body representative organ in these analyses, is relatively deep in the body and therefore its dose calculation involves heavy body shielding of neutrons and a low neutron/gamma-ray ratio. With added follow-up and recently updated doses, we used a data-driven approach to determine the best-fitting neutron RBE for a range of organs of varying depth. Aggregated person-year tables of solid cancer incidence (1958-2009) from the Life Span Study were created with separate neutron and gamma-ray DS02R1 doses for several organs including breast, brain, thyroid, bone marrow, lung, liver and colon. Typical excess relative risk models estimating the linear effect of radiation dose were fitted using a range of neutron weights (1-250) to calculate combined dose for each organ, and model deviances were compared to assess fit. Furthermore, models using separate terms for gamma-ray and neutron dose were also examined, wherein the ratio of the neutron/gamma-ray linear terms indicated the best

estimate of the RBE. The best-fitting RBE value for the traditional weighted colon dose was 80 [95% confidence interval (CI): 20-190], while the RBEs for other organs using weighted doses ranged from 25 to 60, with the best-fitting weights and confidence interval widths both incrementally increasing with greater depth of organ. Models using separate neutron- and gamma-ray-dose terms gave similar results to weighted linear combinations, with a neutron/gamma-ray term ratio of 79.9 (95% CI: 18.8-192.3) for colon. These results indicated that the traditionally modeled RBE of 10 may underestimate the effect of neutrons across the full dose range, although these updated estimates still have fairly wide confidence bounds. Furthermore, the colon is among the deepest of organs and may not be the best choice as a single surrogate organ dose, as it may minimize the role of the neutrons. Future work with more refined organ doses could shed more light on RBE-related information available in the Life Span Study data.

Base de datos	**Embase**
Algoritmo	('nagasaki bomb' OR (nagasaki AND ('bomb'/exp OR bomb))) AND 'congenital malformation' AND radiation AND epidemiology

Radiation risk of individual multifactorial diseases in offspring of the atomic-bomb survivors: a clinical health study.

There is no convincing evidence regarding radiation-induced heritable risks of adult-onset multifactorial diseases in humans, although it is important from the standpoint of protection and management of populations exposed to radiation. The objective of the present study was to examine whether parental exposure to atomic-bomb (A-bomb) radiation led to an increased risk of common polygenic, multifactorial diseases-hypertension, hypercholesterolaemia, diabetes mellitus, angina pectoris, myocardial infarction or stroke-in the first-generation (F1) offspring of A-bomb survivors. A total of 11,951 F1 offspring of survivors in Hiroshima or Nagasaki, conceived after the bombing, underwent health examinations to assess disease prevalence. We found no evidence that paternal or maternal A-bomb radiation dose, or the sum of their doses, was associated with an increased risk of any multifactorial diseases in either male or female offspring. None of the 18 radiation dose-response slopes, adjusted for other risk factors for the diseases, was statistically significantly elevated. However, the study population is still in mid-life (mean age 48.6 years), and will express much of its multifactorial disease incidence in the future, so ongoing longitudinal follow-up will provide increasingly informative risk estimates regarding hereditary genetic effects for incidence of adult-onset multifactorial disease.

Cover-up of the effects of internal exposure by residual radiation from the atomic bombing of Hiroshima and Nagasaki.

The criteria certifying atomic bomb disease adopted by the Japanese government are very different from the actual state of the survivors. The criteria are based on epidemiological research by the Radiation Effects Research Foundation, the successor to the Atomic Bomb Casualty Commission (ABCC). The ABCC studied only the effects of primary radiation from the atomic bombing on the survivors of Hiroshima and Nagasaki, and ignored the damage from residual radiation. Analysis of

the incidence of acute radiation disease, the rate of chromosomal aberrations, and the relative risks of chronic disease among the survivors, shows that the effects of residual radiation from fallout exceeds that of primary radiation in the area more than 1.5-1.7 km distant from the hypocentre of the Hiroshima bombing. The effects of internal exposure due to intake of tiny radioactive particles are more severe than those of external exposure, explaining the difference between the official criteria and the actual state of the survivors.

Non-cancer diseases of Korean atomic bomb survivors in residence at Hapcheon, Republic of Korea

Many Koreans, in addition to Japanese, were killed or injured by the atomic bombs detonated over Hiroshima and Nagasaki, Japan, in 1945. Our study examined non-cancer diseases of Korean A-bomb survivors in residence at Hapcheon, Republic of Korea and evaluated whether they had significantly higher prevalence of non-cancer diseases than non-exposed people. We evaluated a number of tests, including anthropometric measurements, blood pressure, blood chemistry, hepatitis B surface antigen, and urinalysis, of survivors (n=223) and controls (n=372). Univariate analysis revealed significantly lower fasting glucose and creatinine, and higher diastolic blood pressure, aspartate aminotransferase, alanine aminotransferase, and blood urea nitrogen levels in the survivors than in the controls. The calculation of crude prevalence ratios (PRs) revealed that A-bomb survivors had a significantly higher prevalence of hypertension (PR, 1.16; 95% CI, 1.00-1.35) and chronic liver disease (2.20; 1.59-3.06) than controls. After adjusting for covariates (age, sex, body mass index, marital status, education, alcohol consumption, and smoking), A-bomb survivors had a significantly higher prevalence of hypertension (1.24; 1.06-1.44), chronic liver disease (2.07; 1.51-2.84), and hypercholesterolemia (1.79; 1.11-2.90) than controls. This study suggests that A-bomb exposure is associated with a higher prevalence of non-cancer diseases in Korean survivors

Unanswered questions: The legacy of atomic veterans

The Department of Veterans Affairs identifies 195,000 servicemen as being involved in the occupation of Hiroshima and Nagasaki, with an additional 210,000 personnel participating in 200 post-war nuclear tests. In 1995, the Institute of Medicine declined to recommend a study of the reproductive outcomes of Atomic Veterans. This article revisits the Institute of Medicine decision. Health effects and legislation provide the framework for a critical analysis of the Japanese data as it applies to Atomic Veterans. It explores the role of traditional hypothesis testing in legislative decisions and offers an in-depth exploration of paternal contributions to adverse reproductive events. It emphasizes the risks faced by reproductive age males when exposed to environmental hazards such as ionizing radiation

Genetic studies at the atomic bomb casualty commission-radiation effects research foundation: 1946-1997

Delayed effects of external radiation exposure: a brief history.

Within months of Roentgen's discovery of X rays, severe adverse effects were reported, but not well publicized. As a result, over the next two decades, fluoroscope operators suffered lethal skin carcinomas. Later, case reports appeared concerning leukemia in radiation workers, and infants born with severe mental retardation after their mothers had been given pelvic radiotherapy early in pregnancy. Fluoroscopy and radiotherapy for benign disorders continued to be used with abandon until authoritative reports were published on the adverse effects of ionizing radiation by the U.S. NAS-NRC and the UK MRC in 1956. Meanwhile, exposure to the atomic bombs in Japan had occurred and epidemics of delayed effects began to be recognized among the survivors: cataracts (1949),

leukemia (1952) and severe mental retardation among newborn infants after intrauterine exposure (1952). No statistically significant excess of germ-cell genetic effects was detected by six clinical measurements (1956), the F1 mortality (1981), cytogenetic studies (1987) or biochemical genetic studies (1988). Somatic cell effects were revealed by long-lasting chromosomal aberrations in peripheral lymphocytes (1968), and somatic cell mutations were found at the glycophorin A locus in erythrocytes (1992). Molecular biology is a likely focus of new studies based on the function of the gene for ataxia telangiectasia (1995), a disorder in which children have severe, even lethal acute radiation reactions when given conventional doses of radiotherapy for lymphoma, to which they are prone. Also, obligate heterozygote female relatives can be studied for increased susceptibility to radiation-induced breast cancer, as suggested by clinical studies. The tumor registries in Hiroshima and Nagasaki now provide incidence data that show the extent of increases in eight common cancers and no increase in eight others (1994). The possibility of very late effects of A-bomb exposure is suggested by recent reports of increased frequencies of hyperparathyroidism, parathyroid cancers and certain causes of death other than cancer.

Risk calculations for hereditary effects of ionizing radiation in humans

A prediction of the extent to which an additional dose of ionizing radiation increases the natural germ cell mutation rate, and how much such an increase will affect the health status of future human populations is part of the service that human geneticists are expected to offer to human society. However, more detailed scrutiny of the difficulties involved reveals an extremely complex set of problems. A large number of questions arises before such a prediction can be given with confidence; many such questions cannot be answered at our present state of knowledge. However, such predictions have recently been attempted. The 1988 report of the United Nations Scientific Committee for the Effects of Atomic Radiation and the fifth report of the Committee on Biological Effects of Ionizing Radiation of the US National Research Council have presented a discussion of the human genetics problems involved. Empirical data from studies on children of highly radiation-exposed parents, e.g. parents exposed to the atomic bombs of Hiroshima and Nagasaki, or parents belonging to populations living on soil with high background radiation, have been mentioned in this context. Whereas precise predictions are impossible as yet because of deficiencies in our knowledge of medical genetics at various levels, the bulk of the existing evidence points to only small effects of low or moderate radiation doses, effects that will probably be buried in the 'background noise' of changing patterns of human morbidity and mortality.

A case-control study of congenital malformations and occupational exposure to low-level ionizing radiation

In a case-control study, the authors investigated the association of parental occupational exposure to low-level external whole-body penetrating ionizing radiation and risk of congenital malformations in their offspring. Cases and controls were ascertained from births in two counties in southeastern Washington State, where the Hanford Site has been a major employer. A unique feature of this study was the linking of quantitative individual measurement of external whole-body penetrating ionizing radiation exposure of employees at the Hanford Site, using personal dosimeters, and the disease outcome, congenital malformations. The study population included 672 malformation cases and 977 matched controls from births occurring from 1957 through 1980. Twelve specific malformation types were analyzed for evidence of association with employment of the parents at Hanford and with occupational exposure to ionizing radiation. Two defects, congenital dislocation of the hip and tracheoesophageal fistula, showed statistically significant associations with employment of the parents at Hanford, but not with parental radiation exposure. Neural tube defects showed a significant association with parental preconception exposure, on the basis of a small number of

cases. Eleven other defects, including Down syndrome, for which an association with radiation was considered most likely, showed no evidence of such an association. When all malformations were analyzed as a group, there was no evidence of an association with employment of the parents at Hanford, but the relation of parental exposure to radiation before conception was in the positive direction (one-tailed p value between 0.05 and 0.10). Given the number of statistical tests conducted, some or all of the observed positive correlations are likely to represent false positive findings. In view of strong contradictory evidence, based on no demonstrated effects in genetic studies of atomic bomb survivors in Hiroshima and Nagasaki, it is unlikely that these correlations result from a cause and effect association with parental radiation exposure.

Genetic effects of the atomic bombs: A reappraisal

Data are presented on four indicators of genetic effects from studies of children born to survivors of the atomic bombings of Hiroshima and Nagasaki. The indicators are frequency of untoward pregnancy outcomes (stillbirth, major congenital defect, death during first postnatal week); occurence of death in live-born children, through an average life expectancy of 17 years; frequency of children with sex chromosome aneuploidy; and frequency of children with mutation resulting in an electrophoretic variant. In no instance is there a statistically significant effect of parental exposure; but for all indicators the observed effect is in the direction suggested by the hypothesis that genetic damage resulted from the exposure. On the basis of assumptions concerning the contribution that spontaneous mutation in the preceding generation makes to the indicators in question, it is possible to estimate the genetic doubling dose for radiation for the first three indicators (the data base is still to small for the fourth). The average of these estimates in 156 rems. This is some four times higher than the results from experimental studies on the mouse with comparable radiation sources, which have been the principal guide to the presumed human sensitivities. The relevance of these data in setting permissible limits for human exposures is discussed briefly

Selección final de artículos por temática (criterios de inclusión y exclusión de artículos)

Los artículos preseleccionados se obtendrán en texto completo y se les aplicarán los siguientes criterios de selección de acuerdo a cada temática para la selección final

Criterios de selección de artículos

- Se seleccionarán todos los artículos publicados en los distintos idiomas, en los cuales fueron redactados originalmente, que cumplan con los diferentes subtemas y variables a estudiar
- Se tomarán artículos publicados en años anteriores y posteriores a accidente de Chernobyl (1986) y las bombas atómicas en Hiroshima y Nagasaki (1945)
- Se incluirán los artículos de aquellos documentos que se encuentran disponibles para su visualización y descarga en línea.
- Artículos que presenten las repercusiones en la salud (Labio paladar fisurado) de las personas afectadas por la ola radioactiva de los accidentes de Chernobyl, Hiroshima y Nagasaki.

Criterios de exclusión de artículos

- Artículos que incluyen efectos en de la radiación producto de otros accidentes diferentes a los anteriormente nombrados
- Se excluirán artículos que presenten estudios de los efectos biológicos de la radiación es especies diferente a la humana

Proceso de extracción de información de artículos por temática

Se realizará una tabla en Excel para la extracción de datos de cada artículo, en las cuales se pondrá: referencias, abstracts y temáticas de cada artículo, y la extracción de datos de cada temática, para identificar de todos los artículos cuales aplican para cada una de las temáticas, las cuales serán identificadas, con el fin de sustraer de manera organizada la información y facilitar la la presentación de resultados.

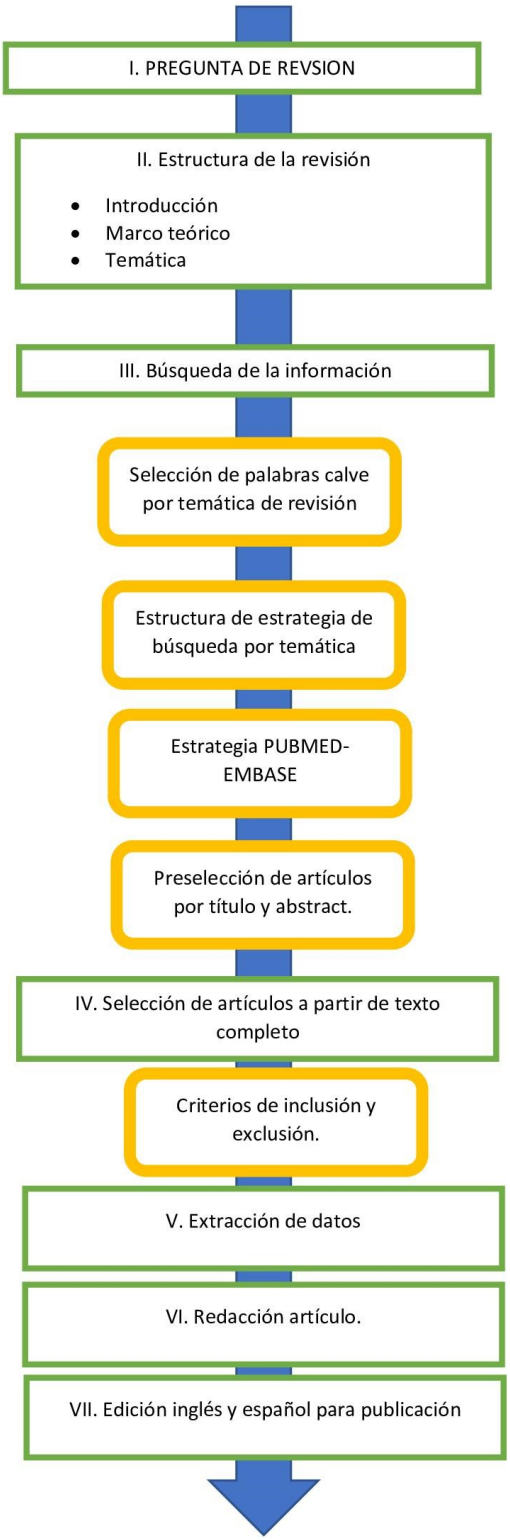
A cada artículo de estudios se le extrajeron los siguientes datos que están consignados en una tabla de Excel:

- Nombre del artículo
- Autores
- Fecha de publicación
- Lugar de estudio
- Efectos estocásticos
- Niveles de contaminación referenciados
- Prevalencia de labio paladar fisurado
- Tiempo transcurrido
- Distancia del foco radioactivo

Proceso de presentación de resultados

Mediante ayudas visuales como lo es el mapa de Europa y Asia representaremos el alcance radioactivo en los diferentes países, el nivel de afectación o contaminación de los mismos.

De igual forma se estructuraran tablas que permitan comparar las diferentes variables de estudio como lo son los diferentes efectos estocásticos,ya sea en mujeres irradiadas embarazadas o aquellas que en un tiempo futuro quedarían embarazadas y estuvieron expuestas, las diferentes prevalencias expuestas en los artículos revisados confrontadas con las diferentes unidades de medida de la contaminación y el tiempo transcurrido para que dichos efectos fueran visibles, así como su discusión escrita en el subyacente cuerpo del trabajo.


I. PREGUNTA DE REVSION
II. Estructura de la revisión
Introducción
Marco teórico
Temática
III. Búsqueda de la información
Selección de palabras calve por temática de revisión
Estructura de estrategia de búsqueda por temática
Estrategia PUBMED-EMBASE
Preselección de artículos por título y abstract.
IV. Selección de artículos a partir de texto completo
Criterios de inclusión y exclusión.
V. Extracción de datos
VI. Redacción artículo.
VII. Edición inglés y español para publicación

Consideraciones en Propiedad Intelectual

Sustento legal

Sustento legal dentro del desarrollo de esta. Este trabajo se realizará de acuerdo a la Ley 1032 del 2006, que modifica el código penal que se relaciona con las violaciones de derechos de autor y derechos conexos y la violacion a los mecanismos de protección de derechos de autor.

Cronograma de actividades

CRONOGRAMA												
Actividad	MESES											
	1er periodo académico				2do periodo académico				3er periodo académico			
	1	2	3	4	5	6	7	8	9	10	11	12
Planteamiento del problema												
Marco teórico												
Estrategias de búsqueda marco teórico												
Objetivos												
Materiales y métodos												
Definición de las variables												
Estrategia de búsqueda												
Selección de artículos												
Criterios de inclusión y exclusión												
Proceso de extracción de información de los artículos												
Proceso de presentación de resultados												
Cronograma												
Presupuesto												

Presupuesto

Rubro	Desembolso nuevo ($)	Desembolso normal ($)	Contrapartida otra institución (Si aplica)		Total ($)
			Contrapartida efectivo ($)	Contrapartida especie ($)	
1. Personal		500.000			
2. Equipos especializados					
2.1. Equipos propios					
3. Materiales y reactivos					
4. Salidas de campo					
5. Refrigerios					
6. Servicios técnicos					
7. Capacitaciones					
8. Adquisición o actualización de software					
9. Evaluación					
10. Otros(Bases de datos)		500.000			
Total					1.000.000

Resultados

La tabla 1 presenta las prevalencias de labio paladar hendido (LPH) o paladar hendido(PH) presentadas por los diferentes autores en países afectados por la lluvia radiactiva del accidente nuclear de Chernobyl, donde se evidencia en general una tendencia a la estabilidad; o aumentos leves que no superan los casos esperados anualmente, por lo que no generan un cambio estadísticamente significativo, en algunos casos, se evidencia un descenso en la prevalencia, y en solo un estudio, la región de Alemania reporta un aumento de 9% de forma no esperada,en la prevalencia de las malformaciones craneofaciales estudiadas, de tipo LPH y LP.

En Gomel y Mogliev regiones de bielorrusia con mayor contaminación (185 a 1480 kBq/m2) a comparación de Minsk y Vitebsk regiones menos contaminadas (37-185 kBq/m2) se identifica una mayor prevalencia de LPH significativamente mayo, teniendo en cuenta que en ambos grupos de regiones se experimentó un aumento moderado de la misma.

Tabla 1. *Prevalencia de labio paladar hendido en diferentes países afectados por la lluvia radioactiva de Chernobyl*

País	Contaminación (nivel de radiación)	Prevalencia control de LPH	Prevalencia posterior de LPH
Rivne Polissia (Ucrania)	301,6 kBq / m2 en 2007	**En regiones con baja contaminación la prevalencia de PH era de 6,1 LPH era de 9.6	La prevalencia de LPH en Riven es de 5.01y para LPH es de 10.6
Minsk y Vitebsk (Bielorrusia)	37-185 kBq/m2	*En el periodo de 1983 -1986 la prevalencia de LPH fue de 1.17, en	En el periodo de 1987-1991 la prevalencia de LPH fue de 1.25 y en 1992-1999 de 1.72
Gomel Mogilev (Bielorrusia)	185 a 1480 kBq/m2	*En el periodo de 1983-1986 la prevalencia de LPH fue de 0.99	En el periodo de 1987-1991 prevalencia de LPH fue de 1.22 y en 1992-1999 1.63
Baviera del norte (Alemania)	0.2mSv	*En el periodo de 1984-1986 prevalencia de PH fue de 0.49 y de LPH fue de 0.79	La prevalencia de PH diciembre del 1986 a febrero de 1987 es de 0.56, de marzo a mayo del 1987 fue de 0.23 La prevalencia de LPH diciembre del 1986 a febrero de 1987 es de 0.80, de marzo a mayo del 1987 fue de 0.99
Baviera del sur (Alemania)	0.6mSv	*En 1984-1986 la prevalencia de PH fue de 0.40, la prevalencia de LPH fue de 0.89.	En el periodo de diciembre del 1986 a febrero de 1987 eL PH fue de 0.37, de marzo a mayo del 1987 en 0.53 en el periodo de junio a agosto de 1987 en 0.34 , en el periodo de septiembre a noviembre de 1987 0.24 La prevalencia de LPH era de 0.89, en el periodo de diciembre del 1986 a febrero de 1987 es

			de 0.68, de marzo a mayo del 1987 de 0.65 en el periodo de junio a agosto de 1987 de 1.01 , en el periodo de septiembre a noviembre de 1987 de 1.08
Kiev(Ucrania)	-18,5 a 74 kBq / m2 para Cs-134 y Cs-137 y 2,6-7,4 kBq / m2 para Sr-90. -9.19 mSv en 1986, 7,29 mSv en 1987, 5,34 mSv en 1988 y 5,03 mSv en 1989.	**Prevalencia control en áreas de baja contaminación (Hungría) 1989 la prevalencia de PH era de 1.0	En el periodo de 1989 en Kiev la prevalencia de PH es de 0.61 en 1990 es de 1.47 en 1991 0.67 en 1992 0.92
Bielorrusia	137Cs de 555 kBq / m2	***Prevalencia control de LPH en áreas de baja contaminación en 1982-1985 era de 0.50 y en 1987-1994 era de 0.89	La prevalencia de LPH en 1982-1985 es de 0.63 en comparación con 1987-1994 1.01
Baviera (Alemania)	53,7 kBq / m2	*La prevalencia control divida de LPH en (1985) fue de 0,00128	La prevalencia dividida de LPH en 1986-1987 0,00137
Alemania	8,8 kBq/m2	*La prevalencia control de LPH en (1983) fue de 2.29	La prevalencia de LPH fue de 2.57 en (1995)
Polissia (Ucrania)	-	**Prevalencia control en regiones de baja contaminación (No Polissia) prevalencia de LPH 8.0 (2000-2014)	En Polissia la prevalencia de LPH fue de 7.0 en (2000-2014)
Rusia	-	**Prevalencia control de LPH en regiones de baja contaminación (1994-2004) de 1,43 +-0,15%	La Prevalencia en Rusia fue de 2,43 +- 0,13% en (1994-2004)
Alemania	0.2-2 mSv	-	Se identifica un aumento de 9.4 % de prevalencia de LP

mSv : (Milisievert) dosis radioactiva absorbida por los seres vivos (varía la unidad de medida de acuerdo al artículo estudiado)
kBq/m2: (Bequerelio sobre metro cuadrado) Actividad radioactiva sobre metro cuadrado, la cual puede ser producto de los diferentes radioisótopos (varía la unidad de medida de acuerdo al artículo estudiado)
***** La prevalencia control se da de acuerdo al tiempo, comparando con prevalencias previas al año de la exposición radioactiva
****** La prevalencia control es determinada en comparación con regiones de baja contaminación
*** La prevalencia control se da determinada por comparación con regiones de baja contaminación y prevalencias previas en tiempo a la exposición radioactiva
PH: Paladar fisurado
LPH: Labio paladar fisurado
- no se reportan valores para esta variable

Los valores de prevalencia se estudian sobre 1000 nacidos vivos

Figura 1. Distancias del foco radioactivo de las ciudades estudiadas

Las ciudades contaminadas por la ola radioactiva producto de las bombas atómicas de Hiroshima y Nagasaki representan una relación radioactiva de 1/100 con respecto al accidente de Chernobyl, dicho esto los datos de prevalencia que afectaron a la población neonata y a su progenitores irradiados relacionadas con las malformaciones craneofaciales de tipo LPH y PH no son expresadas en términos de cifras específicas para estas variables, pues dadas las bajas dosis de exposición no generó un interés investigativo la individualidad de las variables, en su lugar se reportan datos de malformaciones congénitas a nivel general donde no se evidencia un aumento de casos en el periodo en relación a las explosiones atómicas, lo que como se mencionaba anteriormente no incentivo a los investigadores a ahondar en la singularidad de las mismas.

Tabla 2: *Comparación de los sucesos radioactivos estudiados*

País	Geografía	Nivel de Contaminación	Tipo de radiación
Chernobyl	Geográficamente se describe como un amplio valle con abundante arborización	-Niveles de contaminación en el suelo que van de 8,8 kBq/m2 hasta 1480 kBq/m2 en el continente Europeo producto del accidente y en humanos de 9.19 mSv -100 veces más radiación en comparación con las bombas atómicas -Mayor contaminación contenida en el suelo -Ciudad restringida por radioactividad	-Reactor contenía Toneladas de Uranio enriquecido -Liberación de radioisótopos de: Cesio 137 Cesio 134 Estroncio 90 Yodo 131 -Fisión en cadena lenta -Partículas liberadas inicialmente menos tóxicas, con tiempo de vida más largo
Hiroshima	Geográficamente se ubica sobre un valle , considerándose una ciudad casi totalmente llana, lo que generó una reacción expansiva con mayor alcance	-Niveles de contaminación en el suelo de 56,8 Bq m3 Mayor contaminación contenida en el aire -Ciudad próspera actualmente	Little boy 66 kilogramos de Uranio 235 de los cuales implosionaría 1% Fisión en cadena rápida (Liberando energía en milisegundos) Partículas radioactivas altamente tóxicas con tiempo de vida corto
Nagasaki	Geografía montañosa, lo que limitó la ola radioactiva y la expansión de la misma	-Niveles de contaminación en el suelo de 28,5 Bq m-3 -Mayor contaminación contenida en el aire -Ciudad prospera actualmente	Fat Man 64 kilogramos de Plutonio 239 de los cuales se fisionó 1 kilogramo Fisión en cadena rápida (Liberando energía en milisegundos) Partículas radioactivas altamente tóxicas con tiempo de vida corto

Las diferencias geográficas, topográficas y exposición radiactiva así como sus alcances se evidencian en la tabla 2, donde los dos tipos de accidentes radiactivos presentan características particulares a los mismos, dando la relevancia a sus efectos individualmente y asimismo escalereciento los resultados presentes en la tabla 1, en comparación con la ausencia de datos atribuidos a las bombas atómicas de Hiroshima y Nagasaki, estas dos últimas, presentan una menor carga radioactiva y un diferente mecanismo de explosion, donde por el funcionamiento de las mismas (fusión de las partículas) y el transporte e implosión (aéreo), así como el desconocimiento propio de la época, impedían la capacidad destructiva para la que fue creada y de la misma forma los efectos estocásticos atribuidos en la población.

Por otro lado Chernobyl representa un hito en el manejo de la radioactividad, donde su manipulación por un mecanismo de fisión tenía como fin de manipulacion, generar energía, pero de la misma forma representa una afectación que aún hoy en dia se evidencia en la salud de todo el continente Europeo.

Discusión

Las fisuras orofaciales de tipo labio paladar hendido representan una entidad multifactorial que afecta ampliamente a la población en general, entre 1 a 4 de 1000 nacidos vivos alrededor del mundo, rango que oscila dependiendo de muchas variables, entre las que encontramos el origen geográfico, grupos raciales y étnicos y el nivel socioeconómico. Es por esto que esclarecer sus causas probables es de suprema importancia para la población, que le permita de esta forma, su prevención. (2,4)

La radiación ionizante ha sido ampliamente implicada en la teratogenia de diferentes patologías, entre las cuales destaca las malformaciones craneofaciales, dada su capacidad de alterar los enlaces moleculares, generando daños a nivel del ADN y así mismo intracelularmente, en especial, en la vida intrauterina donde la fragilidad de la formación tisular, celular y molecular se encuentran en proceso de fusión y crecimiento permitiendo la generación de una nueva vida. (6) Sin embargo para la inducción de estos daños es necesario unas dosis efectivas que generen consecuencias estocásticas en los fetos. La formación de estas patologías depende del nivel de irradiación (es decir, la dosis) y la etapa del desarrollo embrionario en el que se produce la exposición. La radiación ionizante provoca mutaciones en las células germinales de los padres y puede interferir con los procesos de desarrollo prenatal en sus primeras etapas. Los radionúclidos incorporados en el progenitor materno pueden causar displasia embrionaria, cambios estructurales y funcionales en los órganos y tejidos en desarrollo del embrión y el feto, que pueden conducir a la muerte fetal (en casos de mayor exposición) y a la aparición de malformaciones congénitas. (45)

En esta revisión bibliográfica se estudiaron los efectos producidos por tres grandes eventos radioactivos en la historia, las bombas atómicas en Hiroshima y Nagasaki y el accidente de la planta nuclear de Chernóbil, dos eventos en los cuales las poblaciones afectadas presentaron niveles significativamente altos de radiación ionizante con respecto a la población en general no afectada. Como se mencionaba anteriormente la radiación puede ser producto de diferentes elementos químicos, en estos casos la población fue expuesta a radioisótopos específicos como lo son Cs 137, Cs 134, Sr 90, I131, U 235 y Pu 239, en concentraciones diferentes, tiempos de actividad variable y como se pudo observar con focos de afectación diferente. (30), Las contaminaciones radioactivas medibles en el suelo variaba de entre 8,8 kBq/m2 hasta 1480 kBq/m2, teniendo en cuenta el rango normal de 1kBq/m2, y en la población con dosis efectivas medibles que llegaban a los 9,19 mSv, valores referentes al accidente de Chernobil, sin embargo, en las poblaciones de Nagasaki e Hiroshima los niveles se encontraban por debajo de estas referencias dando niveles de contaminación en el suelo de 28,5 Bq m3 a 56,8 Bq m3 respectivamente.

El Yodo 131 predominante en el accidente de Chernóbil, según E Moser y H D Roedler presentaba una especial afinidad por los tejidos tiroideos, produciendo aumentos en el cáncer de tiroides en especial en la población infantil y neonatal, así como en los casos de trisomía 21 como reporta W Hoffman (43, 29), sin embargo, la vida media de dicho radioisótopo es de 8 días. Por otro lado, elementos como el Cesio y Estroncio tenían vida media más amplias, de 10 y 8 años respectivamente y que particularmente estaban asociados con defectos del tubo

neural, anomalías congénitas, malformaciones craneofaciales, fisuras orofaciales como el labio paladar hendido (29, 30).

Mucha es la variabilidad de la información recolectada a lo largo de los autores, sin embargo, la mayoría llegan a la misma conclusión y es que basados en los estudios de estos dos acontecimientos radioactivos no hay un aumento significativo en la prevalencia de Fisuras labio palatinas producto de la exposición a los radioisótopos, salvo por lo dicho porV Zieglowski y A Hemprich, quienes reportan un aumento significativo de 9.4% en el año inmediatamente posterior al accidente de Chernobil (1987) en dicha prevalencia con respecto a años previos (1980-1986) estudio realizado en, Berlin occidental,Alemania a unos 1150 km del accidente. (37) Contrastado con la publicación realizada por G Lazjuk , P Verger y Col donde en poblaciones con un grado de distancia menor como en el caso de Bielorrusia más específicamente en Gomel y Mogilev a 197 km, si demuestran un aumento en lo referente a los años previos al accidente con respecto al posterior de 0.64%, pero no es una prevalencia significativamente mayor al rango reportado en años previos, caso que se repite en la mayoría de autores. (31)

Por otro lado, en el caso de las bombas atómicas, ni siquiera se observan reportes de estas fisuras en específico, pues como sugieren los autores, en general, la cantidad de radiación no alcanzaba los niveles umbral para generar efectos teratógenos en este ámbito, pues las tazas de malformaciones congénitas en general no evidencian un aumento significativo como lo reporta Nori Nakamura. (44)

Estos hallazgos nos pueden conducir a pensar en varios puntos, el primero y más visible es que efectivamente la radiación ionizante no conduce a un aumento de la prevalencia significativamente de malformaciones craneofaciales de tipo labio paladar hendido como se reporta en las diferentes publicaciones al respecto, por otro lado estos reportes pueden ser producto de diversas variables como los autores lo describen, pues el bajo registro de anomalías craneofaciales puede estar amparado en las desigualdades socioeconómicas de las poblaciones, pues se identifica un subregistro en grupos con menos recursos económicos o comunidades marginales, las cuales no tienen accesos a registros de salud (29). De la misma forma se observan comportamientos contrarios a lo esperado como lo reportan G Lazjuk , P Verger y Col, donde la prevalencia al nacer de todas las anomalías craneofaciales fue significativamente mayor en las regiones menos contaminadas por el accidente de Chernobyl en comparación con las regiones más afectadas, lo que puede ser explicado como ellos bien lo concluyen, por la desigualdad en la rigurosidad de los registros, pues aquellas regiones menos contaminadas albergan los principales y más grandes centros de diagnóstico de anomalías craneofaciales (30)

Otra posible variable se debe a la subestimación que la comunidad internacional muestra ante las bajas dosis crónicas radioactivas que no generan efectos determinísticos como la muerte fetal o la carcinogénesis y la falta de estudio asociada a todo el abanico de repercusiones en la salud que puede generar, entre las cuales están las fisuras orofaciales. (30). Las tendencias al aumento también pueden ser explicadas por una mayor rigurosidad en el seguimiento de las malformaciones craneofaciales producto de la radio vigilancia que se inicia a implementar en Europa a partir del accidente en la planta nuclear de Chernóbil y de la misma forma en la

época de las bombas atómicas en Japón. (30) De la misma forma se observó otro aspecto a valorar, la tasa de nacimientos, que como es mencionado por G Lazjuk , P Verger, y Col descendió de 130.000 anualmente (en 1979-1985) a 64.000(en 1997) en la ciudad de Bielorrusia, fenómeno explicado en gran medida al temor y pánico de la población irradiada a las consecuencias en sus futuros hijos irradiados. (30)

Dada la cantidad de variables involucradas, el conocimiento radiobiológico actual , los reportes de estudio de estas poblaciones afectadas, los efectos sobre la salud y más específicamente el carácter muta génico de la radiación, si los hubiera, no serían medibles con herramientas epidemiológicas, sin embargo, en varios informes independientes, los investigadores han descrito picos aislados en la prevalencia de malformaciones congénitas en la cohorte concebida inmediatamente después del inicio de las consecuencias, pero que como se mencionó, no es posible generar una relación causal a partir de esta información. (29)

Conclusiones

La posibilidad de identificar cambios teratogénicos, mutagénicos que correspondan con las malformaciones craneofaciales de tipo labio paladar hendido en las poblaciones expuestas a los grandes eventos asociados a la radiación (bombas atómicas de Hiroshima y Nagasaki y el accidente nuclear de Chernóbil) es casi nula, dado a que los análisis epidemiológicos realizados no permiten una asociación concreta que controle la amplia gama de variables que se asocia a dicha disrupción de la anatomía normal craneofacial. Sin embargo la prevalencia observada en cuanto a las poblaciones más afectadas por la ola radioactiva no reporta un aumento significativo en el número de casos esperados de esta malformación.

Se espera que futuras investigaciones y estudios aborden el tema de tal forma que permitan definir o refutar una asociación o causalidad definitiva entre la radiación ionizante y el desarrollo de malformaciones craneofaciales de tipo labio y paladar hendido; buscando realizar mejoras de las mediciones de la contaminación radiactiva en el medio ambiente y mejores estimaciones de las dosis de radiación acumuladas en la población.

En los 30 años transcurridos desde el desastre de la central nuclear de Chernobyl, hay evidencia de niveles persistentes de radiación ionizante incorporada en adultos, niños y mujeres embarazadas en el área circundante. Los niveles medidos de cesio-137 varían según la región y pueden verse influenciados por las fuentes de agua y la dieta, así como por la proximidad a las plantas de energía nuclear. Estos niveles de radiactividad han sido relacionados con el aumento de malformaciones congénitas, tales como microcefalia, síndrome de Down, polidactilia, entre otros; sin embargo no hay evidencia significativa de una relación directa con las dosis de radiación y el aumento de la prevalencia de hendiduras craneofaciales de tipo Labio y Paladar Hendido.

Referencias Bibliográficas

1. Sorolla J.P. Anomalías craneofaciales. Rev Médica Clínica Las Condes. 2010;21(1):5-15.
2. Navarro Vila C, dir., García Marín F, coord., Ochandiano Caicoya S, coord. Tratado de cirugía oral y maxilofacial. 2009.
3. Cooper ME, Ratay JS, Marazita ML. Asian oral-facial cleft birth prevalence. Cleft Palate Craniofac J. 2006;43(5):580-9.
4. Stone C. Cleft Lip and Palate: Etiology, Epidemiology, Preventive and Intervention Strategies. Anat Physiol. 2013;04(03):2-6
5. Serrano CP, Ruiz JR, Quiceno LB, Rodríguez MG. Labio y/o Paladar Hendido:Una revisión.Ustasalud 2009; 8: 44 – 52.
6. Land,C. Ionizing radiation.[Internet]. Encyclopedia Britannica, inc.;2019.[Consultado 12 Abr 2020]. Disponible en:https://www.britannica.com/science/ionizing-radiation
7. Weigelt E, Scherb H. Spaltgeburtenrate in Bayern vor und nach dem Reaktorunfall in Tschernobyl. Mund-, Kiefer- und Gesichtschirurgie. 2004;8(2):106–10.
8. Muhamad AH, Watted N, Abdulgani A. Cleft lip : a comprehensive review. Front Pediatr. 2014;338-355.
9. Rytömaa T. Ten Years after Chernobyl. Ann Med. 1996;28(2):83-7.
10. World Health Organization.Ionizing radiation, health effects and protective measures.[Internet].World Health Organization;2016.[Consultado 13 Abr 2020]. Disponible en: https://www.who.int/news-room/fact-sheets/detail/ionizing-radiation-health-effects-and-protective-measures
11. Nakamura N. Genetic Effects of Radiation in Atomic-bomb Survivors and Their Children: Past, Present and Future. J Radiat Res. 2006;47(Supplement B):B67–73.
12. Jordan BR. The Hiroshima/Nagasaki survivor studies: Discrepancies between results and general perception. Genetics. 2016;203(4):1505–12.
13. Scherb H, Weigelt E. Cleft lip and cleft palate birth rate in Bavaria before and after the Chernobyl nuclear power plant accident. Mund Kiefer Gesichtschir. 2004;8(2):106–10.
14. Romance, A. Malformaciones craneofaciales.[Internet].Unidad de Cirugía Maxilofacial. [Consultado 13 Abr 2020]. Disponible https://www.ucm.es/data/cont/docs/420-2014-02-25-Malformaciones%20Craneofaciales.pdf
15. Shkoukani MA, Chen M, Vong A. Cleft Lip – A Comprehensive Review. Front Pediatr. 2013;1:53.
16. Yilmaz HN, Ozbilen EO, Ustun T. The Prevalence of cleft lip and palate patients: a single-center experience for 17 years. Turk J Orthod. 2019;32(3):139-144.
17. Dixon MJ, Marazita ML, Beaty TH, Murray JC. Cleft lip and palate: synthesizing genetic and environmental influences. Nat Rev Genet. 2011 Mar; 12(3): 167–178.
18. Marcucio R, Hallgrimsson B, Young NM. Facial morphogenesis: physical and molecular interactions between the brain and the face.Curr Top Dev Biol. 2015;115:299-320.

19. Agrawal K. Cleft palate repair and variations. Indian J Plast Surg. 2009;42(S 01):S102-S109.

20. Ardila BF. Hiroshima y Nagasaki. Fernando Bermúdez Ardila.El fin del fin. 1 ed.Ediciones Panamericana Formas e Impresos, S.A;200. p. 168-172
21. Ecured contributors .Hiroshima.[Internet].Ecured.1ed;2019.[Consultado 13 Abr 2020]. Disponible en: https://www.ecured.cu/index.php?title=Hiroshima&oldid=3443699
22. Sanchez LG.El terror radiactivo de Hiroshima y Nagasaki [Internet].ABC Ciencia; 2016.[Consultado 13 Abr 2020].Disponible en:https://www.abc.es/ciencia/abci-terror-radiactivo-hiroshima-y-nagasaki-201608131823_noticia.html?ref=https%3A%2F%2Fwww.google.com%2F
23. Donde-está.org.Donde está Chernobil.[Internet].[Consultado 13 Abr 2020]. Disponible en:https://donde-esta.org/chernobyl/
24. Ardila BF.Chernobyl. Fernando Bermúdez Ardila.El fin del fin. 1 ed.Ediciones Panamericana Formas e Impresos, S.A;200. p. 173-178.
25. Van den Akker, A M, Hoeksma JB, Prahl-Andersen B. Incidence of cleft lip and palate in the Netherlands. Ned Tijdschr Tandheelkd. 1987;94(12):520-4.
26. Cereijo AI, Martinez-Frias ML. Prevalence of other birth defects among relatives of oral cleft probands. J Med Genet. 1992;29(7):516.
27. Mapa de Japón. Imagen disponible en:https://es.123rf.com/photo_6883904_mapa-de-jap%C3%B3n-.html. [Consultado Abr 12 2020]
28. Mapa de Ucrania.Imagen disponible en: http://www.consumedland.com/page_01_fr.html.[Consultado Abr 12 2020].
29. Hoffmann W. Fallout from the chernobyl nuclear disaster and congenital malformations in europe. Archives of environmental health. 2001;56(6):478-484. http://www.tandfonline.com/doi/abs/10.1080/00039890109602895. doi: 10.1080/00039890109602895.
30. Dancause KN, Yevtushok L, Lapchenko S, et al. Chronic radiation exposure in the rivne-polissia region of ukraine: Implications for birth defects. American journal of human biology. 2010;22(5):667-674. https://api.istex.fr/ark:/67375/WNG-QMQ4K629-3/fulltext.pdf. doi: 10.1002/ajhb.21063.
31. Lazjuk G, Verger P, Gagnière B, Kravchuk Z, Zatsepin I, Robert-Gnansia E. The congenital anomalies registry in belarus: A tool for assessing the public health impact of the chernobyl accident. Reproductive Toxicology. 2003;17(6):659. doi: 10.1016/s0890-6238(03)00072-8.
32. Jordan B. Les survivants d'Hiroshima/Nagasaki et leur descendance - Les enseignements d'une étude épidémiologique à long terme [Hiroshima/Nagasaki survivors and their offspring: results of longterm epidemiological studies]. Med Sci (Paris). 2018;34(2):171-178. doi:10.1051/medsci/20183402016
33. IRL C, SCHOETZAU A, VAN SANTEN F, GROSCHE B. Birth prevalence of congenital malformations in bavaria, germany, after the chernobyl accident. European journal of epidemiology. 1995;11(6):621-625. https://www.jstor.org/stable/3582164. doi: 10.1007/BF01720294.
34. Buzhievskaya TI, Tchaikovskaya TL, Demidova GG, Koblyanskaya GN. Selective monitoring for a Chernobyl effect on pregnancy outcome in Kiev, 1969-1989. Hum Biol. 1995;67(4):657-672.

35. Lazjuk GI, Nikolaev DL, Novikova IV. Changes in registered congenital anomalies in the republic of belarus after the chernobyl accident. Stem cells (Dayton, Ohio). 1997;15(S1):255-260. https://onlinelibrary.wiley.com/doi/abs/10.1002/stem.5530150734. doi: 10.1002/stem.5530150734.
36. Scherb H, Weigelt E. Spaltgeburtenrate in Bayern vor und nach dem Reaktorunfall in Tschernobyl [Cleft lip and cleft palate birth rate in Bavaria before and after the Chernobyl nuclear power plant accident]. Mund Kiefer Gesichtschir. 2004;8(2):106-110. doi:10.1007/s10006-004-0524-1
37. Zieglowski V, Hemprich A. Spaltgeburtenrate der ehemaligen DDR vor und nach dem Reaktorunfall in Tschernobyl [Facial cleft birth rate in former East Germany before and after the reactor accident in Chernobyl]. Mund Kiefer Gesichtschir. 1999;3(4):195-199. doi:10.1007/s100060050129
38. Jordan BR. The Hiroshima/Nagasaki Survivor Studies: Discrepancies Between Results and General Perception. Genetics. 2016;203(4):1505-1512. doi:10.1534/genetics.116.191759
39. Wertelecki W, Chambers CD, Yevtushok L, et al. Chornobyl 30 years later: Radiation, pregnancies, and developmental anomalies in Rivne, Ukraine. Eur J Med Genet. 2017;60(1):2-11. doi:10.1016/j.ejmg.2016.09.019
40. Les fentes labiopalatines et l'environnement en Russie
41. Korsakov AV, Geger EV, Lagerev DG, Pugach LI, Mousseau TA. De novo congenital malformation frequencies in children from the Bryansk region following the Chernobyl disaster (2000-2017). Heliyon. 2020;6(8):e04616. Published 2020 Aug 17. doi:10.1016/j.heliyon.2020.e04616
42. Little J. The Chernobyl accident, congenital anomalies and other reproductive outcomes. Paediatr Perinat Epidemiol. 1993;7(2):121-151. doi:10.1111/j.1365-3016.1993.tb00388.x
43. Moser E, Roedler HD. 131Jod: Biokinetik, Strahlenexposition sowie Risikoabschätzung im Zusammenhang mit dem Reaktorunfall in Tschernobyl [Iodine 131: biokinetics, radiation exposure and risk assessment with reference to the reactor accident at Chernobyl]. Rofo. 1987;146(6):711-716.
44. Nakamura N. Genetic effects of radiation in atomic-bomb survivors and their children: past, present and future. J Radiat Res. 2006;47 Suppl B:B67-B73. doi:10.1269/jrr.47.b67
45. Korsakov, A. V., Geger, E. V., Lagerev, D. G., Pugach, L. I., & Mousseau, T. A. (2020). De novo congenital malformation frequencies in children from the Bryansk region following the Chernobyl disaster (2000-2017). Heliyon, 6(8), e04616. https://doi.org/10.1016/j.heliyon.2020.e04616