

# II Jornadas Científicas de la UNED

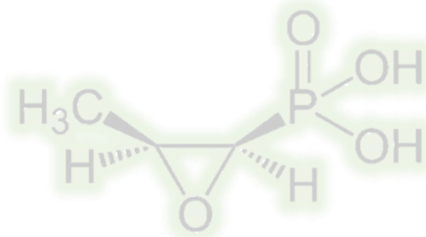
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## PROGRAMA DE DOCTORADO EN CIENCIAS BIOMÉDICAS Y SALUD PÚBLICA

Equipo 6: Investigación epidemiológica y bases genéticas de enfermedades raras

### TÍTULO PROVISIONAL DE LA TESIS

Uso de fosfomicina durante el embarazo y defectos congénitos: Estudio caso-control en una serie consecutiva de 3.178.291 nacimientos en España durante el periodo 1.980-2.018



### DOCTORANDO

Carlos Dévora Figueroa

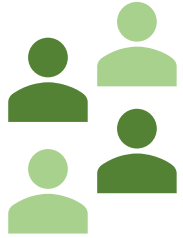
### DIRECTORA DE TESIS

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## BREVE INTRODUCCIÓN: Enfermedad rara: concepto y cifras

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Aquella que no afecta a más de  
**5** de cada **10.000** habitantes



**6-8 %** de la población mundial

Organización Mundial de la Salud  
**+ 6.000** enfermedades raras

Más de

**3**

MILLONES DE PERSONAS  
conviven con alguna de estas  
patologías en **España**

## BREVE INTRODUCCIÓN: Defectos congénitos: definición e importancia

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Los **defectos congénitos**, también llamados **anomalías congénitas**, constituyen un conjunto de alteraciones que tienen lugar durante el **periodo embrionario y/o fetal** y que pueden manifestarse durante el **transcurso del embarazo**, en el **momento del nacimiento** o, incluso, **pasado algún tiempo**.

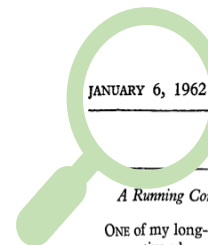
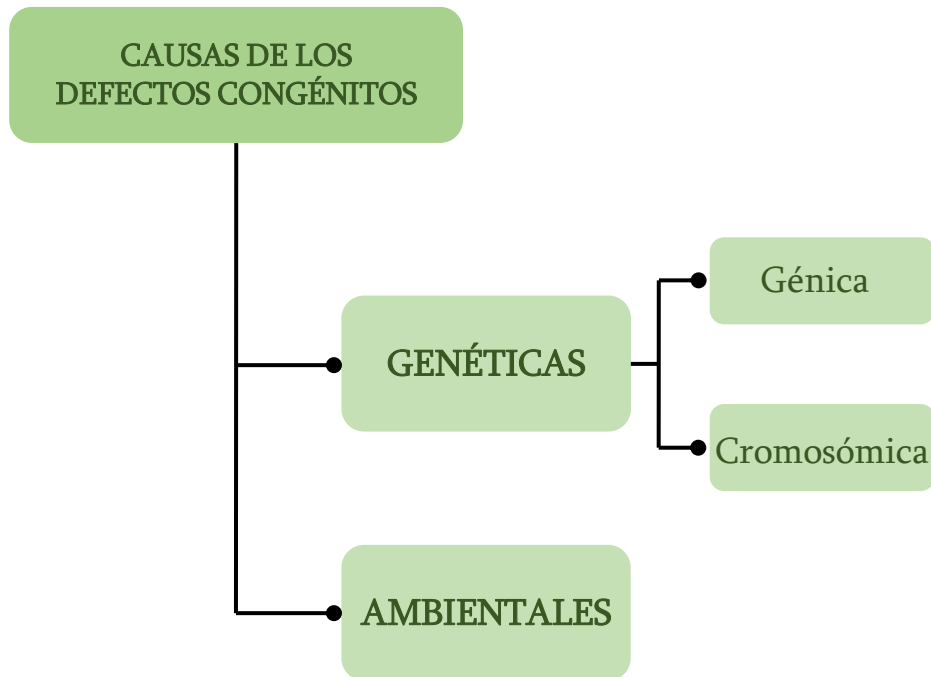
“ La mayor parte de defectos congénitos tiene la **consideración de Enfermedad Rara** ” .

### Importancia cualitativa y cuantitativa...

- ✓ Muerte prematura.
- ✓ Morbimortalidad infantil.
- ✓ Discapacidad a largo plazo.

# BREVE INTRODUCCIÓN: Defectos congénitos: causas

## Algunos fármacos pueden provocar defectos congénitos...



JANUARY 6, 1962

IN ENGLAND NOW—LETTERS TO THE EDITOR

THE LANCET 45

In England Now

Letters to the Editor

*A Running Commentary by Peripatetic Correspondents*

ONE of my long-term analytic patients, who is going through a very active phase of his analysis, had a bad anxiety attack on his way home after a session. His wife called in the family doctor who, to be on the safe side, sent the patient into hospital with the comment "coronary thrombosis" perforated ulcer. He was first seen by the surgeon, who found nothing to justify operative interference. When the wife explained that her husband was undergoing analysis "for his nerves" he took one glance at the patient and said: "I see nothing nervous about him," but transferred him to the physician.

The physician ruled out coronary thrombosis on ordinary physical examination, but arranged for an E.C.G. none the less and threw in a barium meal as an extra. When, as expected, all results were negative, he sat down at—or should I say on—the bedside to "reassure" the patient. The patient related some of the analytic findings of the past two years, and received a reassuring pat on the back from the physician. Later, reporting to the wife, the physician said: "Your husband need not have gone all that time to the psychiatrist to find out what happened in his childhood. I got it out of him in five minutes."

\* \* \*

"Hark! the herald angels sing, . . ." came over the radio as we plugged in the electric kettle for tea for breakfast. "This kettle's taking a long time to boil. Has it gone phut again?" "That was a new element and flex and plug that I had put in a week ago. Better look at the plug, it has a fuse in it." And so the investigation began; and the radio continued, "Peace on earth, and mercy mild . . ." The water in the kettle was warm, but wouldn't boil, yet the flex and all parts seemed all right. I unplugged the kettle and plugged in the bed-lamp—no light. The dressing-room light was out too—power failure. The radio continued—transistorised. Our house is near-all-electric. True, the central-heating is gas-operated, but the cooker that was to have been on gas is an electric model. You can't boil a kettle on a central-heating gas-boiler, but we remembered the gas-poker at the lounge fire-place. Saved again—but were we? Try holding a kettle

### THALIDOMIDE AND CONGENITAL ABNORMALITIES

SIR,—Dr. McBride (Dec. 16) describes congenital abnormalities in babies delivered of women who have taken thalidomide. I have seen 52 malformed infants whose mothers had taken 'Contergan' in early pregnancy, and I understand that contergan is a synonym of thalidomide, others being 'Distaral', 'Softenon', 'Neurosedyn', 'Isomin', 'Kedavon', 'Telargan', and 'Sedalis'.

Since I discussed the possible aetiological role of contergan in human malformations at a conference on Nov. 18, 1961, I have received letters from many places in the German Federal Republic, as well as from Belgium, England, and Sweden, reporting 115 additional cases in which this drug was thought to be the cause.

Though these malformations are variable, they are of a rather specific nature. It is usually possible to infer from the type of the abnormalities alone whether contergan has been taken. Typical of a contergan history are defects of the arms (amelia, atypical phocomelia with absence of the thumbs and sometimes of other fingers as well, aplasia of the radius, defects of the long bones of the legs, especially the femora and tibiae, absence of the auricles, haemangiomas of the nose and the upper lip [wine-spot variety], atresia of the oesophagus, the duodenum, or the anus, cardiac anomalies, and aplasia of the gallbladder and of the appendix).

Judging from case histories of more than 300 women who have borne normal infants, and of whom none had taken contergan between the 4th and the 8th week after conception, the risk to a fetus of a mother taking contergan during this period may be definitely higher than 20%. I venture the estimate that at least 2000, possibly more than 3000, "contergan" babies have been born in Western Germany since 1959.

Universitäts-Kinderklinik,  
Hamburg-Eppendorf, Germany.

W. LENZ.

## ¿Existe riesgo teratogénico tras la administración del antibiótico fosfomicina en mujeres embarazadas?



Review

Comparison of single-dose fosfomycin tromethamine and other antibiotics for lower uncomplicated urinary tract infection in women and asymptomatic bacteriuria in pregnant women: A systematic review and meta-analysis

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Women  
Pregnancy  
Meta-analysis

### ABSTRACT

**Introduction:** This systematic review and meta-analysis investigated the efficacy and safety of single-dose fosfomycin tromethamine (FT) versus other antibiotic agents in women suffering from lower uncomplicated urinary tract infection (uUTI) and pregnant women with uUTI or asymptomatic bacteriuria (ASB).

**Methods:** MEDLINE, EMBASE and the Cochrane library were searched to identify relevant literature. Twenty-one studies were identified. Nine of the 21 studies enrolled 21 22 patients and were used to compare the clinical resolution of uUTI between non-pregnant and pregnant women. Given that uUTI and ASB are assessed using similar microbiological evaluation methods, all 3103 patients in the identified 21 studies were pooled to determine microbiological resolution between uUTI or ASB patients. Safety outcomes of the treatments were analysed in 15 studies.

**Results:** The results showed that single-dose FT was comparable with other antibiotic agents in clinical resolution of uUTI (OR 0.89; 95% CI 0.71–1.10;  $P = 0.41$ ) in non-pregnant ( $P = 0.32$ ) and pregnant women ( $P = 0.64$ ). Moreover, single-dose FT was equal to other antibiotics in microbiological resolution, and there was no difference in overall microbiological resolution (OR 1.11; 95% CI 0.92–1.34;  $P = 0.29$ ) among non-pregnant women with uUTI ( $P = 0.48$ ), pregnant women with uUTI ( $P = 0.81$ ) and pregnant women with ASB ( $P = 0.30$ ). There were no serious fosfomycin-related adverse events and most frequent adverse events were mainly gastrointestinal.

**Conclusion:** This meta-analysis suggests that single-dose fosfomycin tromethamine produces equivalent clinical outcomes to comparator antibiotics in terms of clinical efficacy and microbiological efficacy. It is therefore clinically effective and safe for women with uUTI and pregnant women with uUTI or ASB, and has higher patient compliance.

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Ficha técnica de X medicamento  
conteniendo fosfomicina

### 4.6. Fertilidad, embarazo y lactancia

#### Embarazo:

Los datos disponibles sobre la seguridad del tratamiento con fosfomicina durante el 1.º trimestre del embarazo (n = 152) son limitados. Por el momento, estos datos no revelan signos de potencial teratogénico. Fosfomicina atraviesa la placenta. Los estudios en animales no sugieren efectos perjudiciales directos ni indirectos en términos de toxicidad para la reproducción (ver sección 5.3).

sólo se debe utilizar durante el embarazo si es estrictamente necesario.

# MI TESIS DOCTORAL...

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## OBJETIVOS ESPECÍFICOS:

- a) Estudiar el consumo de fosfomicina durante el embarazo, en sus distintas etapas y a lo largo de los años en madres de niños y niñas con defectos congénitos y sin dichas patologías y comparar ambos grupos.
- b) Realizar un **análisis multivariante**, controlando la influencia de otros factores y variables sobre la posible relación entre la exposición prenatal a fosfomicina y la presencia de defectos congénitos en el recién nacido.
- c) Elaborar, en base a los resultados obtenidos, las **pautas preventivas** que correspondan, enfocadas a la prevención primaria de defectos congénitos.



## ¿DE QUÉ DATOS DISPONEMOS?

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Se han utilizado los datos del **Estudio Colaborativo Español sobre Malformaciones Congénitas (ECEMC)** del periodo comprendido entre 1.980 y 2.018.

**3.178.291** nacimientos consecutivos, de niños con defectos congénitos (**CASOS**) y sin ellos (**CONTROLES**).

**+ de 300 variables para analizar**

**Información sobre el ECEMC**



Páginas - Grupos de investigación del IIER-ECEMC

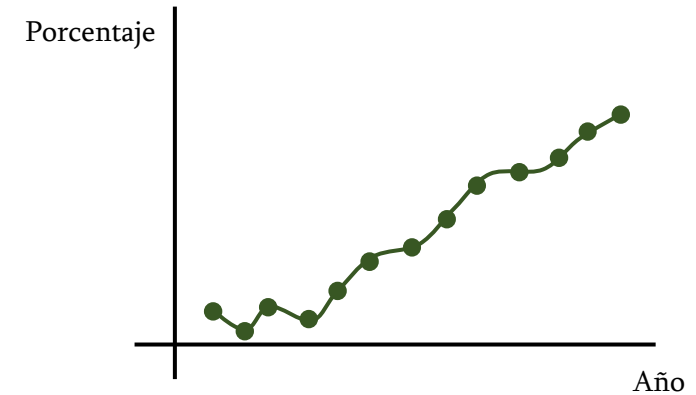


# ¿QUÉ HEMOS HECHO HASTA AHORA?

- INMERSIÓN EN EL CONOCIMIENTO DE LOS DEFECTOS CONGÉNITOS Y SUS CAUSAS. BÚSQUEDA BIBLIOGRÁFICA



- EVOLUCIÓN DEL CONSUMO DE FOSFOMICINA EN ESPAÑA



- PRINCIPIOS DE BIOESTADÍSTICA Y EPIDEMIOLOGÍA



$$\chi^2 = \sum \left( \frac{(f_o - f_e)^2}{f_e} \right)$$

- SELECCIÓN DE VARIABLES Y PREPARACIÓN DE LOS FICHEROS DE DATOS PARA EL ESTUDIO MULTIVARIANTE

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## ALGUNOS MENSAJES FINALES...

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“ La coordinación y los esfuerzos conjuntos de diversos organismos e instituciones contribuyen al avance en la investigación Biomédica ” .

### Esperamos...



- ✓ Mejor conocimiento sobre la fosfomicina.



- ✓ Que las mujeres embarazadas puedan recibir tratamiento para un grupo frecuente de patologías y dolencias en el embarazo, con mayor seguridad, basado en ese mejor conocimiento.



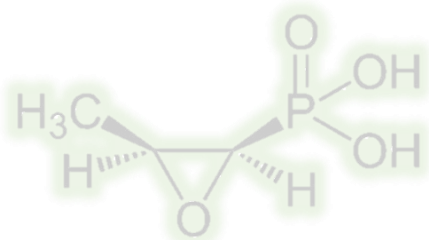
- ✓ Facilitar la prevención de defectos congénitos y contribuir, por tanto, a que los niños y niñas nazcan sanos.



# ¡Gracias!

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“Y a la UNED, al ISCIII y al ECEMC  
por esta oportunidad para poder llevarlo a cabo”



Más información sobre el Programa de Doctorado en la página  
de la UNED. ¡Anímate!