Authors' objectives
To critically review the literature on use of antidepressants during breast-feeding.

Searching
MEDLINE was searched from 1966 to 1995 using the individual names of all antidepressant drugs used during lactation or breast-feeding.

Study selection
Study designs of evaluations included in the review
Single case studies or case series were included.

Specific interventions included in the review
Amitriptyline, nortriptyline, desipramine, clomipramine, doxepin, dothiepin, fluoxetine, sertraline, and bupropion.

Participants included in the review
Breast-feeding mothers and their infants were included. In the included studies, the infants' ages ranged from 1 to 60 weeks.

Outcomes assessed in the review
Maternal and infant serum levels of drugs and drug metabolites (ng/ml) were measured.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined by a narrative review.

How were differences between studies investigated?
Differences in outcomes between the studies were not investigated statistically.

Results of the review
Fifteen studies representing data from 29 breast-feeding mother-infant pairs were included.

Amitriptyline, nortriptyline, desipramine, clomipramine, dothiepin and sertraline were not found in quantifiable amounts in nurslings, and no adverse effects were reported. With the exception of dothiepin, tricyclic parent drugs were
not detectable at levels as low as 1 to 10 ng/ml in nursling serum. For other drugs the limits of detection were: amitriptyline, 5 ng/ml; nortriptyline, 4 to 5 ng/ml; desipramine, 1 ng/ml; clomipramine, 10 ng/ml; and dothiepin, 2 ng/ml. Adverse effects were described in some young infants whose mothers had been treated with doxepin or fluoxetine during breast-feeding.

Authors' conclusions
Amitriptyline, nortriptyline, desipramine, clomipramine, dothiepin and sertraline were not found in quantifiable amounts. Therefore, these are the drugs of choice for breast-feeding women. Adverse effects were described in some young infants whose mothers had been treated with doxepin or fluoxetine during breast-feeding. The collective serum level data suggest that infants older than 10 weeks are at low risk for adverse effects of tricyclics, and there is no evidence of accumulation.

CRD commentary
The review is mainly limited by the primary studies: these studies are so small (the largest has seven mothers) that a convincing investigation of the risk of infrequent side-effects is difficult. The literature search is restricted to MEDLINE; a wider search strategy (including a search of bibliographies of retrieved studies) may have retrieved more primary research. Therefore, the results regarding safety could be viewed as inconclusive.

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