BJOG: an International Journal of Obstetrics and Gynaecology
November 2004, Vol. 111, pp. 1254–1260
DOI: 10.1111/j.1471-0528.2004.00405.x

Is induced abortion a contributing factor to tubal infertility in Mexico? Evidence from a case–control study

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Objective To determine the contribution of induced abortion to tubal infertility in Mexico.

Design Population- and hospital-based case-control study.

Setting Tertiary hospitals in Mexico City.

Sample Women between 20 and 40 years with infertility and controls of the same age: 251 cases, 502 hospital controls, 502 neighbourhood controls.

Methods A case–control study was conducted in four tertiary hospitals in Mexico City with 251 cases and 1004 controls (two hospital and two neighbourhood controls per case, matched by age [±2 years]). Cases were infertile women, aged 20–40, with tubal occlusion confirmed by laparoscopy. Controls were fertile women, who had carried a pregnancy to term within the last two years. Participants completed a previously validated questionnaire asking about reproductive history and induced abortion.

Results Our study did not show an association between induced abortion and tubal infertility among women that did not relate both events (cases *vs* hospital controls: OR = 1.57, 95% CI: 0.29–8.65; cases *vs* neighbourhood controls: OR = 0.82, 95% CI: 0.07–8.99) using conditional logistic models adjusting by marital status, number of pregnancies, age at first sexual intercourse and history of pelvic inflammatory disease. In contrast, early age at sexual debut and history of pelvic inflammatory disease significantly increased the risk of tubal infertility.

Conclusions In Mexico, the lack of association between induced abortion and tubal damage causing infertility observed in this population might be explained by a shift toward 'safer' abortion practices.

INTRODUCTION

Safe abortion, as provided in most developed countries, is not a risk factor for infertility, except when infection occurs.[1] Whether or not unsafe abortion[2] increases the risk of infertility is inconclusive.[3–8] Differential measurement error (i.e. recall bias) of unsafe abortion history, lack of control of confounding factors, insufficient statistical power, lack of a standardised definition of 'unsafe abortion' as well as difficulties to differentiate between post-abortion or postpartum complications, are factors that might explain the inconsistent relationship between unsafe abortion and infertility. However, it is reasonable to assume that in settings where abortion is illegal or legally restricted, women terminate unwanted pregnancies under clandestine and unsafe conditions, therefore increasing the rate of infection and subsequent complications including infertility.

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In Mexico, abortion is legally restricted and clandestine abortions are common. Indeed, it is estimated that, each year, between a quarter to a half million unsafe abortions take place.[2,9,10] Most abortions are performed during the first trimester (before completion of the 12th week of gestation).[10] A common acute complication of induced abortion under unsafe conditions is infection,[2] which can be limited to the endometrium (endometritis), affect the Fallopian tubes (salpingitis) or, in severe cases, evolve into pelvic inflammatory disease. The inflammatory process, either the acute salpingitis or pelvic inflammatory disease, can cause tubal occlusion by means of intraluminal scars or adhesion formation.[11] Tubal occlusion, also known as 'tubal factor', is responsible for about a third of female infertility cases in developed countries, but its contribution to infertility in developing countries is estimated to be much higher: from 40% to 85%.[12]

It is estimated that 10% of Mexican couples suffer from infertility[13]; in countries where the ability to procreate is highly valued, infertility often carries a huge psychological burden of personal dissatisfaction, stigma and depression for both women and couples.[14]

As part of a large portfolio of studies aimed at investigating the social and medical consequences of unsafe abortion,[15–19] between July and November of 2002 we conducted a case–control study in Mexico City to explore whether or not induced abortion is a risk factor for tubal

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Table 1. Socio-demographic characteristics, cases *versus* controls.

Characteristic	Cases (n = 251)	Controls	
		Hospital (n = 502)	Neighbourhood (n = 502)
Age (years)			
Mean	33.43	33.0	33.02
Min–Max	23–40	22–40	21–40
Marital status (%)			
Married	96.81	89.24*	92.03**
Unmarried	3.19	10.76	7.97
Education attainment (%)			
High school	37.85	61.95*	56.18**
Undergraduate	15.54	13.94	15.54
Graduate	23.51	15.54	18.13
Postgraduate	23.11	8.57	10.16
Residence (%)[a]			
Rural	13.55	30.28*	20.12**
Urban	86.45	69.72	79.88

[a] Until 15 years of age.
* Cases *vs* hospital controls, $P < 0.05$.
** Cases *vs* neighbourhood controls, $P < 0.05$.

infertility. In this article, we present and discuss our findings in the context of current abortion practices in Mexico.

METHODS

For this study, we recruited two clinical and two neighbourhood controls per case, matched by age (±2 years). In total, 251 cases and 1004 controls were enrolled. The protocol was reviewed and approved by the Internal Review Boards of the participating institutions. Each participating woman signed an informed consent form in which the study was clearly described and which stated that the information provided by the participants would be treated as confidential.

Cases consisted of women residents of Mexico City, aged between 20 and 40, who were diagnosed with tubal factor infertility confirmed by laparoscopy.

Women were invited to participate by their treating physician in the infertility units of three tertiary hospitals in Mexico City (one public and two social security). Out of a total of 266 eligible cases, we recruited 251 cases (acceptance rate: 94.36%).

Two controls with a history of pregnancy during the two preceding years or who were pregnant at the date of interview were selected for each case. They were matched by age (±2 years) with the index case. These controls were recruited in two of the three participating tertiary units in Mexico City (one social security and one public), since in one of them only non-eligible hospital controls are attended.

Hospital controls included women who attended the hospital for obstetric or gynaecological reasons other than infertility (prenatal care, breast diseases and pap smear) (12.15%), ear, nose and throat diseases (5.38%), gastrointestinal diseases (4.98%), osteomuscular problems (3.39%), skin problems (3.19%), urinary diseases (3.19%), neurological problems (we excluded those women whose capacity to answer our questionnaire was reduced for medical reasons) (2.59%), cardiovascular diseases (2.19%), endocrine problems (2.99%), ophthalmological diseases (1.79%), respiratory diseases (1.79%), allergies (1.99%), infectious diseases (0.60%) and haematological problems (0.60%). We also recruited a group of women attending preventive services (6.77%), others seeking paediatric care for their children (30.08%), as well as some companions of patients (15.34%). From a total of 511 eligible controls, 502 accepted to participate in the study (response rate of 98.24%).

Neighbourhood controls included fertile women living on the same block or nearby (no more than three blocks away) the index case's household. For each case, we identified two neighbours that were matched by age (±2 years), and had been pregnant during the two preceding years, or who were pregnant at the date of the interview. Controls were identified following a standardised methodology for field studies, which does not involve a visit to the index case at home.[20] From a total of 508 eligible controls, 502 accepted participating in the study (acceptance rate: 98.82%).

The termination of pregnancy brought on purposefully by drugs (i.e. medical abortion) or mechanical means (i.e. surgical abortion) was considered as induced abortion and it was investigated using a pre-standardised self-administered questionnaire that had been used in previous studies.[21] We evaluated the reproducibility of this instrument in a random subsample of 41 women from this study: the same interviewer administered it twice to the same woman in the same place, with a seven-month lapse in between. This strategy allowed us to estimate the magnitude of measurement error of induced abortion with our instrument; we further adjusted the specific measures of association, as it has been suggested elsewhere.[22]

The questionnaire was designed to be self-administered [n = 879 (70%)]. However, in some cases we performed face-to-face interviews [e.g. in the case of illiterate women or those who requested it; n = 376 (30%)]. Cases and clinical controls were interviewed at the hospitals in a private room, and neighbourhood controls were interviewed in their households.

The questionnaire included the following sections: socio-demographic information, reproductive history, including the history and procedure of abortion (person who performed it, place where it was carried out, etc.), as well as ever signs and symptoms related to pelvic inflammatory disease, namely, a history of vaginal discharge, fever and/or painful sexual intercourse. The administration of the questionnaire (either self-administered or face to face) took an average of 8 minutes.

Table 2. Reproductive history, cases *versus* controls.

Characteristic	Cases (n = 251)	Controls	
		Hospital (n = 502)	Neighbourhood (n = 502)
Age at sexual debut (%)			
<20	51.63	58.57	52.82
≥20	48.37	41.43	47.18
No. of sexual partners (%)			
1	60.89	60.88	67.07
2	27.02	28.34	23.98
≥3	12.10	10.78	8.94
Induced abortion (%)			
Yes	3.19	4.58	2.19
No	96.81	95.42	97.81
History of pelvic inflammatory disease (%)[a]			
Yes	31.47	23.51*	18.53**
Probable	10.36	17.13	8.37
No	58.17	59.36	73.11
No. of pregnancies (%)[b]			
1	49.64	20.72*	14.74**
2	32.37	28.09	33.86
3 or more	17.99	51.20	51.39
Unplanned pregnancy (%)			
Yes	13.15	45.42*	41.43**
No	86.85	54.58	58.57
Miscarriages (%)			
None	72.51	80.68*	82.67**
1	19.12	13.75	15.14
2 or more	837	5.58	2.19
Ectopic pregnancies			
Yes	16.33	0.80*	0.60**
No	83.67	99.20	99.40
Preterm birth			
Yes	10.07	25.50*	16.14
No	89.93	74.50	83.36
Caesarean section			
Yes	18.71	51.79*	53.78**
No	81.29	48.21	46.22
Adverse reproductive index[c]			
Yes	3.60	0.80*	0.40**
No	96.40	99.20	99.60

[a] Pelvic inflammatory disease: No = no symptoms; Yes = vaginal discharge, painful sexual intercourse and fever; Probable = some of these symptoms.
[b] Included only women with one or more pregnancies.
[c] Index includes: molar pregnancy, anembryonic pregnancy and intrapartum death.
* Cases *vs* hospital controls, $P < 0.05$.
** Cases *vs* neighbourhood controls, $P < 0.05$.

At the end of the interview, we asked both cases and controls if they thought that induced abortion had specifically affected their health. We included this question to identify those women who might relate their history of induced abortion to their infertility (recall bias).

All women who rejected participating in the study provided information about their age, education and marital status. The main reason for not participating was lack of interest in the study.

Using χ^2 and ANOVA statistics, we compared the following variables: frequency of induced abortion, duration of interview, total number of interviews and total number of missing values as related by the five interviewers, in order to evaluate any differential pattern that may appear as a result of a poorly conducted interview.

A dichotomous index of adverse reproductive outcomes was generated based on the history of molar pregnancy, anembryonic pregnancy and stillbirth. This index was positive when one of these events had taken place, and negative otherwise. Also, we created a proxy variable for pelvic inflammatory disease as follows: negative, in the absence of vaginal discharge, painful sexual intercourse and fever history; positive, when all these events were recorded; and probable otherwise.

Table 3. Factors associated with induced abortion.

Characteristics	Induced abortion	
	Yes (n = 42)	No (n = 1213)
Age (years)		
Mean	34.26	33.05*
Min–Max	25–40	21–41
Marital status (%)		
Married	80.95	92.25*
Unmarried	19.05	7.75
Age at sexual debut (years)		
Mean	18.30	19.95*
Min–Max	12–30	12–39
No. of sexual partners		
Mean	2.88	1.54*
Min–Max	1–35	1–21
History of pelvic inflammatory disease (%)[a]		
Yes	28.57	22.92
Probable	59.52	55.98
No	11.90	21.10
No. of pregnancies		
Mean	3.71	2.41*
Min–Max	1–9	0–10
Unwanted pregnancy (%)		
Yes	85.71	35.70*
No	14.29	64.30

[a] Pelvic inflammatory disease: No = no symptoms; Yes = vaginal discharge, painful sexual intercourse and fever; Probable = some of these symptoms.
* $P < 0.05$.

Table 4. Multivariate odds ratios for the effect of induced abortion, pelvic inflammatory disease and age at first sexual intercourse on infertility.

Characteristic	Cases *vs* hospital controls				Cases *vs* neighbourhood controls			
	Model 1[a]		Model 2[b]		Model 1[a]		Model 2[b]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Induced abortion								
No	1.0	–	1.0	–	1.0	–	1.0	–
Yes	4.29	1.25–14.64	1.57	0.29–8.65	4.09	0.65–25.56	0.82	0.07–8.99
Pelvic inflammatory disease								
No	1.0	–	1.0	–	1.0	–	1.0	–
Probably	3.44	1.54–7.67	3.12	1.40–6.97	6.12	2.62–14.3	6.01	2.59–13.97
Yes	4.51	1.91–10.62	4.3	1.81–10.24	14.3	5.10–40.06	15.76	5.48–45.39
P for trend				0.02				<0.001
Age at first sexual intercourse (years)								
≥20	1.0	–	1.0	–	1.0	–	1.0	–
<20	3.1	1.71–5.52	2.8	1.58–5.13	3.71	1.99–6.91	3.52	1.82–6.77

[a] Adjusted by age, marital status and number of pregnancies.
[b] Model excluded four cases that associated induced abortion with infertility and their corresponding hospital controls (8) and neighbourhood controls (8).

Socio-demographic and reproductive characteristics (including the adverse reproductive outcome index and the pelvic inflammatory disease proxy variable) of the study population were compared using χ^2 and *t* test statistics; the Fisher correction was used for cells with counts of less than five subjects.

To assess the relationship between induced abortion and tubal infertility, we used conditional logistic regression models. The variables considered as potential confounders included civil status, number of pregnancies, age at sexual debut and history of inflammatory pelvic disease.

The possibility that recall bias may be operating in this study was evaluated according to the recommendation made elsewhere[23] that is to directly ask respondents to identify 'exposures' which they believe are relevant factors for the disease, and compare multivariated models with and without those respondents.

The reproducibility of the questionnaire used in this study was evaluated according to the Kappa coefficient. Under the assumption of non-differential measurement error, the under-estimation of the observed ratios was corrected using the formula $OR_{real} = [OR_{observed} - 1/Kappa] + 1$.[22]

The statistical analysis was performed with the software. STATA 7.0.

RESULTS

First, we compared selected variables across interviewers (i.e. induced abortion, duration of interview, etc.) to detect differential response patterns. No important differences were detected (data not shown). Likewise, we did not find any differences between participating and non-participating women regarding age (33.17 *vs* 33.10 years), number of years of education (87.89% *vs* 82.14% < undergraduate) and marital status (married: 91.87% *vs* 100%).

The general characteristics of the study population are displayed in Table 1. On average, the age of the participants was 33 years, with no differences between cases and controls, as had been foreseen in the design. Cases were statistically significantly more likely than control women to be married, to have a better education and to be residents of urban areas until 15 years of age, probably reflecting the composition of the population that attend infertility clinics.

The reproductive characteristics of the participating women are shown in Table 2. Similar distributions of age at sexual debut (<20 years, ≥20 years) were observed among cases and controls The proportion of women who reported ≥3 sexual partners was lower among neighbourhood controls, compared with cases and hospital controls (difference not statistically significant). The frequency of induced abortion was not statistically different across groups, and varied from 2.19% among neighbourhood controls to 4.58% among hospital controls. A history of pelvic inflammatory disease, ectopic pregnancy and an adverse reproductive index were significantly more frequent among cases than controls. Contrastingly, as it was expected, the distribution of pregnancies, unplanned pregnancies, history of miscarriages, preterm births and caesareans were significantly lower among the cases, compared with clinical and neighbourhood controls.

Compared with women with no history of induced abortion, women who reported an induced abortion were, on average, one year older (34.26 *vs* 33.05 years), more often unmarried (19.05% *vs* 7.75%), had a statistically significant lower age of sexual debut (18.3 *vs* 19.95 years), reported more sexual partners (2.88 *vs* 1.54), had a larger number of pregnancies (3.71 *vs* 2.41) and reported a higher

frequency of unwanted pregnancies (85.71.% *vs* 35.70%). The antecedent of pelvic inflammatory disease was higher among women with a previous induced abortion, compared with those with no history (Table 3), but the difference was not statistically significant.

After adjusting for potential confounders, a significant odds ratio of 4.29 (95% CI: 1.25–14.64) was estimated for the effect of induced abortion on infertility, when cases were compared with hospital controls; however, the magnitude and significance of this association disappeared when four women who believed that induced abortion was associated with their infertility (and their corresponding controls) were dropped from the analysis, yielding an odds ratio of 1.57 (95% CI: 0.29–8.65). A similar situation was found when cases were compared with neighbourhood controls: after eliminating the abovementioned women from the analysis, the adjusted and non-significant odds ratios dropped from 4.09 to 0.82 (95% CI: 0.07–8.99) (Table 4).

A history of suggestive pelvic inflammatory disease significantly increased the risk of infertility. Compared with clinical controls, women with pelvic inflammatory disease history had 4.30 times greater risk of infertility than those with no history. This risk was much higher when neighbourhood controls were used as the referent group (OR = 15.76; 95% CI: 5.48–45.39). The effect of pelvic inflammatory disease on infertility showed a significant linear trend: the higher the prevalence of signs and/or symptoms related to pelvic inflammatory disease, the higher the probability of tubal infertility. This effect remained even after excluding those women who related their history of induced abortion with infertility (Table 4).

We also found a statistically significant association between age at sexual debut and tubal infertility: the lower the age at sexual debut the higher the risk of infertility [OR = 3.1 (95% CI = 1.71–5.52) and 3.71 (95% CI = 1.99–6.91) for hospital and neighbourhood controls, respectively]. The effect of early age at sexual debut on infertility did not change after excluding those women who associated their history of induced abortion to their infertility (Table 4).

The Kappa coefficient of reproducibility for the question on induced abortion was 0.78.

DISCUSSION

While the results of this study do not support the hypothesis that induced abortion increases the risk of tubal infertility in Mexico, we found that some factors associated with sexually transmitted infections (i.e. early age of sexual debut and a history of pelvic inflammatory disease) are risk factors for tubal infertility, as suggested in other studies.[24,25]

Our findings are not in line with those reported from a study performed in Kenya[26] where infertile women had almost twice the antecedent of previous induced abortion, compared with their controls. However, a recent study performed in Vietnam,[27] a developing country where abortion is legal and services—although considered of poor quality—are widely available, showed no association between induced abortion and infertility.

A possible explanation for the lack of association between abortion and infertility in our study, is that the techniques women use to terminate their pregnancy might be safer than we expected. We collected some data that support this hypothesis: firstly, 60% of women who had had an abortion reported obtaining the procedure at a clinic, and 96% of those informed that the provider was a physician. Secondly, only 5% reported having inserted, by themselves or by someone else, an object into the vagina. This low prevalence of self-induced unsafe abortion contrasts with a much higher percentage documented in Mexico some years ago,[28] when self-induced abortion (particularly with catheters, but also with other sharp objects) was one of the most common methods used, even among urban women. Third, 38% of women reported taking a medication to abort (data not shown). Although we did not inquire about the type of drug they used, it is highly likely that most of them used misoprostol, a prostaglandin analogue with abortive properties, that is extremely safe under recommended use conditions (timing, dose and purpose). A retrospective cohort study of 1804 women treated for abortion complications in a hospital in Brazil found that infection was lower in women stating they had used misoprostol (4.2%) than in those who reported that the abortion had not been induced (7.9%), and 12 times lower than in women who had used other abortion methods (49.4%).[29] Focus groups with gynaecologists in Brazil established that doctors perceive that the use of this drug has a strong influence on the reduction of complications related to illegal abortions.[30] Misoprostol is widely available in Mexico, but so far no reports have been published regarding its use for termination of pregnancy.

Another possible explanation for our findings is that safer abortion may be the result of almost 20 years of a post-abortion care program, whose aim is to decrease the negative health consequences of induced abortion on women's health.[31] However, further research is required to confirm either of these two hypotheses.

Although our study had limited statistical power, some methodological features in the development of our protocol and its implementation contribute to the validity of our results. The acceptability rates in both cases and controls were high (above 95%). Furthermore, we inquired about the general characteristics of the non-participating women to evaluate if they were substantially different from participating women, which would have biased the study population, but no differences were found in either age, years of education or civil status (data not shown).

The representativeness of clinical controls is a concern in case–control studies. To overcome this limitation, we included a group of community-based controls, which is a

strong feature of this study. No important differences were found between the two types of controls in terms of age, years of education, civil status and number of pregnancies, thus reducing the probability of having a selected sample of clinical controls.

Because 7.37% of the clinical controls were women with gynaecological problems that might be potentially linked to infertility, we ran multivariate models eliminating those women, and no differences were found when they were excluded from the models: the odds ratios with and without them were 1.57; 95% CI: 0.29–8.65 and, 1.95; 95% CI: 0.32–11.85, respectively (data not shown). Moreover, because a history of painful sexual intercourse is not necessarily a symptom of pelvic inflammatory disease, as in the case when it is linked to endometriosis which could also affect infertility, we use a strict definition of suggestive pelvic inflammatory disease including only those women that reported three symptoms: vaginal discharge, painful sexual intercourse and fever history.

Cases with no history of pregnancy that might have had primary infertility or an induced abortion event associated with secondary tubal infertility were included in the case group. To evaluate the potential effect of the former group on the association between induced abortion and tubal infertility, we excluded them from the adjusted multivariate models, and no important differences were detected: odds ratios of 1.57; 95% CI: 0.29–8.65 (hospital controls) and 0.82; 95% CI: 0.07–8.99 (neighbourhood controls) were estimated to be 1.32; 95% CI: 0.33–5.19 (hospital controls) and 0.71; 95% C.I: 0.17–2.99 (neighbourhood controls), when potential cases of primary infertility were excluded from the analysis (data not shown).

Compared with Mexican national averages,[32] our study population had a very high educational level. A possible explanation for this particular asset of our population is that we only recruited urban women with access to tertiary health care facilities. Therefore, the results of our research should not be extrapolated to women of lower socioeconomic status or years of schooling.

We also addressed the possible existence of measurement error in the reporting of induced abortion and evaluated three potential sources: the performance of interviewers, the reproducibility of our instrument (non-differential measurement error) and the potential existence of recall bias (differential measurement error).

The interviewers that participated in this study had extensive experience in field research, they were all trained by the same member of the research team and they were not aware of the hypothesis of the study, although they were not blinded (i.e. they knew the case–control status of the participants). When we compared the responses to selected questions (including the frequency of induced abortion) by interviewer, no statistical differences were found reducing the probability of interviewer-induced response. Moreover, we compared the responses to key selected questions from self-administered questionnaires with those administered by interviewers and did not find any significant differences (data not shown).

The reproducibility of our instrument was fairly good. In particular, the reproducibility of the question inquiring about the history of induced abortion was 0.7835. Assuming the presence of non-differential measurement error, the lack of a 100% reproducible question will bias the corresponding odds ratio towards the null value; in other words, we were able to capture about 78% of the magnitude of the association between the history of induced abortion and tubal infertility. After adjusting for limited reproducibility, the observed odds ratios of 1.57 (hospital controls) and 0.82 (neighbourhood) would be 1.73 and 1.3, respectively.[22] These differences do not change the conclusions of this study.

Recall bias is a special type of differential measurement error, and should be a major concern when evaluating the reporting of sensitive past events, such as induced abortion. Consequently, we included a question to identify those women that related their history of induced abortion to infertility.[23] When those women were included in the analysis, the odds ratios for induced abortion and infertility were artificially high (because all these women were cases, and we did not identify any controls that related their history of induced abortion to infertility). By contrast, women did not relate other characteristics such as pelvic inflammatory disease and age at first sexual intercourse with abortion. We did not find previous studies that showed quantitatively the potential existence of recall bias concerning induced abortion.

In Mexico, abortion is legally restricted and its complications still constitute the fourth cause of maternal mortality, especially among women who live in rural and poor urban settings.[33,34] While these women resort to clandestine and unsafe services for the termination of pregnancy due to lack of information about safer options and/or inability to afford the safer care that some private physicians provide, women who have economic resources access low risk pregnancy termination services and receive quality care. From an ethical and human rights point of view, as well as a public health perspective, this inequality is unacceptable. This is particularly true in Mexico, where the Constitution establishes that all citizens have the right to health protection.

Acknowledgements

This study was supported by the David and Lucile Packard Foundation. The authors would like to thank the health authorities of all participating hospitals, particularly: Dr Fidelina Ortiz, from the Hospital General de México; Dr Juan Carlos Hinojosa from the Centro Médico Nacional La Raza; Dr Felipe Vadillo Ortega and Dr Sergio Villalobos Acosta from the Instituto Nacional de Perinatología;

Dr Salvador Gaviño and Dra Silvia Pacheco from the Hospital 20 de Noviembre. The authors would also like to express their gratitude to all women who kindly accepted to participate in this study.

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Accepted 15 July 2004