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Intrauterine adhesions, peritubal adhesions and tubal occlusion on hysterosalpingography: Any significant correlations with clinical history of previous pelvic inflammatory disease, dilatation and curettage and other pelvic surgeries among patients with secondary infertility?

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Abstract

Pelvic Inflammatory Disease (PID), Dilatation and Curettage (D&C) and other abdominopelvic surgeries are often presumed to cause female infertility. This can occur through adhesions formation that can result in Intrauterine Adhesions (IUA), Peritubal Adhesions (PTA) and Tubal Occlusion (TO). Hysterosalpingography (HSG) can be used to diagnose IUA, PTA, and TO; and the correlations of these findings with the histories of PID, D&C and other abdominopelvic surgeries statistically tested. The available literature shows very few of such correlation tests. The objective of this study was to document HSG diagnosis of IUA, PTA and TO, and test their correlation with histories of previous PID, D&C and abdominopelvic surgeries among women with secondary infertility. This is a prospective descriptive study of 158 subjects, analyzed with SPSS version 21. For correlation test, $p \leq 0.05$ is considered significant. There was history of previous PID in 53 subjects (33.5%), D&C in 114 (72.2%), and abdominopelvic surgery in 80 (50.6%). The important findings included: IUA in 20 subjects (12.7%), TO in 53 (33.5%) and PTA in 30 (19.0%). Significant correlation was found between D&C and PTA, but not between PID and IUA, PID and TO, PID and PTA, D&C and IUA, D&C and TO, abdominopelvic surgery and IUA, abdominopelvic surgery and TO, or abdominopelvic surgery and PTA. Tubal occlusion, followed by PTA and by IUA were detected in that order as the possible causes of infertility in our subjects; and these did not correlate well with the history of PID, D&C and other abdominopelvic surgeries.

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Introduction

Adhesions formation is one of the sequelae of injury to an organ or tissue. The injury could be infective, traumatic, iatrogenic, neoplastic or secondary to radiation exposure. Intrauterine Adhesions (IUA) may partially or completely obliterate the uterine cavity,[1] and severe form of IUA can in addition to obliteration of the uterine cavity, cause tubal occlusion, while IUA at the conus can cause conual occlusion. Similarly, adhesions or scarring on the luminal surface of the fallopian tube may cause tubal occlusion and adhesions occurring around the fallopian tubes may result in Peritubal Adhesions (PTA) with various manifestations. All these may lead to subfertility or infertility.

Intrauterine Adhesions (IUA) are commonly caused by injury to the basal layer of the endometrium.[1,2] The uterus is most susceptible to this type of injury following onset of pregnancy, for instance as a result of Dilatation and Curettage (D&C) for termination of pregnancies, incomplete miscarriages or removal of retained products of conception.[1-2] Among women with infertility, the above scenarios are only obtainable in secondary infertility setting. Other causes of IUA include; injury to the myometrium (as

happens in myomectomy or caesarian section), hysteroscopy, mullerian duct malformation, genital tuberculosis, and insertion of intrauterine devices.[1,3] Asherman's syndrome is a severe form of IUA associated with amenorrhoea or hypomenorrhea and may result in abnormal placentation, pregnancy loss or infertility.[3] Some authors reported the risk of Asherman's syndrome after one episode of D&C as 16% and that after three or more D&Cs as 32%.[3,4]

PTA can result from abdominopelvic surgeries or pelvic infections.[5-7] It can affect the proximal part of the tube (proximal adhesions) or the distal part (distal adhesions) and may or may not present with tubal occlusion.[5-7] Some authors have noted that occlusion of the fallopian tube by PTA is a common cause of infertility.[5-7] Tubal occlusion secondary to PTA can take an anatomic form by blocking the tubal canal or the abdominal orifice of the fallopian tube.[7,8] It may also take a functional form by retracting the ovary and/or the tube, thus widening the gap between the oocyte and the fimbriae, and hindering the oocyte pick up.[5,7] Certain radiographic criteria are used to diagnose PTA on HSG. These include one or a combination of the following: convoluted fallopian tube, ampullary dilatation, loculation of spillage of contrast medium into the peritoneal cavity, peritubal halo effect, and vertical fallopian tube.[5,6]

Apart from IUA and PTA, other causes of tubal obstruction/occlusion include: tubal scarring secondary to infection, endometrial polyps, fibroids (especially submucosal), mucus plug, tubal spasm, and congenital malformations.[6,8-10] Though some authors use tubal obstruction and tubal occlusion interchangeably, others use the term 'obstruction' to imply a temporary process which can be reversible (like spasm and mucus plugging), and 'occlusion' to imply a permanent organic damage as seen in peritubal adhesions (typified by hydrosalpinges and perifimbrial adhesions), intrauterine adhesions and tubal scarring secondary to infections.[6,8-9,11] The proximal, mid or distal portions of the tube may be involved in tubal lesion and this may be unilateral or bilateral.[6,9]

Secondary infertility is the inability to conceive after an earlier pregnancy which may or may not have led to term delivery of live baby.[12,13] It has been reported by a good number of authors to be more prevalent than primary infertility in the developing countries like ours [14-17] It has also been estimated that 15-20% of all cases of secondary infertility are due to adhesions,[7,10] and that up to 10% of female infertility are due to uterine factors which include IUA.[18-19] Other authors opine that 25% of female infertility are due to tubal and peritoneal factors,[20-21] and that more than 50% of the causes of tubal factor infertility are due to PID.[22]

The modalities used in assessing intrauterine, tubal and peritubal pathologies include Hysterosalpingography (HSG), Sonohysterography (SHG), laparoscopy, Computerized Tomographic Virtual Hysterosalpingography (CT-VHSG) and Magnetic-Resonance Virtual Hysterosalpingography (MR-VHSG).[5-6,14,18] However because of its minimal risk, accuracy, and ease of performance, HSG is regarded as a procedure of choice in the initial investigation of infertility due to tubal diseases or PTA,[5-6] and is commonly used to evaluate the uterine cavity and the fallopian tubes in female infertility workup.[23] This is so, despite the fact that many infertility centers regard laparoscopy as the modality of choice for investigating tubal patency and pelvic structure.[6] In comparison to laparoscopy as the gold standard for diagnosis of tubal patency, HSG is said to have a sensitivity of 72-85% and specificity of 68-89%.[6,24]

A global study observed a sharp increment of prevalence of secondary infertility with age, increasing from 2.6% in women aged 20-24 y to 27.1% in women aged 40-44 years.[25] The above observed age dependent prevalence was also noted to became less pronounced when calculated as a percent of the whole women in the study population.[25]

A study in Oman, south-east Asia, found history of previous PID in 3% of women presenting for HSG on account of secondary infertility.[26] It also found positive history of previous pelvic surgeries in 50% of the same population.[26] In Benin, south-south Nigeria, Eze *et al.*[27] found positive history of previous D&C in 67.5% of women with infertility while a study in Ile-Ife, south-west Nigeria by Famurewa *et al.*[7] noted it in 59.2%. The reasons for the variations between the results of these studies both of which were done in Nigeria and in similar population, though not obvious; may be explained by changes in time, educational and economic status of people involved at various times.

In HSG study carried out in India among women with secondary infertility, the uterus was found normal in 18.11% and abnormal in 81.89%. [12] Using HSG, Nwankwo and Akani in PortHarcourt, south-south Nigeria,[28] noted IUA in 12.8% of the infertile women and Eze *et al.*[27] reported uterine synechia in 7% of such women. The reasons for the variations in the two studies are not obvious since they were of similar study population using similar modality. None of them reported the frequency of this lesion among the secondary infertility subgroup, hence the need for a study like ours to bring this subgroup into focus.

A study in Ilorin, north-central Nigeria, noted tubal occlusion in 18.7% of women presenting for HSG with history of secondary infertility.[29] The lesion was found to be bilateral in 8.3% and unilateral in 10.4%.[29] But a HSG study in Oman found higher frequency of tubal obstruction (28.7%) in the secondary infertility group, being bilateral in 2.97% and unilateral in 25.74%.[26] And another study in Ilorin, north-central Nigeria, found even higher frequency; it reported tubal occlusion in 72.41%, being bilateral and unilateral in 32.75% and 39. 66% respectively. [30] Using HSG and diagnostic laparoscopy, Dutta *et al.*[31] in India noted right sided PTA in 36% and 52% respectively and the left PTA in 20% and 28% respectively.

Among women with infertility, strong association was found between tubal blockage and past medical history suggestive of previous PID by Toufig *et al.*[32] and this is in concordance with that obtained in Ile-Ife.[7] But, the report of a strong association between tubal abnormalities and history of previous abdominopelvic surgery by Toufig *et al.*[32] is at variance with the report by a study in Benin[27] that found no correlations between tubal blockage and history of previous pelvic surgery. The finding of significant association between tubal blockage and positive history of previous D&C by a study in Ile-Ife[7] also differs from the report of no significant correlation between the two variables by another in Benin.[27]

Our search did not show the documented results of correlation of the above clinical histories with either IUA, TO or PTA among women with secondary infertility. The objective of this study is to ascertain whether HSG diagnosis of intrauterine adhesions, tubal occlusion and peritubal adhesions correlate well with clinical histories of previous PID, abdominopelvic surgeries and D&C among women with secondary infertility. The result will be useful to clinicians, patients and policy formulators on the need for improvement in preventive medicine and also of improved quality of medical and surgical interventions in women of child bearing age especially in our environment where secondary infertility has been reported to be high by many authors; [14-17] and reported to be as high as 80% by a study in Ilorin.[29]

Materials and Methods

This is a prospective descriptive study of 158 women with secondary infertility and was carried out simultaneously at the department of Radiation Medicine of the University of Nigeria Teaching Hospital Ituku-Ozalla, Enugu state, Nigeria; and Hansa Clinics (a radiology centre located in Enugu), over a period of six months (September 2011 to February 2012). Institutional ethical clearance was obtained prior to the study. The subjects were women booked for HSG on account of secondary infertility and who gave their consent to be included for the study. The recruitment was in a consecutive pattern. Those who declined to be recruited for the study and those booked for other reasons than secondary infertility were excluded from the analysis.

The 10-day rule was adhered to in the booking of the patients. The investigation was explained to each patient and counseling given. An antispasmodic agent, (Hyoscine bromide, 20mg) was administered intravenously (none of the subjects in our study had positive history of glaucoma). Subject was placed in lithotomy position and asceptic protocols were observed in cleaning the vulva, vagina and cervix. Cusco's speculum was introduced into the vagina, the anterior lip of the cervix was then held firmly in place with a volsellum forceps, and the uterus sounded. Leech-Wilkinson's cannula was inserted into the cervical canal and through that, about 5-60ml of water soluble contrast medium, sodium diatrizoate/meglumine diatrizoate 76% (Urografin 76%) was slowly injected into the uterine cavity. Injection was done in stages to demonstrate the cervical canal, uterine cavity, fallopian tubes and peritoneal spill, since there was no functional fluoroscopy machine during the period of study. Films were taken at breath-holding and in anterioposterior projection. Additional projections were taken when necessary. The images were acquired with screen-film combination and processed manually.

Data were analyzed with the Statistical Package for the Social Sciences (SPSS) version 21.0 by IBM Corp. Armonk, New York, USA. Frequency tables, measures of central tendencies and measures of dispersion were carried out. Appropriate variables were further analyzed by pairing and carrying out Pearson's correlation tests. $p \leq 0.05$ was considered statistically significant. Cases of missing data were excluded from the analyses.

Results

One of the patients with secondary infertility who presented for the study was excluded on account of incomplete data; and a total of 158 subjects were used for the analysis. The age ranged from 21 years to 49 years with a mean of 33.5 years, median of 33.5 years and mode of 35 years. The range of duration of infertility and the mean duration were 1-17 years and 4.0 years respectively. The clinical history findings included the following: history suggestive of previous PID in 53 subjects (33.3%), D&C in 114 (72.2%), abdominopelvic surgery (with or without D&C) in 80 (50.6%), D&C and or other abdominopelvic surgery (which included appendicectomy, myomectomy and Caesarian section) in 141 (89.2%). All the 114 patients with history of D&C also had positive history of abortion.

As seen in Table 1, diagnosis of intrauterine adhesions (see also Figure 1) were made in 20 subjects (12.7%). Tubal occlusions were diagnosed in 53 (33.5%) which included bilateral 28 (17.7%),

Table 1. Frequencies of some variables.

Variable	Frequency	Percentage
PID	53	33.5
D&C	114	72.2
ABPS	80	50.6
IUA	20	12.7
Tubal occlusion	53	33.5
Peritubal adhesions	30	19.0

ABPS: abdominopelvic surgery; D&C: dilatation and curettage; IUA: intrauterine adhesions; PID: pelvic inflammatory disease.

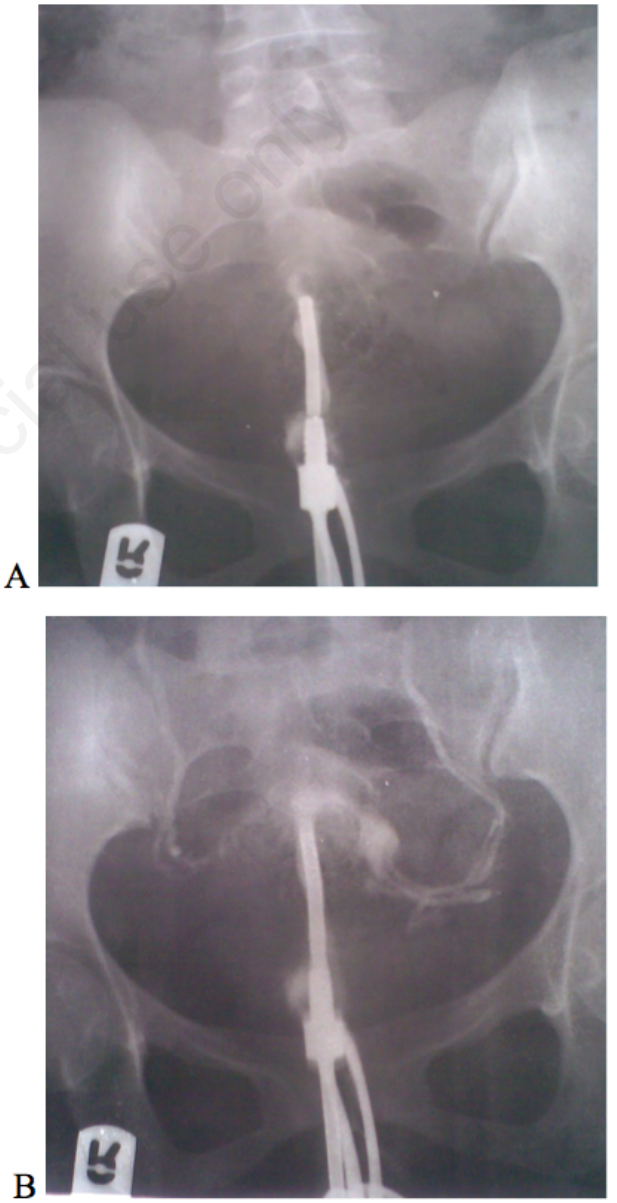

Figure 1. Case of Asherman's syndrome: severe intrauterine adhesions in a patient with amenorrhoea. In film A the uterine cavity is completely obliterated and fallopian tubes occluded; and in a later film B venous intravasation of contrast is seen bilaterally.

right unilateral 15 (9.5%, and left unilateral 10 (6.3%). Peritubal adhesions (see Figure 2) were detected in 30 (19.0%) and bilateral in 9 (5.7%), right unilateral in 8 (5.1%), and left unilateral in 13 (8.2%).

The Pearson's correlation test (see Table 2) shows no significant correlation between the following pairs of variables: PID and IUA, PID and tubal occlusion, PID and peritubal adhesions, D&C and IUA, D&C and tubal occlusion, history of abdominopelvic surgery and IUA, abdominopelvic surgery and tubal occlusion, abdominopelvic surgery and PTA. There was also no significant correlation between; age and IUA, age and PTA, duration of infertility and IUA, duration of infertility and tubal occlusion and, duration of infertility and PTA. The pair of D&C and peritubal adhesions, as well as, age and tubal occlusion showed significant correlation.

Discussion

In our study, the commonest age group was 30-39 years. The age ranges in women undergoing HSG on account of secondary infertility is scarce in the available literature. However, our finding was in agreement with 30-39 years recorded in a study of women with infertility done in Ile-Ife[7] in a society of predominantly different ethnic and cultural group from ours, but of the similar racial and religious disposition; but differed from 26-36 years age group recorded by Toufig *et al.*[32] in a different country with different cultural, religious and educational background. This suggests a cultural, religious and educational influence.

The mean age of secondary infertility in our study (35.0 years) was higher than 27.21±6.5 obtained in India among women with secondary infertility, but the mean duration (4.0 years) obtained in our study was lower than theirs which was 5.34±3.5 years.[12] The reasons for these variations are not obvious. However, it appears that in that clime, marriage is contracted earlier than in ours.

The positive history suggestive of previous PID among women with secondary infertility in our study (33.3%), was higher than that obtained by a study in Oman (3.0%).[26] This may be due to differences in awareness of PID and the ease of accessibility to quality healthcare in the two environments. However, the history of pelvic surgery occurred in approximately equal frequency in both our study and theirs (50.6% and 50.0% respectively).[26]

Our finding of positive history of D&C in 72.2% was higher than 67.5% recorded by a study in Benin[27] and 59.2% noted in Ile-Ife.[7] The reasons for ours being higher than both studies can be explained by difference in the scope of population studied, since ours was women with secondary infertility while theirs included women with primary and secondary infertility. Since positive history of D&C indicates that there was an earlier conception, no patient with primary infertility can possibly have this history.

Table 2. Correlation results of some paired variables.

Pairs	P-value	Interpretation
PID *vs* IUA	0.722	Not significant
PID *vs* TO	0.937	Not significant
PID *vs* PTA	0.978	Not significant
D&C *vs* IUA	0.448	Not significant
D&C *vs* TO	0.929	Not significant
D&C *vs* PTA	0.049	Significant
ABPS *vs* IUA	0.171	Not significant
ABPS *vs* TO	0.780	Not significant
ABPS *vs* PTA	0.377	Not significant
AGE *vs* IUA	0.434	Not significant
AGE *vs* TO	0.001	Significant
AGE *vs* PTA	0.404	Not significant
DI *vs* IUA	0.935	Not significant
DI *vs* TO	0.084	Not significant
DI *vs* PTA	0.299	

ABPS: abdominopelvic surgery; DI: duration of infertility; D&C: dilatation and curettage; IUA: intrauterine adhesions; PID: pelvic inflammatory disease; PTA: peritubal adhesions; TO: tubal occlusion.

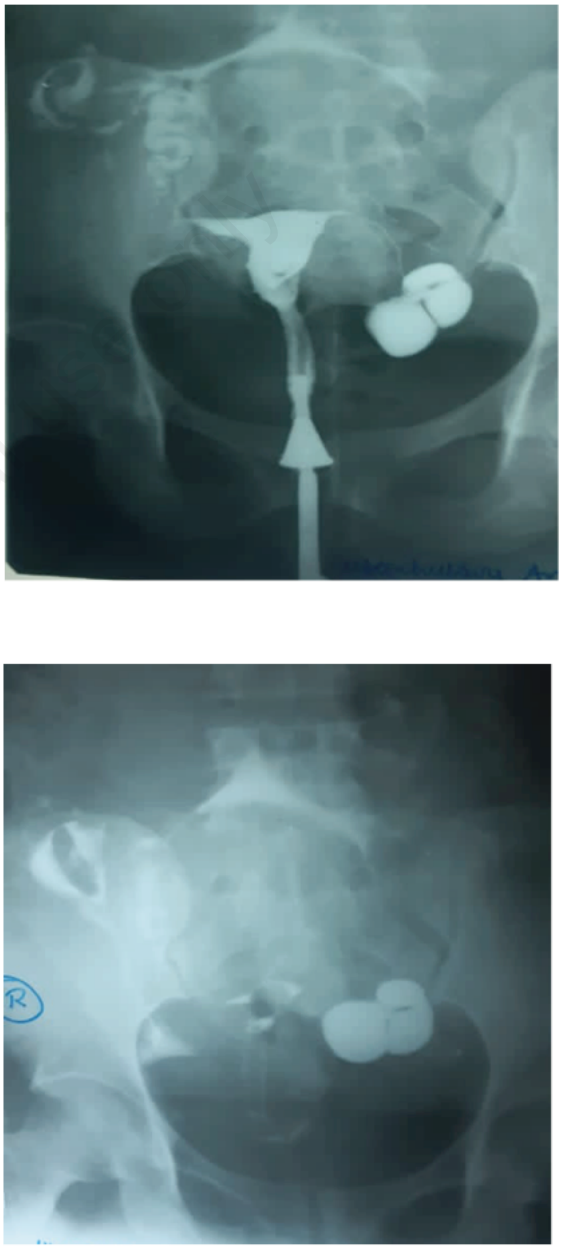

Figure 2. A (taken with cannula intact) and B (taken after cannula withdrawal): Peritubal adhesions with left tubal obstruction. Left tube shows convoluted appearance and ampullary dilatation (hydrosalpingx) with no spill of contrast into the peritoneal cavity (occlusion), while right shows vertically oriented fallopian tube with restricted spill of contrast in the peritoneal cavity.

Therefore inclusion of patients with primary infertility in the analysis will reduce the percentage obtained. This further underscores the need for a study of the secondary infertility subgroup as done in ours.

The frequency of intrauterine adhesions in our study (12.7%) of women with secondary infertility approximates 12.8% recorded by in PortHarcourt,[28] using similar procedure of HSG but among women with infertility (including the primary and secondary types). The reason for this similarity is not obvious. However, the value in our study is higher than 7% recorded in Benin among a population involving primary and secondary infertility.[27]

Tubal occlusions were diagnosed in 33.5% of our study population. This is higher than 18.7% reported in by a study in Ilorin[29] and 28.7% reported in Oman,[26] but less than 72.41% reported by another study in Ilorin;[30] all of which studies were of female with secondary infertility and carried out with HSG. In terms of laterality, both the bilateral and unilateral involvements detected in our study were higher than those recorded by a study in Ilorin[29] but lower than those recorded by another study in Ilorin.[30] On the other hand, while the bilateral involvements found in our study were higher than that reported by a study in Oman, the unilateral involvements were lower.[26] Both the right and left sided PTA seen in our study were lower than those reported in India[31] among women with infertility.[31] Again, our finding of left peritubal adhesions higher than right was at variance with that obtained in India that found the right sided to be higher than left.[31] The reasons for variations are not obvious.

The finding of no significant correlation between PID and tubal occlusion or peritubal adhesions in our study differed from the report of both Famurewa *et al.*[7] and Toufig *et al.*[32] The finding of no significant correlation between D&C and tubal occlusion in our study agreed with that obtained in Benin[27] but was in discordant with that obtained in Ile-Ife.[7] Similarly, the absence of significant correlation between history of abdominopelvic surgery and tubal occlusion in our study was in concordance with that of Eze *et al.*[27] but disagreed with that of Toufig *et al.*[32]

Though the reasons for these variations are not obvious, the observations agree with the assertion by Toufig *et al.*[32] that there are variations in the HSG findings in infertility globally. However, general improvement in the available medical expertise and the level of education over time may most likely play a role in explaining the changes. As most of our subjects were patients from a tertiary health care facility and may have had received improved medical and surgical attentions, improved management may have helped to reduce the likelihood of tubal complications following both abdominopelvic surgeries and the treatment of PID.

However, the significant correlation of history of D&C with peritubal adhesions in our study seems to suggest otherwise. But, the fact that the 114 patients with history of D&C in our study also had positive history of abortion may explain the apparent disparity. In our environment, abortion is not legalized and abortion carries a social stigma. As a result, most abortions are procured in secrecy, without regards for aseptic procedures and in the hands of unqualified healthcare personnel. Hence, the peritubal complications noted may be a reflection of post abortal complications among these patients rather than complications of D&C per se. Neither among female with infertility nor among the secondary infertility subgroup did the available literature show the correlation of IUA with either PID, D&C or abdominopelvic surgeries.

Conclusions

Tubal occlusion is the commonest finding in the possible causes of secondary infertility in our study. Though this did not correlate well with the history of PID or abdominopelvic surgeries or D&C, there is still need to improve the medical and surgical management of women of reproductive age as this may affect the fertility outcome.

There are few correlation studies on the variables both in secondary infertility group and in entire infertility population in the available literature. More of such studies are therefore recommended. Moreover, the studies should also inculcate the type of institution where the PID were treated and where the D&C or abdominopelvic surgeries were performed.

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