

# Diagnostic and management dilemmas in secondary abdominal pregnancy: A case report and literature review of 314 cases from 1930-2021.

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## Abstract

Background- Abdominal pregnancy remains a diagnostic and management challenge Objective- Highlighting diagnostic and management dilemmas in secondary abdominal pregnancy Search strategy- MEDLINE, EMBASE, PubMed and Web of Science searched from 1930-2021. Selection criteria- Articles on secondary abdominal pregnancies Data collection and analysis- An illustrative case report of a woman at 13 weeks gestation referred from a primary health centre with vague abdominal pain. Imaging confirmed secondary abdominal pregnancy with hemoperitoneum. Emergency laparotomy revealed significant hemoperitoneum, a live floating fetus in the abdominal cavity and placental attachment to the left cornu and fallopian tube which were removed and cornual repair performed. Recovery was uneventful. We reviewed the literature on secondary abdominal pregnancies, early and advanced from 1930-2021 and summarised management and outcomes of 314 such cases. Main Results- Among the 314 cases reviewed, 295 cases (93.9%) were surgically managed and 19 (6%) required hysterectomy. Post-surgery methotrexate was given in 9 cases (2.9%). Following primary methotrexate administration in 18 patients, 10 required surgery (55.5%). Complete placental removal was achieved in 264 cases (84%), partial in 27 (8.6%) and left in situ in 16 (5.1%). Seventy-four cases (23.6%) required blood transfusion. There were 15 maternal deaths (4.8%). Twenty-seven fetuses (8.6%) were live born, 6 (1.9%) were neonatal deaths and 46 (14.6%) were fetal demise. Conclusion- Maternal mortality and morbidity is of serious concern in abdominal pregnancies requiring a high index of suspicion and management expertise. Funding- None Keywords- abdominal pregnancy, primary peritoneal pregnancy, secondary abdominal pregnancy, hepatic pregnancy, omental pregnancy, diaphragmatic pregnancy.

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**Shortened running title:** Diagnostic and management dilemmas in secondary abdominal pregnancy

## Abstract:

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## Data collection and analysis-

An illustrative case report of a woman at 13 weeks gestation referred from a primary health centre with vague abdominal pain. Imaging confirmed secondary abdominal pregnancy with hemoperitoneum. Emergency laparotomy revealed significant hemoperitoneum, a live floating fetus in the abdominal cavity and placental attachment to the left cornu and fallopian tube which were removed and cornual repair performed. Recovery was uneventful.

We reviewed the literature on secondary abdominal pregnancies, early and advanced from 1930-2021 and summarised management and outcomes of 314 such cases.

**Main Results-** Among the 314 cases reviewed, 295 cases (93.9%) were surgically managed and 19 (6%) required hysterectomy. Post-surgery methotrexate was given in 9 cases (2.9%). Following primary methotrexate administration in 18 patients, 10 required surgery (55.5%). Complete placental removal was achieved in 264 cases (84%), partial in 27 (8.6%) and left in situ in 16 (5.1%). Seventy-four cases (23.6%) required blood transfusion. There were 15 maternal deaths (4.8%).

Twenty-seven fetuses (8.6%) were live born, 6 (1.9%) were neonatal deaths and 46 (14.6%) were fetal demise.

**Conclusion-** Maternal mortality and morbidity is of serious concern in abdominal pregnancies requiring a high index of suspicion and management expertise.

**Funding-** None

## Introduction

Abdominal pregnancy is a rare obstetric entity accounting for 1.4% of ectopic pregnancies and is associated with a high maternal and perinatal morbidity and mortality (1). Defined as an implantation in the peritoneal cavity, exclusive of tubal, ovarian or intraligamentary pregnancy (2), the estimated incidence is 1:10,000 live births (3). Though there are several theories about the pathophysiology, it is broadly classified into two types, namely primary and secondary abdominal pregnancies (4). Risk factors associated with abdominal pregnancies include dilation and curettage, uterine surgeries, history of tubal pregnancy and artificial insemination (5). Studdiford, as early as 1944, proposed the diagnostic criteria of primary abdominal pregnancy which included the following: 1-normal tubes and ovaries, 2- no evidence of uteroperitoneal fistula, 3-pregnancy related solely to the peritoneal surface, and 4- no evidence of secondary implantation following initial primary tubal nidation (6). Allibone et al. defined the ultrasound criteria necessary to diagnose an abdominal pregnancy namely: 1-fetus outside the uterus, 2- failure to see a uterine wall between the fetus

and the urinary bladder, 3-close approximation of fetal parts and maternal abdominal wall, 4- eccentric position/attitude of the fetus, 5-placenta outside the uterine cavity, and 6- visualisation of the placenta immediately adjacent to the fetal chest and head with no amniotic fluid (7). Despite defined diagnostic criteria, diagnosis maybe hindered by factors such as an anterior uterine leiomyoma, retroflexed uterus and bicornuate uterus (8). A high index of suspicion is required to diagnose this condition as its clinical features and presenting symptoms vary widely and are non-specific. The more common presenting symptoms include persistent abdominal pain, missed periods, bloody vaginal discharge and vague gastrointestinal symptoms like nausea and vomiting (9). We report a case of secondary abdominal pregnancy at 13 weeks of gestation which was managed surgically.

**Objective :** To highlight the diagnostic and management dilemmas in secondary abdominal pregnancies

**Methods:** Case report and literature review on 314 abdominal pregnancies.

Case report:

A 32-year-old primigravida at 13 weeks 5 days of gestation, presented to OBG emergency department, with complaints of generalised pricking abdominal pain and mild chest pain for 5 days which was gradually worsening and spotting per vagina for one day. Five days prior to her presentation at our hospital, she had been admitted at a local hospital with complaints of vomiting and mild abdominal pain. On evaluation there, hemoglobin was 5.7 g/dl and ultrasonography reported a live intrauterine fetus with a crown rump length of 4.57 cm corresponding to 11 weeks of gestation. Fetal heart rate was 175 bpm and maternal ascites along with fluid in the Morissons pouch was noted. She received two units of packed red cells transfusion and repeat hemoglobin on 6<sup>th</sup> June 2020 was 9.4 g%. As her symptoms persisted she was referred to our centre, Kasturba Medical College Hospital, Manipal, a tertiary care hospital.

She had an uneventful antenatal course prior to 13 weeks of gestation and no risk factors were identified. On examination she was alert and cooperative, heart rate 92 bpm and blood pressure 110/70 mmHg. Cardio-vascular and respiratory system examination were normal. Per abdominal examination revealed abdominal distension, minimal tenderness, no guarding or rigidity and uterus was not palpable. Per speculum examination showed a posterior, long, closed cervix and no evidence of bleeding or clots. Laboratory investigations showed hemoglobin of 8.9 g/dl and the coagulation profile, liver and renal function tests were within normal limits. Admission  $\beta$ -HCG level was 60,614 mIU/ml. Transvaginal sonography revealed an empty uterus measuring 7x4 cm, a left adnexal mass of 7x7 cm and a collection in the Pouch of Douglas measuring approximately 4x3x3 cm. There was evidence of hemoperitoneum with fluid collections in the hepatorenal and splenorenal pouches. An extrauterine live fetus was noted above the uterine fundus, more towards the left side, corresponding to 11 weeks of gestation. There was no communication demonstrable between the fetus/placenta and uterine contour. The couple was counselled in detail about the abdominal pregnancy, the need for surgical removal of the pregnancy and possible complications. A multidisciplinary team including urologist, general and vascular surgeons were on standby and adequate blood products were arranged. After obtaining high risk consent, emergency laparotomy was performed. Intraoperatively, hemoperitoneum was confirmed and a live fetus was lying in the abdominal cavity above the uterine fundus towards the left, just below the abdominal wall. A 500g clot was evacuated. The umbilical cord was ligated and a fetus measuring 6.5x2x2 cm, weighing approximately 20 g was removed (Figure 1). There was evidence of sealed rupture on the left fallopian tube and left uterine cornu; and part of placental tissue was attached to the site. Following a left salpingectomy and uterine cornual repair the bleeding was controlled. On further exploration, bulk of the placental tissue was found attached to the small bowel mesentery and partly to the omentum. With intra operative assistance from surgeons, bulk of the placental tissue was separated. An on-table decision was taken to leave a very minimal amount of placental tissue in situ (<1cm), which was firmly attached to the vascular mesentery in order to avoid massive hemorrhage. Both ovaries and the right fallopian tube appeared normal. Two intra-abdominal drains were left in situ. The total intra operative blood loss was 1370 ml. Intraoperatively she received 3 units of packed red blood cells and 2 units of fresh frozen plasma. Immediate post-operative period was uneventful. Fibrinogen levels and thromboelastography evaluation were normal. She received broad spectrum intravenous antibiotics. Postoperative Hb was 8 g/dl. Both intraabdominal

drainage tubes were removed on the 2<sup>nd</sup> post-operative day. She recovered well and was discharged after counselling regarding birth spacing and future pregnancies.

Review of literature on 314 abdominal pregnancies:

We performed a literature review of 314 abdominal pregnancies from 1930-2021 using electronic searches in MEDLINE, EMBASE, PubMed, Web of Science and bibliographies of relevant articles. The review was limited to human studies in English. Case reports, case series and systematic reviews were included. Data recorded included site of the ectopic, gestational age at diagnosis, surgical and/or medical management, blood loss and transfusions, maternal morbidity and mortality and fetal outcomes. Descriptive statistics are provided.

## Results

We reviewed 314 cases of abdominal pregnancies, both early and advanced, from 1930-2021. Table 1 outlines the details reported by various authors and table 2 summarises the management and maternal and fetal outcomes. In our current series, 295 cases (93.9%) were surgically managed and 19 cases (6%) required hysterectomy. Post-surgery adjuvant methotrexate was given in 9 cases (2.9%) and ultrasound guided percutaneous microwave ablation was performed in one patient with diaphragmatic ectopic. Ten out of 18 patients (55.5%) required surgical intervention following primary methotrexate. Complete removal of the placenta can be a daunting task in certain cases. We found that complete removal was achieved in 264 cases (84%), partial in 27 cases (8.6%) and left in situ in 16 cases (5.1%). Due to lack of longterm follow-up and paucity of data, the postoperative complications like intraabdominal sepsis and bleeding where the placenta was left insitu could not be analysed. Maternal mortality and morbidity is a matter of serious concern in abdominal pregnancies and a high index of suspicion and management expertise is required. In this series, 74 cases (23.6%) required transfusion of blood and blood products. There were 15 maternal deaths (4.8%).

Regarding the neonatal outcome, 241 cases (76.8%) were abdominal pregnancies <20 weeks of gestation. In the advanced abdominal pregnancies after 20 weeks of gestation, 27 fetuses (8.6%) were live born, 6 (1.9%) were neonatal deaths and 46 (14.6%) were fetal demise in utero or stillborn.

## Discussion

### Main findings and interpretation

The first abdominal pregnancy was reported in 1708 as an autopsy finding and many cases have been reported worldwide ever since (3). While in a primary abdominal pregnancy the fertilized ovum implants directly in the abdominal cavity (10), in a secondary abdominal pregnancy the embryo or fetus continues to grow in the abdominal cavity after expulsion from its primary site of development (11). There are several theories about the pathophysiology of an abdominal pregnancy. Berghella V et al hypothesised that an omental pregnancy is secondary to a primary tubal or ovarian pregnancy that subsequently implants on the omentum (12), while Cavanagh stated that fertilization may occur in the posterior cul-de-sac where sperms accumulate and the ovum is transported via dependent flow of peritoneal fluid (13). Paternoster DM et al suggested delayed ovulation associated with a reversed tubal course by retrograde menstrual flow as a possible mechanism and further emphasised the role of intraperitoneal fluid flow in carrying the zygote from the cul-de-sac to different intraperitoneal sites (14). Dmowski et al and Hall et al postulated a spontaneous migration of the embryo from the uterus to the retroperitoneal space along lymphatic channels (15,16). Abdominal pregnancies post hysterectomy have been explained by migration of the fertilised ovum via fistulous tracts (17).

Though the ectopic pregnancy rates are on an incline, the risk of abdominal pregnancies, with ruptured ectopic pregnancy among one of its many causes, is on a declining trend due to improved antenatal care and diagnostic methods (11). Despite the availability of defined criteria by Studdiford, its diagnosis proves challenging and requires a high degree of suspicion. In addition to its vague non-specific clinical presentation, initial misdiagnosed ultrasound reports may interfere with timely diagnosis, like in our case. The most common physical examination findings include abdominal tenderness (100%), abnormal fetal lie (70%), easily palpable fetal parts and a displaced cervix (9). Our patient presented with symptoms of generalised

pricking abdominal pain, mild chest pain and spotting per vagina at 13 weeks of gestation. This vague presentation was misleading and resulted in a delay in diagnosis till evaluation at our centre. More often than not a transvaginal ultrasound confirms the diagnosis but in case of a dilemma, MRI can provide further clarity regarding the diagnosis.

Gestational age at diagnosis and maternal hemodynamic stability are the main factors dictating management. The two main modalities of treatment are medical and surgical, surgical being more common as patients usually present as an acute emergency with intra-abdominal bleeding (4). The choice between laparoscopy and laparotomy depends on multiple factors including period of gestation at diagnosis, maternal hemodynamic stability and availability of resources and skill (18). With increasing early ultrasonography, ectopic pregnancies are being identified prior to complications like rupture, providing an opportunity to attempt medical management with KCl or methotrexate individualised for each case (4). Less commonly used agents include hyperosmolar glucose, prostaglandins, danazol, etoposide and mifepristone (18).

The management of the placenta ranges from complete or partial removal of the placenta to leaving the complete placenta in situ (18). The use of adjuvant methotrexate for the placental remnants is controversial. While some believe that it helps accelerate the involution of the placenta others say that rapid degeneration results in higher amounts of necrotic tissue accumulation forming a nidus for infection thereby increasing sepsis rates (18). The use of methotrexate at advanced gestation is debatable, as it works best on rapidly dividing cells and is less likely to help in case of a mature placenta (19). We did not administer methotrexate to our patient as very minimal placental tissue <1 cm was left behind.

Abdominal pregnancy, especially when advanced, is known to be associated with high maternal and neonatal morbidity and mortality (18). The maternal mortality rate ranges from 0.5-20% (20). Severe hemorrhage, perforation, bowel obstruction, fistula, disseminated intra-vascular coagulation and sepsis contribute to the increased morbidity and mortality. Our patient was transfused with 3 units of packed red blood cells and 2 units of fresh frozen plasma and did not have any other post operative morbidity. Perinatal mortality rates of 40%-95% have been reported and 21-90% of surviving fetuses have serious birth defects due to anhydramnios and subsequent compression and also vascular disruption (20). Surviving neonates frequently develop torticollis, flattening of the head, facial or cranial asymmetry, thoracic malformations, limb defects, joint abnormalities and CNS malformations (9,20).

In a systematic review done by Poole A et al on 225 abdominal pregnancies diagnosed/treated at less than 20 weeks of gestation, from 1965 to 2009, 8% of the early abdominal ectopics occurred with an intrauterine device in situ. Mean gestational age at treatment was 10 weeks. The commonest sites of early abdominal ectopics were pouches around the uterus (24.3%), serosal surface of uterus and tubes (23.9%) and other sites (12.8%). Primary surgical management was done in 208 cases (87.8%). Non-surgical adjuvant or primary therapy included intramuscular methotrexate, intralesional methotrexate, intracardiac KCl and uterine artery embolization. The overall maternal mortality was 3% (4).

Nkusu ND et al reviewed 163 cases of advanced abdominal pregnancy after 20 weeks of gestation from 1946 to 2008. Forty five percent cases were diagnosed preoperatively. Fetal/ perinatal mortality was 72% and pressure deformities were common among survivors. Maternal postoperative complications like hemorrhage and infection were noted in 55%, transfusion of blood products in 80%. Maternal mortality was 12% (20).

In the current review of 314 cases of early and advanced abdominal pregnancy by various authors from 1930-2021, we observed a maternal morbidity in terms of transfusion of blood and blood products in 74 cases (23.6%) and maternal deaths in 15 cases (4.8%). The maternal mortality rate we noted in our review is marginally higher than the systematic review done by Poole A et al(4) but is significantly lower compared to the rate quoted by Nkusu ND (12%)(20). This difference could be attributed to the period of gestation used as inclusion criteria. Early versus advanced abdominal pregnancy is an important factor influencing the varied maternal mortality and morbidity rates reported by different authors and higher rates have been reported at advanced gestations. We also noted that 93.9% of the cases were surgically managed and 6% required hysterectomy. These rates are comparable to that noted by Poole A et al. In addition, multiple

other factors may have contributed to the reduction in maternal mortality rates over the years like early diagnosis, advanced imaging modalities, increased patient and physician awareness, improved surgical and non-surgical techniques, blood product availability and better access to tertiary care centres over the years. Regarding the overall neonatal outcome, 8.6% were live born, 76.8% were fetal losses <20 weeks of gestation, 14.6% were IUFD/ stillborn and 1.9% were neonatal deaths.

### **Strengths and limitations**

This is one of the largest reviews of literature of 314 cases of secondary abdominal pregnancy focussing on its management and outcomes. As an overlap of few study periods was noted, we acknowledge the possibility of repetition of cases among the various authors included in this review. The inclusion criteria too, varied in terms of gestational age and management.

### **Conclusion**

Abdominal pregnancy is a rare type of ectopic gestation which remains a diagnostic challenge. Of concern is the high maternal and perinatal morbidity and mortality, especially at advanced gestations. The diagnosis may be missed despite early ultrasound and requires a high index of suspicion and a skilled sonologist for timely diagnosis. MRI is a useful adjunct when the ultrasound is inconclusive. Early surgical intervention is imperative to decrease complications and improve outcomes. It is essential to ensure the availability of adequate blood and blood products as hemorrhage in these cases can be sudden and massive. Surgery remains the mainstay of management and medical methods are not usually successful. However, the rarity of this condition and the myriad presentations preclude sound recommendations to be made.

### **Disclosure of interests**

The authors declare no conflict of interest.

### **Contribution to Authorship**

Machado N was involved in the clinical care of the patient, conceptualisation of the study, performed the data collection, data analysis and wrote the manuscript. Vasudeva A, the corresponding author, was involved in clinical care and management of the patient, contributed to the study design, data analysis and has the final responsibility for the decision to submit the article. Bharatnur S, Kanchan S and Hoskeri V were involved with the clinical care of the patient.

### **Details of Patient's consent**

The patient's written consent for publication was obtained .

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### **Details of Ethics Approval**

Not applicable

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**Table 1. A review of 314 cases of abdominal pregnancies from 1930-2021**

Author	Year of publication (Study period)	No. of cases	Gestational age at diagnosis	Management	EBL	Placental removal	Maternal morbidity/mortality	Neonatal outcome
Ware HH et al (21)	1948 (1930-1946)	13	28 weeks-48 weeks	13-Surgical	NA	3-Complete 3-Partial 6-Left in situ 1-NA	3-Deaths	5-Live 8-Still b



Author	Year of publication (Study period)	No. of cases	Gestational age at diagnosis	Management	EBL	Placental removal	Maternal morbidity/mortality	Neonatal outcome
Cross JB et al (22)	1951 (1936-1950)	19	15 weeks-40 weeks	19-Surgical	10 had excessive bleeding	11-Complete 4-Partial 4-Left in situ	4- Deaths	2-Live 2-NND 8-IUFD <20 weeks
Yahia C et al (23)	1956 (1933-1955)	8	5 $\frac{1}{2}$ months - 39 weeks	8- Surgical (5-Hysterectomy)	NA	6-Complete 2-Left in situ	Nil mortality	3-Live 1-NND 4-IUFD
Dixon HG et al (24)	1960	10	22 weeks-51 weeks	10- Surgical (6-Hysterectomy)	NA	10-Complete	Nil mortality	4-Live 5-Still b 1-NND
Beacham WD et al (25)	1946 (1937-1945)	20	4 months- 9 months	19- Surgical (8- Hysterectomy 1- Post mortem diagnosis)	NA	16-Complete 1-Partial 2-Left in situ 1-NA	12-Transfused 1-Death	18-IUFD Stillborn 1-Lived NND
Gupta P et al (26)	2009	3	14 weeks-36 weeks	3-Surgical (1-Preoperative IM methotrexate 1-Incidental laparotomy finding)	200 ml	3-Partial (absorbed in 1-6 months)	2-Transfused	1-IUFD
Poole A et al (4)	2012 (1965-2009)	225	6 weeks- 16 weeks 4 days	208-Primary Surgical 9-Medical 8-Medical followed by surgery	50- 7500 ml	210-Complete 15-Partial	56-Transfused 7-Deaths	—
Jain V et al (27)	2012	1	33 weeks	Surgical	800- 1000 ml	Complete	Transfused	Female, kg. NICU-F
Srinivasan A et al (28)	2014	1	8 weeks 5 days	Surgical - partial omentectomy (omental ectopic)	NA	NA	Nil mortality	—

Author	Year of publication (Study period)	No. of cases	Gestational age at diagnosis	Management	EBL	Placental removal	Maternal morbidity/mortality	Neonatal outcome
Singh Y et al (29)	2016	1	35 weeks	Surgical (Incidental finding on emergency LSCS)	Massive bleeding	Complete	Nil mortality	Live fetus 2.6 kg
Gidiri MF et al (30)	2015	3	21 weeks-35 weeks	3-Surgical (1-Incidental finding at LSCS)	1500-2000 ml	2-Complete 1-Left in situ (absorbed in 6 mths)	Nil mortality	1-Male, 1-fetus, 1-IUFD
Cosentino F et al (31)	2017	1	12 weeks	Surgical-laparoscopy	500 ml	Complete	Nil mortality	—
Tolefac PN et al (18)	2017	1	25 weeks	Surgical-laparotomy	NA	Left in situ (absorbed in 3 mths)	Nil mortality	Live male fetus, 1150 g
AbdulJabbar NA et al (32)	2018	2	7 weeks-14 weeks	2-Surgical (1-laparoscopy 1-Laparotomy)	150-3000 ml	2-Complete	1-Transfused	NA
Trail CE et al (33)	2018	1	6 weeks	Surgical cum medical- (Hepatic flexure ectopic) diagnosed laparoscopically. Post op methotrexate x 2 doses	500 ml	—	Nil	NA
Shurie S et al (34)	2018	1	35 weeks	Surgical-laparotomy (anterior abdominal wall and mesentery ectopic)	NA	—	Nil	IUFD

Author	Year of publication (Study period)	No. of cases	Gestational age at diagnosis	Management	EBL	Placental removal	Maternal morbidity/mortality	Neonatal outcome
Gurjar R et al (35)	2019	1	37 weeks	Surgical (Incidental LSCS finding)	NA	Partial	Transfused	Live Male, 2.45 kg
Odelola O et al (36)	2019	1	9 weeks-initial diagnosis	Surgical-Emergency laparotomy at 33 weeks 5 days	1500 ml	Complete	Transfused	Live female, 2.2 kg
Qian H et al (37)	2020	1	8 weeks 6 days	Ultrasound-guided percutaneous microwave ablation of diaphragmatic ectopic	NA	NA	Nil	—
Van Antwerp E et al (38)	2021	1	10 weeks	Surgical management-laparoscopy-partial omentectomy (omental ectopic)	800 ml	NA	Nil	—

**Abbreviations used in Table 1 :** EBL- Estimated Blood Loss, NND- Neonatal Death, IUFD- Intra Uterine Fetal Demise, NA- Not Available, NICU- Neonatal Intensive Care Unit, RDS- Respiratory Distress Syndrome, LSCS- Lower Segment Cesarean Section, Mths- months

**Table 2:** Summary of management and maternal and fetal outcomes in 314 cases

Total number of cases reviewed= 314

Management	Number of cases	Percentage
Surgical	295	93.9%
Hysterectomy	19	6%
Post-surgery Adjuvant methotrexate	9	2.9%
Primary Methotrexate followed by surgery	10	3.2%

USG guided percutaneous microwave ablation	1	0.3%
Placental removal		
Complete	264	84%
Partial	27	8.6%
Left in situ	16	5.1%
NA (not available)	7	2.3%
Maternal morbidity/mortality		
Transfusions	74	23.6%
Death	15	4.8%
Neonatal morbidity/mortality		
<20 weeks gestation	241	76.8%
Live born (including NND)	27	8.6%
Fetal demise (IUFD/stillborn)	46	14.6%
NND	6	1.9%

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