Breast cancer during lactation

Dr Jocelyn Lippey
18th January 2016
Case 1 - DD

- 37yo female
- 2 previous pregnancies
- Mild asthma but otherwise well
- 32/40 admitted with polyamnios & cervical incompetence
- Noticed right breast lower inner quadrant mass
Breast mass in Pregnancy/lactation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy or lactational change</td>
<td>50%</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>22%</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>12%</td>
</tr>
<tr>
<td>Cysts</td>
<td>10%</td>
</tr>
<tr>
<td>Lactating adenoma</td>
<td>1%</td>
</tr>
<tr>
<td>Non-diagnostic samples (benign on F/U)</td>
<td>2%</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>3%</td>
</tr>
</tbody>
</table>

Gupta RK. The Breast Journal 1997; 3(3): 131-134
Baby delivered via LCSC at 38/40 (breech presentation)
4.1g boy
2hrs in SCN for hypoglycaemia
Tubal ligation performed simultaneously
Successfully breastfeeding
Started to develop paraesthesia in R arm prompting GP review and referral to breast surgical service
Seen by surgeon 11 weeks post partum
Risk factors
- Breast fed all 3 children
- First pregnancy at 34

Family history
- 2 maternal aunts with breast cancer at 34 and 39 – one deceased
- Maternal great grandmother breast cancer

O/E: 25mm palpable mass in R LIQ with 10cm area of surrounding erythema
- Large palpable fixed axillary nodes
- Swelling extending up to clavicle with palpable infraclavicular lymph node
Initial plan:
- Biopsy mass
- Staging investigations
  - CT chest/abdomen/pelvis
  - Bone scan
- Refer to medical oncology
Core biopsy of breast

- G3 invasive carcinoma with medullary features
- ER negative, PR negative, HER2 negative

Staging CT and bone scan clear for visceral metastatic disease

- Extensive axillary disease

Started on chemotherapy

- NAC
Overview

- Case presentation
- Breast cancer in young women
- Breast cancer in pregnancy and lactation
  - Epidemiology
  - Pathogenesis
  - Presentation and Diagnosis
  - Treatment
  - Prognosis
  - Psychological aspects
- Summary
Breast cancer in young women

- Around 1500 women under 45yo are diagnosed with breast cancer every year in Australia
- 100 women per year in Australia and NZ diagnosed with BC during or shortly after pregnancy
- All ages, 15,000 women per year in Australia are diagnosed with breast cancer
- 5yr survival for women <40yrs ranges between 55 and 75% (overall 5yr survival in Australia is 89%)
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- Summary
Pregnancy associated breast cancer - PABC

Groups breast cancer during pregnancy with diagnosis within 1 year of delivery as PABC

Hard to tease out differences in literature

Breast cancers discovered during lactation do have more aggressive traits and higher rates of cause-specific death.

Can not be explained by or adjusted for age, extent of disease or pregnancy hormones.

Confirmed in mouse models


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  - Prognosis
  - Psychological aspects

- Summary
Epidemiology - PABC

- Most common cancer during pregnancy
- 1-3 in 10,000 pregnancies
- Likely to increase in incidence as maternal gestational age increases
WA Gestational Breast Cancer Project

- Used WA Data Linkage System to identify women under 45 who had PABC
  - 1982 to 2003 women with breast cancer
  - n=2539
  - 475,000 births (about 627,000 pregnancies)

- Reviewed chart, pharmacy data, pathology labs, midwife records

- Epidemiology, patterns of care and outcomes

- Psychosocial issues

- Pregnancy after breast cancer

WA gestational breast cancer results

- 150 cases identified ~8p.a. in WA
- 6.25% of breast cancers in WA in women <45yo
- 1/3 were pregnant
- 23.6 per 100,000 pregnancies
- Some treatment differences – more mastectomies
- Tumour comparisons 53.8% tumour >2cm size (39.7% control), 54.5% lymph node positive (40.6% control)
- Compared with other young women diagnosed with breast cancer similar survival overall but significantly worse if diagnosed just after birth rather than during
- 73% 5yr survival

AMOSS – Australasian Maternity Outcomes Surveillance System
Gestational Breast Cancer (GBC)

• **Aims:**
  – Determine incidence, obstetric and cancer management and perinatal outcomes of women who give birth with a first diagnosis of breast cancer during pregnancy or within 6 weeks post partum
  – Explore health care-related experiences of women diagnosed with GBC to inform clinical care

• **Methods:**
  – Prospective, Australia & NZ
  – 1/1/13 to 30/6/14
  – Quantitative and Qualitative design aspects

Aims to address rare conditions <1:1000 and to find evidence on these Maternity units >50 deliveries/yr
AMOSS – Australasian Maternity Outcomes Surveillance System
Gestational Breast Cancer (GBC)

• National results
  – 47 cases
    • 39 Australia
    • 8 NZ
  – Estimated incidence 8.5 per 100,000 births
  – Timing of diagnosis
    • 40 cases diagnosed during pregnancy
    • 7 cases diagnosed within 6 weeks post partum
### AMOSS Cancer characteristics

<table>
<thead>
<tr>
<th></th>
<th>Diagnosed</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pregnancy</td>
<td>Postpartum n=7</td>
<td></td>
</tr>
<tr>
<td>Breast symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>32 (80.0%)</td>
<td>36 (76.6%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>3 (7.5%)</td>
<td>4 (8.5%)</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td>5 (12.5%)</td>
<td>7 (14.9%)</td>
</tr>
<tr>
<td>Cancer site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Single</td>
<td>38 (95.0%)</td>
<td>44 (93.6%)</td>
</tr>
<tr>
<td></td>
<td>Bilateral</td>
<td>1 (2.5%)</td>
<td>1 (2.1%)</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td>1 (2.5%)</td>
<td>2 (4.3%)</td>
</tr>
<tr>
<td>Cancer foci</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unifocal</td>
<td>23 (57.5%)</td>
<td>25 (53.2%)</td>
</tr>
<tr>
<td></td>
<td>Multifocal</td>
<td>10 (25.0%)</td>
<td>12 (25.5%)</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td>7 (17.5%)</td>
<td>10 (21.3%)</td>
</tr>
<tr>
<td>Tumour grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>3 (7.5%)</td>
<td>3 (6.4%)</td>
</tr>
<tr>
<td></td>
<td>Intermediate</td>
<td>4 (10.0%)</td>
<td>5 (10.6%)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>23 (57.5%)</td>
<td>26 (55.3%)</td>
</tr>
<tr>
<td></td>
<td>NA/NK</td>
<td>10 (25.0%)</td>
<td>13 (27.7%)</td>
</tr>
</tbody>
</table>

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Duration of breast symptoms prior to diagnosis: 1-12 weeks
Mean(±SD) 4.8±3.9 weeks, median 3.5
## Onset Labour and mode of birth

<table>
<thead>
<tr>
<th></th>
<th>Diagnosed</th>
<th>Pregnancy n=40</th>
<th>Postpartum n=7</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Induction of labour</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>26(65.0%)</td>
<td>3(42.9%)</td>
<td>29(61.7%)</td>
<td></td>
</tr>
<tr>
<td><em>GBC as reason for induction</em></td>
<td>21(52.5%)</td>
<td>NA</td>
<td>21(44.7%)</td>
<td></td>
</tr>
<tr>
<td>Other reasons</td>
<td>5(12.5%)</td>
<td>3(42.9%)</td>
<td>8(17.0%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>13(32.5%)</td>
<td>4(57.1%)</td>
<td>17(36.2%)</td>
<td></td>
</tr>
<tr>
<td>Not known</td>
<td>1(2.5%)</td>
<td>0(0.0%)</td>
<td>1(2.1%)</td>
<td></td>
</tr>
<tr>
<td><strong>Mode of birth</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unassisted vaginal birth</td>
<td>23(57.5%)</td>
<td>4(57.1%)</td>
<td>27(57.4%)</td>
<td></td>
</tr>
<tr>
<td>Forceps/Vacuum extraction</td>
<td>4(10.0%)</td>
<td>1(14.3%)</td>
<td>5(10.6%)</td>
<td></td>
</tr>
<tr>
<td>Caesarean section</td>
<td>13(32.5%)</td>
<td>2(28.6%)</td>
<td>15(31.9%)</td>
<td></td>
</tr>
</tbody>
</table>
## Maternal outcomes

<table>
<thead>
<tr>
<th>Diagnosed</th>
<th>Pregnancy n=40</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Complications due to breast cancer</strong></td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1(2.5%)</td>
</tr>
<tr>
<td>Abscess in left breast at site of the lumpectomy</td>
<td>1(2.5%)</td>
</tr>
<tr>
<td>Left lower lobe pneumonia secondary to neutropenia</td>
<td>1(2.5%)</td>
</tr>
<tr>
<td>Secondary spread to femoral head causing pain, difficulty weight bearing</td>
<td>1(2.5%)</td>
</tr>
<tr>
<td>Thrombocytopenia secondary to systemic therapy</td>
<td>4(10.0%)</td>
</tr>
<tr>
<td><strong>Postpartum haemorrhage</strong></td>
<td>3(7.5%)</td>
</tr>
<tr>
<td><strong>Return to theatre after birth</strong></td>
<td>1(2.5%)</td>
</tr>
<tr>
<td><strong>Admitted to ICU</strong></td>
<td>2(5.0%)</td>
</tr>
<tr>
<td><strong>Admitted to HDU</strong></td>
<td>1(2.5%)</td>
</tr>
</tbody>
</table>
AMOSS Conclusions

- Majority of women had breast symptoms prior to diagnosis
- Communication and planned multi-disciplinary integrated care critical
- Majority of women diagnosed in 2\textsuperscript{nd} and 3\textsuperscript{rd} trimester
- High rate of preterm birth reflects the use of induction for planned early delivery to support cancer therapy
- Perinatal outcomes are reassuring in the small case series
- Almost half of women diagnosed in pregnancy initiate breastfeeding
- Longer term follow up is warranted to monitor infant morbidity
Overview

- Case presentation
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- Summary
Pathogenesis

- Differences in pathogenesis (all theoretical)
  - Elevated levels of circulating hormones during pregnancy act on cancer cells to increase biologic aggressiveness
  - Hormonal changes during pregnancy increase vascularisation and inflammatory cell recruitment

- Significant changes to vasculature, adipose tissue and extracellular matrix during lactation
  - Adipocyte and stromal remodeling required for increased nutritional and metabolic demands of the expanding epithelium as well as the paracrine endocrine function

- 15% of women <40yo with breast cancer will have a genetic mutation yet may have a scant family history of breast cancer
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Presentation

- Typically longer duration of symptoms prior to management than in age matched cohorts
  - 2 to 15 months from first symptom to diagnosis
  - Delay of 1 month in diagnosis translates into a 0.9% risk in the odds of lymph node metastasis

  Raphel J, Turdeau ME, Chan K. Curr Oncol 2015 22;Supplement1: S8-18

- Age for age, compared to non-pregnant women with breast cancer, pregnant women with breast cancer are diagnosed at later stages
  - More aggressive biology
  - Significant breast changes delaying diagnosis

- Detecting abnormalities in breast tissue with examination is more difficult whilst lactating

- Breast lumps during pregnancy should be investigated promptly
Diagnosis

**Imaging**
- Ultrasound should be the first investigation
  - Breast parenchyma has a very different appearance during gestation and lactation
- MMG is safe but decreased sensitivity in young women with dense breasts especially during lactation
  - Shield during pregnancy
  - Generally clinicians reluctant to use
  - Should be 2nd test after FNA or core biopsy shows suspicion
- MRI unsafe during pregnancy but safe during lactation
  - Gadolinium contrast – unknown affect during pregnancy
    - Express milk for 24hrs after administration of gadolinium and discard
  - High magnetic fields

Webb JA, Thomsen HS, Sameh K et al. Eur Radiol 2005; 15: 1234-1240
Diagnosis

- Difficulties in diagnosis
- Concern about milk fistula and bleeding after core biopsy
  - Although actual incidence of fistula is very low safer to start with FNA
  - Blood flow increased 180% during pregnancy
Palpable lump

Bilateral breast ultrasound

Complex cystic or solid lesion
  - Direct FNA
  - FNA +/- Core biopsy
  - Simple Cyst
    - Routine review
  - Malignant
    - Benign
      - Bilateral mammography
      - Clinical follow-up

Consider CE Breast MRI on case by case basis
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- Summary
Management

- Guidelines
  - USA, UK, European and Canadian but no Australian guidelines

- General breast cancer management no different

- Breast feeding usually advised to stop before surgery, chemotherapy and further adjuvant treatments

- Medications and lactation
  - Unknown whether trastuzumab and tamoxifen are excreted in breast milk but advised not safe to breastfeed
  - Chemotherapy does cross into breast milk
    - Should be at least 14 days between last chemotherapy session to start of breastfeeding
Surgical management

- Generally tumours are larger so mastectomy is required.

- Rates of recurrence after breast conservation unacceptably high?
  - 38% LRR at 10yrs for <35yo

  Bollet MA, Sigal-Zafrani B, Mazeau et al. Radiotherapy and Oncology 2007; 82: 272-280

- Breast conservation and radiotherapy is possible.
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- Summary
Prognosis

- Conflicting data about worse prognosis in PABC
  - Some studies show similar prognosis in age matched cohorts and some worse especially in lactation/post partum group
  - All retrospective cohort studies some with poorly matched groups
  - On average larger tumours and more nodal involvement

- Overall estimate 5yr survival approximately 50%
Norweigan population study

- Used national registry of both cancers and pregnancy to analyse 42,000 women aged 16-49 who had any type of cancer between 1967 and 2002.

- 516 of those 42,000 women were pregnant around the time of their cancer diagnosis.

- Cause specific mortality was the same for the pregnant vs non pregnant group except in the breast and ovarian lactating groups.
<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Crude HR</th>
<th>95% CI</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Not pregnant</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Pregnant</td>
<td>1.77</td>
<td>1.20 to 2.60</td>
<td>1.23</td>
<td>0.83 to 1.81</td>
</tr>
<tr>
<td>Lactating</td>
<td>3.44</td>
<td>2.40 to 4.92</td>
<td>1.95*</td>
<td>1.36 to 2.78</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Not pregnant</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Pregnant</td>
<td>1.23</td>
<td>0.83 to 1.84</td>
<td>1.52*</td>
<td>1.01 to 2.31</td>
</tr>
<tr>
<td>Lactating</td>
<td>0.92</td>
<td>0.55 to 1.53</td>
<td>1.10</td>
<td>0.65 to 1.85</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Not pregnant</td>
<td>0.96</td>
<td>0.51 to 1.64</td>
<td>0.89</td>
<td>0.52 to 1.53</td>
</tr>
<tr>
<td>Pregnant</td>
<td>0.81</td>
<td>0.37 to 1.69</td>
<td>0.94</td>
<td>0.46 to 1.77</td>
</tr>
<tr>
<td>Lactating</td>
<td>0.61</td>
<td>0.37 to 1.03</td>
<td>0.94</td>
<td>0.46 to 1.77</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Not pregnant</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Pregnant</td>
<td>1.09</td>
<td>0.74 to 1.61</td>
<td>1.15</td>
<td>0.77 to 1.70</td>
</tr>
<tr>
<td>Lactating</td>
<td>0.72</td>
<td>0.44 to 1.18</td>
<td>0.89</td>
<td>0.54 to 1.46</td>
</tr>
<tr>
<td>Thyroid cancer</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Not pregnant</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Pregnant</td>
<td>1.34</td>
<td>0.81 to 2.31</td>
<td>1.26</td>
<td>0.73 to 2.22</td>
</tr>
<tr>
<td>Lactating</td>
<td>2.12</td>
<td>1.17 to 3.84</td>
<td>1.70</td>
<td>1.08 to 2.70</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Not pregnant</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Pregnant</td>
<td>0.17</td>
<td>0.06 to 0.46</td>
<td>0.46</td>
<td>0.17 to 1.23</td>
</tr>
<tr>
<td>Lactating</td>
<td>0.93</td>
<td>0.44 to 1.96</td>
<td>2.23</td>
<td>1.05 to 4.73</td>
</tr>
</tbody>
</table>

NOTE. Univariate analyses are presented as crude HR. Multivariate analyses (right column) are adjusted for age, diagnostic period and initial extent of disease. Abbreviations: HR, hazard ratio; ref, reference. *Indicates significant HRs; P < .05.
Aged matched cohort studies about prognosis

Norwegian cancer registry between 1954 and 1981 identified 35 women <45yo with breast cancer
- 20 were pregnant at the time of diagnosis
- 15 were lactating

Compared these to aged matched controls

Diagnosis delay
- 2.5 months in pregnancy group
- 6 months in lactation group
Figure 1: Survival (%) by time after diagnosis. Pregnancy group versus two control groups.

Figure 3: Survival (%) by time after diagnosis. Lactating group versus two control groups.
Future pregnancies

- Advice generally is to wait 2 years

- Advantages
  - Survival
    - Rate of recurrence is highest in first 3 years
  - Psychological
  - Treatment

- Disadvantages
  - Decreased fertility

- Association with future pregnancies reducing risk of death by 41% “healthy mother effect”

- Future pregnancies and breastfeeding
  - Single breast
  - Radiotherapy fibrosis makes successful lactation in affected breast unlikely
  - No evidence previous chemotherapy affects the safety of breastfeeding

Information needs

- BCNA Young Pink Sisters
- Hope for Two
  http://www.hopefortwo.org/
- Fertile Hope
  http://www.livestrong.org/we-can-help/fertility-services/

Specific information on
- Premature menopause
- Fertility
- Contraception
- Sexuality
- Reconstruction
- Grief and loss
Psychosocial issues of PABC

- Feeling of isolation
- Lack of support/information – want facts to make their own choices
- Options/choice – want support for their choice and not to be judged
  - 60% had children but wanted to consider more
- Need for improved support networks
- Unique range of experiences for women in this group


15 women qualitative study
I think I was concerned about being able to continue breastfeeding but ultimately I thought it was probably better for me to just be alive. A formula fed baby will be fine and better to have a mother than not.

You can try and change the position, so feed him on that side, then turn him around to this side and um have another go at feeding him. But then my nipple was getting so sore. So I went down to the nursery and I sat in the chair to feed and I asked one of the midwives something about the feeding and she said oh yes dear, but um. You only feed for ten minutes on that side and then ten minutes on the other side. And I said oh, I'm sorry but I've had the mastectomy. And she said oh, oh, you're that lady. Oh sorry. And she was so apologetic. And she was going I'm sorry, I'm sorry, I'm so sorry. I'm like – that's OK and then I took the baby and just went back to my room. So it was like, um...I didn't belong in the maternity ward.
AMOSS – Australasian Maternity Outcomes Surveillance System
Gestational Breast Cancer (GBC)

- Qualitative arm – 17 women all diagnosed pre delivery
- Semi-structured interviewed with thematic analysis of transcripts
- Emergent themes
  - Take women seriously
  - Prompt referral
  - Involve women in treatment planning
  - Uniform response
  - Consistent information
  - Well co-ordinated care
  - Access to breast care nurse
During treatment

• Agreed approach to proposed treatment
• Consistent information conveyed to the woman
• Well coordinated obstetric and oncology care
  • “And in the maternity ward: They had obviously made sure that every single nurse who was on knew what was going on with me, so that when they walked in, I didn’t have to explain anything…
  • I was given such good care, and they all knew when my radiation was supposed to start; they asked how I was feeling about that; how I was— if they could do anything extra for me. I was just given just beautiful care.” (Participant 6)
During treatment

I found that when I was dealing with the cancer—because I was sort of basically dealing with two departments: the maternity department and the cancer department, and when I was in the cancer ward, that was fine, and they could deal with me— I was a pregnant woman—but it was more when I was dealing with the maternity department. They really struggled to deal with me because I didn’t really fit it into any boxes. (Participant 13)
Common concerns

- Will a future pregnancy cause a recurrence?
- How will my partner cope with kids if I die?
- How will my children cope with a sick mother?
- Will the cancer affect my children?
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  - Treatment
  - Prognosis
  - Psychological aspects

Summary
Take home points

- Breast cancer in young women is uncommon but incidence is increasing
- Any breast mass presenting during lactation which persists beyond 72hrs needs medical assessment
- No need to stop breast feeding for biopsy
- Unique range of psychological issues needed in this group
Acknowledgments

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