A man and a woman are shown in profile, looking out a window. The man is on the left, wearing a dark sweater, and the woman is on the right, wearing a red and yellow patterned top. They are both looking towards the right. A large, stylized graphic overlay consisting of several curved, overlapping bands in shades of blue and pink dominates the left and center of the image. The background is a bright, out-of-focus view of greenery through a window.

Diagnostic  
Evaluation  
for Recurrent  
Pregnancy Loss

*ReproSource*<sup>®</sup>  
ILLUMINATING PATHWAYS TO REPRODUCTIVE HEALTH™

# Evaluating recurrent pregnancy loss (RPL)

ReproSource provides high-quality diagnostic testing to help determine the causes of recurrent pregnancy loss

## ASRM<sup>1</sup> and ACOG<sup>2</sup> recommendations:

### Who should be tested?

- ✓ Couples with  $\geq 2$  miscarriages<sup>1</sup>

### What should be evaluated?

#### Family history and physical evaluation

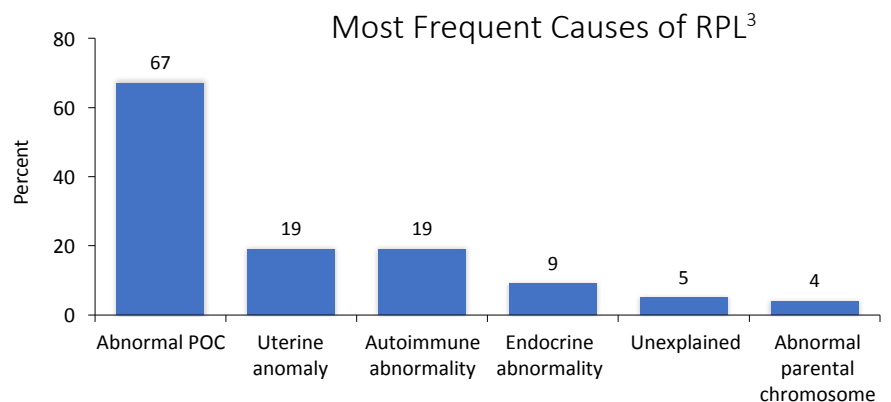
- ✓ Uterine anatomy: Sonohysterogram, hysterosalpingogram, hysteroscopy
- ✓ Lifestyle: Smoking, obesity, drugs & alcohol

#### Laboratory evaluations

- ✓ Endocrine: Thyroid stimulating hormone
- ✓ Coagulation: Lupus anticoagulant
- ✓ Immunology: Anticardiolipin, Anti- $\beta 2$ -glycoprotein 1
- ✓ Genetics: POC & parental chromosome analysis

POC=products of conception

**Chromosomal abnormalities** in POC are the most frequent cause of recurrent pregnancy loss<sup>3</sup>



Data does not add up to 100% because more than one problem was identified in some cases.

# ReproSource offers an RPL evaluation that is aligned with ACOG and ASRM guidelines and is easy to interpret

ReproSource Pregnancy Evaluation Report is carefully curated as per medical society guidelines and includes testing of the most common causes of RPL: genetic abnormalities, antiphospholipid syndrome, and endocrine disorders

300 Trade Center, Suite 6540  
Woburn, MA 01801 USA  
tel: 800.667.8893 USA only  
tel: 781.937.8893  
fax: 781.935.3068  
CLIA#: 22D0884531

## Pregnancy Evaluation Report

### RPL Standard Panel 1.3

*ReproSource*<sup>®</sup>  
ILLUMINATING PATHWAYS TO REPRODUCTIVE HEALTH™

Patient: Example, Patient	Clinician: Clinician Example
Gender: F Age: 28 Date of Birth: 01/03/1990	Telephone: 413.555.5555 Fax: 413.555.5556
Specimen: T00001390	Address: Example Clinic
Reported: 11/04/18	123 Example Street
Received: 11/02/18 Time: 10:00 am	Example City, EX 55555
Collected: 11/01/18 Time: 10:30 am	

#### RESULTS OVERVIEW\*\*

CATEGORY	TESTS	UNITS	RANGE	IN RANGE	BORDER-LINE	OUT OF RANGE	NOTE	
Endocrine	Thyroid stimulating hormone (TSH)	mIU/L	0.40–4.50	1.52				
Coagulation	Lupus anticoagulant (LA)	N/A	negative	negative				
Immunology	Anticardiolipin (aCL)	IgG	GLP	0-14	7			
		IgM	MLP	0-14	4			
	Anti-β <sub>2</sub> Glycoprotein I (aBGPI)	IgG	SGU	0-20			50	positive
		IgM	SMU	0-20			31	positive
Genetics	Maternal Karyotype (blood)	N/A	46, XX			X	46,XX,t(3;4;14)[q21;p14;q22.3] see comments	
	Chromosomal Microarray, POC ClariSure® Oligo-SNP	N/A	46,XX OR 46,XY	46,XX			no maternal cell contamination	

#### COMMENTS:

\*\*THIS RESULTS OVERVIEW PAGE IS NOT INTENDED TO PROVIDE COMPLETE INFORMATION. PLEASE REVIEW THE INDIVIDUAL TEST RESULTS THAT FOLLOW:\*\*

- Out of range results obtained for anti-B2 glycoprotein I IgG and IgM. Please review full results in detail.
- An abnormal female chromosome complement with an apparently balanced complex rearrangement involving chromosomes 3, 4, and 14 is seen. Please review full results in detail.
- POC: normal female microarray result. No maternal cell contamination. Please review full results in detail.

Please contact ReproSource Client Services with any questions **tel:** 800 667 8893 option 1 **email:** clientservices@reprosource.com **web:** www.reprosource.com

#### CURRENT TESTING GUIDELINES FOR RECURRENT PREGNANCY LOSS (RPL)

Recurrent Pregnancy Loss Testing		ACOG	ASRM	ACG	ESHRE	Opinion
CRITERIA	TESTS					
2 or 3 or more intrauterine pregnancy losses	Thyroid Stimulating Hormone	Yes	Yes	Yes	Yes	Yes
	Lupus anticoagulant (LA)	Yes	Yes	Yes	Yes	Yes
	Anticardiolipin (aCL) IgG IgM	Yes	Yes	Yes	Yes	Yes
	Anti-β <sub>2</sub> GPI IgG IgM	Yes	Yes	Yes	Yes	Yes
	Karyotype X2 (both parents)	Yes	Yes		Yes	Yes

**REFERENCE SOURCES**

ACOG: American College of Obstetrics & Gynecology  
ASRM: American Society of Reproductive Medicine  
ACG: Antiphospholipid Consensus Group  
ESHRE: European Society of Human Reproduction & Embryology  
Opinion: Expert Opinion Papers & Reviews

**REFERENCES**

- ACOG Practice Bulletin 150 (2015) Early Pregnancy Loss
- ACOG Practice Bulletin 132 (2012) Antiphospholipid Syndrome
- ASRM Committee Opinion (2013) Evaluation and Treatment of RPL
- ACG International Consensus Statement (2006) Antiphospholipid Syndrome (APS) Recommendations
- ESHRE Practice Guidelines (2017) Recurrent Pregnancy Loss
- Stephenson M. Clinical Obstetrics & Gynecology (2007) Evaluation and Management of Recurrent Early Pregnancy Loss
- Kutteh W. Seminars in Reproductive Medicine (2015) Novel Strategies for the Management of Recurrent Pregnancy Loss

# ReproSource provides actionable results

## Test results lead to finding care management solutions<sup>1</sup>

Test Category	Targeted Testing	Clinical Application	Care Management Options*
Endocrine <sup>1</sup>	<ul style="list-style-type: none"> <li>• Thyroid stimulating hormone</li> </ul>	<ul style="list-style-type: none"> <li>• Assessment of ovulatory function and possible endocrine-related disorders</li> <li>• Evaluation for thyroid dysfunction</li> </ul>	<ul style="list-style-type: none"> <li>• Levothyroxine</li> </ul>
Coagulation <sup>1,2,4</sup>	<ul style="list-style-type: none"> <li>• Lupus anticoagulant</li> </ul>	<ul style="list-style-type: none"> <li>• Evaluation for antiphospholipid syndrome and other autoimmune disorders</li> </ul>	<ul style="list-style-type: none"> <li>• Heparin + aspirin<sup>†</sup></li> </ul>
Immunology <sup>1,2,4</sup>	<ul style="list-style-type: none"> <li>• Anti-β<sub>2</sub>-glycoprotein IgG, IgM</li> <li>• Anticardiolipin (aCL) IgG, IgM</li> </ul>	<ul style="list-style-type: none"> <li>• Evaluation for antiphospholipid syndrome and other autoimmune disorders</li> </ul>	<ul style="list-style-type: none"> <li>• Heparin + aspirin<sup>†</sup></li> </ul>
Genetics <sup>1,5</sup>	<ul style="list-style-type: none"> <li>• Parental karyotype</li> <li>• Chromosomal microarray of product of conception (POC)</li> </ul>	<ul style="list-style-type: none"> <li>• Evaluation for genetic abnormalities in POC (e.g., trisomy) or parents (e.g., translocations)</li> </ul>	<ul style="list-style-type: none"> <li>• Genetic counseling</li> <li>• Preimplantation genetic diagnosis for balanced translocation</li> </ul>

\*This information is provided for informational purposes only and is not intended as medical advice. A physician's test selection and interpretation, diagnosis, and patient management decisions should be based on their education, clinical expertise, and assessment of the patient. Physicians should refer to the manufacturer's approved labeling for prescribing, warnings, side effects and other important information.

†Syphilis infection should also be excluded as it can give a false-positive test for antiphospholipid syndrome

*"By adding this tool, which is microarray testing of the fetal tissue [to the standard ASRM RPL workup], we're able to almost double the number of couples that we can give an answer to...and provide them with an explanation."*

—Dr William Kutteh<sup>‡</sup>

*Clinical Professor, Vanderbilt University Medical Center, Memphis, TN.  
Director, Recurrent Pregnancy Loss Center, Fertility Associates of Memphis, TN.*

*Successful outcomes can be achieved with appropriate management*

**5 years** after a first consultation

**67% of all women** and

**72% of women with 3 miscarriages**

*achieve a live birth<sup>6</sup>*



<sup>‡</sup>Dr Kutteh has served as a paid speaker for ReproSource.

# Convenient specimen collection & shipping

## ReproSource RPL diagnostic test specifications

Test	Chromosomal Microarray, POC, ClariSure® Oligo-SNP	Maternal Cell Contamination Study, STR-Analysis	Parental* Chromosomal Analysis (Karyotype)	Recurrent Pregnancy Loss Standard Panel
<b>Test code</b>	Fresh tissue: T4209 FFPE block: T4202	T4201	T4411	P7300
<b>Indication</b>	Detects fetal chromosomal abnormalities	Provides assurance that test results from fetal specimens are not influenced by contaminating maternal material	Detects balanced chromosome rearrangement in couples	Evaluates maternal immune, coagulation and endocrine factors
<b>Performed on</b>	POC	Peripheral blood	Peripheral blood	Peripheral blood
<b>Sample requirements</b>	2 x 3 mm of tissue from product of conception in transport media in POC kit FFPE block acceptable (use code above)	5 mL whole blood collected in an EDTA (lavender-top) tube in MCC box within the POC kit	5 mL whole blood collected in a sodium heparin (green-top) tube in Parental Karyotype kit	Complete requisition and fax to 1.781.935.3068 ReproSource customer service group will facilitate scheduling at a Quest PSC or shipment of dry ice for in office draw
<b>Minimum volume</b>	2 x 3 mm (tissue)	3 mL	1 mL	See kit instruction
<b>Test notes</b>	Low assay failure rate	Test run in conjunction with Chromosomal Microarray, POC, ClariSure Oligo-SNP	Separate sample and requisitions for patient and her partner are required	Specifically tests for: <ul style="list-style-type: none"> <li>• Lupus anticoagulant</li> <li>• Thyroid-stimulating hormone</li> <li>• Anticardiolipin IgG and IgM</li> <li>• Anti-β2 -Glycoprotein IgG and IgM</li> </ul>
<b>Shipping notes</b>	Transport refrigerated Do not freeze DO NOT PUT IN FORMALIN	Ship at room temperature Do not freeze	Ship at room temperature Do not freeze	Ship frozen in dry ice box provided by ReproSource client services

**Note: Panel components can be ordered separately.**

EDTA: ethylenediaminetetraacetic acid; FFPE tissue: formalin-fixed paraffin embedded tissue; MCC: maternal cell contamination; POC: products of conception; PSC: patient service center.

\*When a POC microarray is abnormal, a parental follow up (karyotype) can help further pinpoint the cause of the miscarriage.

ReproSource is not enrolled in Medicare or Medicaid and is unable to submit claims and bill those entities for testing.

## Give peace of mind to your patients<sup>7</sup>

- Both men and women feel extremely or very upset about the thought of a miscarriage
- More than 75% of patients would like to know the cause of their miscarriage

## RPL diagnostic testing can help you and your patients find answers

- Identify events unlikely to re-occur
- Evaluate underlying immunologic, hematologic or structural issues that can be addressed
- Help identify appropriate actions or solutions

### Experts on hand to help with test selection, interpret results, and advise on next steps:

- **Specimen kits & shipping supplies:**

ClientServices@ReproSource.com or 1.800.667.8893  
press option 1

- **Interpreting test results:**

QuestClinicianSupport@ReproSource.com or  
1.800.667.8893 press option 1

- **To reach a Quest Diagnostics genetic counselor for assistance with interpretation of Chromosomal Microarray, POC, ClariSure® Oligo-SNP results call:**

1.866.GENE.INFO (1.866.436.3463)

- **Patient billing:**

BillingInquiries@ReproSource.com or  
1.800.667.8893 press option 3

- **Need to see or hear from your account executive:**

Sales@ReproSource.com or  
1.800.667.8893 press option 1

- **Specimen requirements & processing:**

ClientServices@ReproSource.com or  
1.800.667.8893 press option 1

- **Online reporting instructions, usernames & passwords:**

ITsupport@ReproSource.com or  
1.800.667.8893 press option 1

#### References

1. Practice Committee of the American Society for Reproductive Medicine. Evaluation and treatment of recurrent pregnancy loss: a committee opinion. *Fertil Steril*. 2012;98:1103-1111.
2. ACOG. Repeated miscarriages. Available at: <https://www.acog.org/Patients/FAQs/Repeated-Miscarriages>. Accessed December 12, 2018.
3. Popescu F, Jaslow CR, Kutteh WH. Recurrent pregnancy loss evaluation combined with 24-chromosome microarray of miscarriage tissue provides a probable or definite cause of pregnancy loss in over 90% of patients. *Hum Reprod*. 2018;33:579-587.
4. Committee on Practice Bulletins - Obstetrics, ACOG. Practice Bulletin No. 132: Antiphospholipid syndrome. *Obstet Gynecol*. 2012;120:1514-1521.
5. ACOG. Practice Bulletin No. 162 Summary: Prenatal diagnostic testing for genetic disorders. *Obstet Gynecol*. 2016;127:976-978.
6. Lund M, et al. Prognosis for live birth in women with recurrent miscarriage: what is the best measure of success? *Obstet Gynecol*. 2012;119:37-43.
7. Bardos J, Hercz D, Friedenthal J, Missmer SA, Williams Z. A national survey on public perceptions of miscarriage. *Obstet Gynecol*. 2015;125:1313-1320.