doi: 10.13241/j.cnki.pmb.2020.19.042

不同放散试验对新生儿 ABO 溶血病的诊断价值对比 *

相 莲[1] 高 琳[2] 王 蓓[3] 颜 晖[4△] 马 莹[4]

（1 西安医学院第一附属医院输血科 陕西 西安 710077；2 西安医学院第一附属医院儿保科 陕西 西安 710077；
3 西安市儿童医院中心实验室 陕西 西安 710072；4 西安市中心医院检验科 陕西 西安 710003）

摘要 目的：分析与比较不同放散试验对新生儿 ABO 溶血病的诊断价值。**方法：**选择 2017 年 9 月至 2019 年 6 月在本院进行 ABO 溶血病检测的新生儿 240 例，取所有新生儿的静脉血样本 2~3 mL，采用冷冻复融放散试验方法与改良热放散试验方法检测新生儿 ABO 溶血病的发生情况，并比较单独诊断和联合诊断的价值。**结果：**在 240 份标本中，冷冻复融放散试验检出新生儿 ABO 溶血病阳性 130 例，阳性检出率为 54.2 %；改良热放散试验检出新生儿 ABO 溶血病阳性 94 例，阳性检出率为 39.2 %；二者联合检出新生儿 ABO 溶血病阳性 100 例，阳性检出率为 41.67 %，联合检出新生儿 ABO 溶血病阳性率和冷冻复融放散试验检出新生儿 ABO 溶血病阳性率显著高于改良热放散试验检出新生儿 ABO 溶血病阳性率(P<0.05)。临床最终诊断为新生儿 ABO 溶血病 101 例，阳性率为 42.08 %，患儿 ABO 血型包括 A 型 56 例，B 型 45 例。冷冻复融放散试验诊断新生儿 ABO 溶血病的敏感性和特异性为 73.8 %和 95.5 %，ROC 曲线面积 0.775；改良热放散试验检诊断为新生儿 ABO 溶血病的敏感性和特异性为 100 %和 95.2 %，ROC 曲线面积 0.853；二者联合诊断对新生儿 ABO 溶血病的敏感性和特异性为 90.0 %和 97.85 %，ROC 曲线面积 0.872，联合诊断特异性优于改良热放散试验检诊和冷冻复融放散试验诊断，且改良热放散试验检诊敏感性优于冷冻复融放散试验诊断。**结论：**相对于冷冻复融放散试验，改良热放散试验对新生儿 ABO 溶血病的诊断敏感性更高，且不影响诊断特异性，两种放散方法联合检测具有更好的应用价值。

关键词：冷冻复融放散试验；改良热放散试验；新生儿 ABO 溶血病；敏感性；特异性

中图分类号：R725.5；R457.1 **文献标识码：**A **文章编号：**1673-6273(2020)19-3792-05

Comparison of the Diagnostic Values of Different Release Tests for the Neonatal ABO Hemolytic Disease*

XIANG Lian[1], GAO Lin[2], WANG Bei[3], YAN Hui[4△], MA Ying[4]

(1 Department of Blood Transfusion, the First Affiliated Hospital of Xi'an Medical College, Xi'an, Shaanxi, 710077, China;
2 Department of Pediatrics, the First Affiliated Hospital of Xi'an Medical College, Xi'an, Shaanxi, 710077, China;
3 Central Laboratory of Xi'an Children's Hospital, Xi'an, Shaanxi, 710072, China;
4 Department of Laboratory Medicine, Xi'an Central Hospital, Xi'an, Shaanxi, 710003, China)

ABSTRACT Objective: To explore and compare the diagnostic values of different radiation tests for neonatal ABO hemolytic disease. **Methods:** From September 2017 to June 2019, 240 cases of neonates were selected for ABO hemolytic disease testing in our hospital, and 2~3 mL of venous blood samples from all newborns were collected. The freezing thawing test method and the improved thermal elution test methods were to detect the occurrence of ABO hemolytic disease in newborns and compare the value of individual diagnosis and combined diagnosis. **Results:** There were 130 cases of neonatal ABO hemolytic disease were detected by the freezing thawing test in the 240 cases, and the positive detection rate was 54.2 %. In the improved thermal elution test, 94 cases of neonatal ABO hemolytic disease were positive, and the positive detection rate was 39.2 %. The combined detection of 100 cases of neonatal ABO hemolytic disease was positive, with a positive detection rate of 41.67 %. The positive rate of neonatal ABO hemolytic disease combined with the freezing thawing test was significantly higher than that of the improved thermal elution test for neonatal ABO hemolytic disease (P<0.05). The final clinical diagnosis were 101 cases of neonatal ABO hemolytic disease, with a positive rate of 42.08 %. The ABO blood type of children included 56 cases of type A, 45 cases of type B. The sensitivity and specificity of the freezing thawing test to diagnose neonatal ABO hemolytic disease were 73.8 % and 95.5 %, and the ROC curve area was 0.775. The sensitivity and specificity of the improved thermal elution test to diagnose neonatal ABO hemolytic disease were 100 % and 95.2 %, and the ROC curve area was 0.853. The sensitivity and

* 基金项目：国家自然科学基金青年基金项目(81602902)

作者简介：相莲(1981-)，女，本科，主管检验师，研究方向：新生儿溶血病的诊断、贫血的输血治疗，
电话：15091335579，E-mail：xlan6696@163.com
△ 通讯作者：颜晖(1980-)，男，本科，主管检验师，研究方向：贫血的实验诊断、血细胞形态学检验，
电话：13891911904，E-mail：307919351@qq.com

(收稿日期：2020-01-30 接受日期：2020-02-26)

specificity of the combined diagnosis of the two for neonatal ABO hemolytic disease are 90.0 % and 97.85 %, and the ROC curve area is 0.872. The specificity of the combined diagnosis is superior to the improved thermal elution test diagnosis and freezing thawing test diagnosis. The diagnostic sensitivity of the improved thermal elution test is better than that of freezing thawing test. **Conclusion:** Compares with the freezing thawing test, the improved thermal elution test was more sensitive to the diagnosis of ABO hemolytic disease in newborns without affecting the diagnostic specificity. The combined detection of the two release methods have better application value.

Key words: Freezing thawing test;Improved thermal elution test; ABO hemolytic disease of newborn; Sensitivity; Specific

Chinese Library Classification(CLC): R725.5; R457.1 Document code: A

Article ID: 1673-6273(2020)19-3792-05

前言

新生儿溶血病(hemolytic disease of the newborn,HDN)在临床上比较常见[1],可引起胎儿血管外溶血、黄疸外,严重者可出现肝脾大、心力衰竭、贫血、水肿等症状[2,3]。如果新生儿肝脏功能发育不够完善,可导致黄疸症状继续加重,累及神经系统症状,严重情况下可导致新生儿死亡[4,5]。

新生儿溶血病的原因根据血型系统主要分为 ABO 血型不合和 ABO 以外的血型不合，其中 ABO 血型是人类第一个发现的血型系统,由该系统引起新生儿溶血病的几率占绝大多数[6,7]。早期实验室诊断对 HDN 的临床治疗与干预有重要意义，当前常用的检测方法主要有化学放散、酸放散、热放散等[8]。改良热放散实验是通过缩短振荡时间,降低放散液的溶血程度,也可使得实验工作简单化[9,10]。特别是经过木瓜蛋白酶处理的红细胞具有强抗原 - 抗体系统的反应活性，能够提高检测的灵敏性[11,12]。本研究具体比较了不同放散试验对新生儿 ABO 溶血病诊断价值,以提高新生儿 ABO 溶血病的早期检出率。现总结报道如下。

1 资料与方法

1.1 研究对象

选择 2017 年 9 月至 2019 年 6 月在本院进行 ABO 溶血病检测的新生儿 240 例,纳入标准:血液标本来源于拟诊为新生儿 ABO 溶血病者;新生儿日龄 1~12 d;母婴血型不合并伴有黄疸的新生儿;母亲为 O 型血,父亲为非 O 型血型;患儿家长知情同意;病历资料完整;经本院伦理委员会批准。排除标准:血液标本来源于有输血史或者换血史的新生儿;临床与检测资料缺乏者。

其中男 124 例,女 116 例;日龄最短 1 d,最长 12 d,平均 7.82± 1.35 d。

1.2 检测方法

1.2.1 试剂与仪器 标准 ABO 细胞由上海血液生物医药有限责任公司提供(批号:2019093016),木瓜蛋白酶由国药集团化学试剂有限公司提供(批号:64006884),新生儿血型卡、抗人球蛋白检测卡、血型检测卡购自长春博迅生物技术有限责任公司,低离子介质购自珠海贝索生物技术有限公司。Diana 半自动血型处理系统及其专用离心机、孵育器购自美国 sigma 公司,ThermoForma702 型超低温冰箱购自美国 BD 公司。

1.2.2 血液采集 取所有新生儿的 EDTA 抗凝后静脉血样 2~3 ml,3000 r/min 离心 5 min 后,吸出压积红细胞 2 mL,生理盐水洗涤 4 遍,同时做两种放散试验检测。

1.2.3 放散试验方法 (1)冷冻复融放散试验:取洗涤后的压积红细胞 6 滴于试管中,加入 3 滴生理盐水,混匀,-80℃冷冻 15 min 后进行复融,3 000 r/min 离心 5 min 后,取上清液体(放散液)。取 2 滴低离子溶液、2 滴放散液、1 滴 3 %~5 %标准 ABO 细胞悬液,混匀,37℃水浴 15 min 后,生理盐水洗涤 3 次,干燥后于试管中加入单克隆抗 IgG 抗体 2 滴。离心后肉眼判断阳性标准:试管中出现凝集块。(2)改良热放散试验方法:取洗涤后的压积红细胞,加入 2 份 1 %木瓜蛋白酶溶液孵育 30 min,使用生理盐水配置木瓜蛋白酶处理标准 ABO 细胞悬液。取洗涤后患儿压积红细胞 6 滴于等量生理盐水,混匀,56℃水浴 10 min,并轻轻振荡 1 min,3 000 r/min 离心 5 min 后,取上清液体(放散液)。在抗人 IgG 检测卡对应位置标孔中,分别加入瓜蛋白酶处理标准 ABO 细胞悬液 50 μL 和放散液 25 μL 后，置于半自动卡式孵育器孵育 15 min,放入专用离心机离心 9 min 后。肉眼判断阳性标准:反应孔中出现凝集块。

1.3 统计学分析

选择 SPSS 19.0 进行数据分析,计量数据以($\bar{x}\pm s$)示,组间比较行 t 检验;计数数据以(%)表示,组间比较行 x^2 检验,以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 三种试验检测的阳性检出率对比

在 240 份标本中，冷冻复融放散试验检出新生儿 ABO 溶血病阳性 130 例,阳性检出率为 54.2 %。改良热放散试验检出新生儿 ABO 溶血病阳性 94 例,阳性检出率为 39.2 %,冷冻复融放散试验检联合改良热放散试验检出新生儿 ABO 溶血病阳性 100 例,阳性检出率为 41.67 %,冷冻复融放散试验检联合改良热放散试验检出新生儿 ABO 溶血病阳性率和冷冻复融放散试验检出新生儿 ABO 溶血病阳性率显著高于改良热放散试验检出新生儿 ABO 溶血病阳性率($P<0.05$),见表 1。

2.2 临床对新生儿 ABO 溶血病的确诊结果

在 240 份标本中，临床最终诊断为新生儿 ABO 溶血病 101 例,阳性率为 42.08 %,患儿 ABO 血型包括 A 型 56 例,B 型 45 例。

2.3 三种试验对新生儿 ABO 溶血病的诊断价值

在 240 份标本中，冷冻复融放散试验诊断新生儿 ABO 溶血病的敏感性和特异性为 73.8 % (96/130)和 95.5 % (105/110),ROC 曲线面积 0.775。改良热放散试验检诊断为新生儿 ABO 溶血病的敏感性和特异性为 100 % (94/94) 和 95.2 % (139/146),ROC 曲线面积 0.853。冷冻复融放散试验与改良热放散试验诊断新生儿 ABO 溶血病的敏感性和特异性为 90.0 %

(98/100)和 97.85 %(137/140),ROC 曲线面积 0.872,联合诊断特异性优于改良热放散试验诊断和冷冻复融放散试验诊断,且改良热放散试验诊断敏感性优于冷冻复融放散试验诊断,见表 2、3、4 和图 1。

表 1 240 份全血标本的不同放散试验的阳性检出率对比(例,%)

Table 1 Comparison of positive detection rates of 240 different whole blood specimens in different release tests (n, %)

Experiment method	n	Number of positive specimens	Positive detection rate
Freezing thawing test	240	130	54.2
Improved thermal elution test	240	94	39.2*
Joint test	240	100	41.67*

Note: Compared with the freeze-thaw release test, *P<0.05.

表 2 冷冻复融放散试验诊断新生儿 ABO 溶血病的敏感性和特异性(n=240)

Table 2 The sensitivity and specificity of the freezing thawing test in diagnosing neonatal ABO hemolytic disease

Freezing thawing test	Clinical final diagnosis		Total
	Positive	Negative	
Positive	96	34	130
Negative	5	105	110
Total	101	139	240

表 3 改良热放散试验诊断新生儿 ABO 溶血病的敏感性和特异性(n=240)

Table 3 The sensitivity and specificity of improved thermal elution test for diagnosis of neonatal ABO hemolytic disease (n=240)

Improved thermal elution test	Clinical final diagnosis		Total
	Positive	Negative	
Positive	94	0	94
Negative	7	139	146
Total	101	139	240

表 4 联合试验诊断新生儿 ABO 溶血病的敏感性和特异性(n=240)

Table 4 The sensitivity and specificity of the combined test to diagnose neonatal ABO hemolytic disease (n=240)

Joint test	Clinical final diagnosis		Total
	Positive	Negative	
Positive	98	2	100
Negative	3	137	140
Total	101	139	240

3 讨论

新生儿溶血病的临床表现为黄疸、贫血、水肿等,可伴发胆红素脑病,导致神经系统损伤,严重情况下可威胁到患儿的生命[13,14]。ABO 血型不合是当前临床最为常见的新生儿溶血疾病,新生儿 ABO 溶血病约占所有新生儿溶血病的 70.0 %左右[15]。该病的发生机制还不明确,在妊娠后期,如果胎盘局部破裂,可导致胎儿红细胞即渗入母体血液循环,刺激母体内产生与胎儿红细胞不配合的 IgG 性质的血型抗体,为免疫性溶血的发生创造了条件[16,17]。胎盘绒毛膜仅有的一层单体细胞,伴随着胎儿的生长,胎盘绒毛膜的破裂容易造成胎盘屏障的渗漏。新生儿 ABO 溶血病的及早检测和诊断可以避免后续症状的发生,减轻疾病对新生儿造成损伤[18]。

目前,放散试验是新生儿 ABO 溶血病的主要诊断依据[19]。传统试管法抗人球试验是经典的试验方法,微柱凝胶法是抗人球试验与微柱凝胶技术的结合,具有检测敏感度高、特异度强、结果准确等特点,能减少结果判定的人为误差,在一定程度上可以全取代传统试管法[20]。有研究显示在近千例的试管法抗人球试验与微柱凝胶法平行试验中,相符率都为 100 %[21]。本研究的 240 份标本中,冷冻复融放散试验的阳性检出率为 54.2 %,而改良热放散试验的阳性检出率为 39.2 %,二者联合检测的阳性率为 41.67 %,临床最终诊断为新生儿 ABO 溶血病 101 例,阳性率为 42.08 %,患儿 ABO 血型包括 A 型 56 例,B 型 45 例。从机制上分析,母体的 IgG 抗 A 或抗 B 经过胎盘进入胎儿血循环,相对比较容易发生新生儿 ABO 溶血病[22]。改良热放散试验方法主要是采用了木瓜蛋白酶处理标准红细胞,降低红细

胞表面负电荷，并可结合微柱凝胶卡法检测放散液中的抗体，能够破坏红细胞表面的唾液酸，有利于 IgG 抗体与具有相应抗原的红细胞结合，降低红细胞表面负电荷，减少红细胞之间的排斥力，产生凝集反应[23,24]。

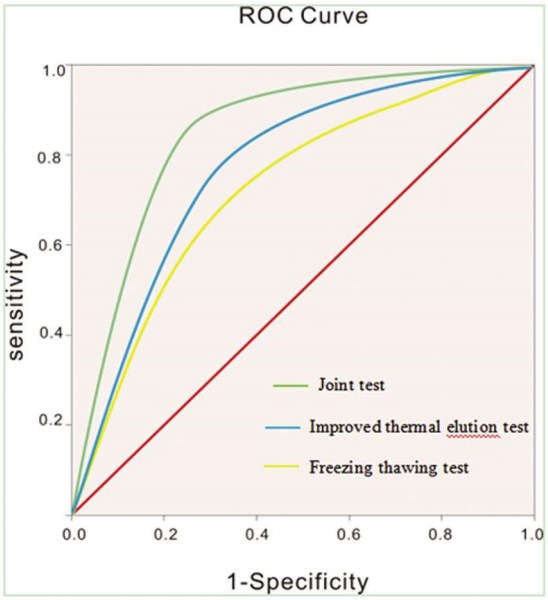

图 1 三种试验对新生儿 ABO 溶血病的 ROC 曲线

Fig.1 ROC curve of three trials on neonatal ABO hemolytic disease

ABO 血型是人类第一个发现的血型系统，由该系统引起新生儿溶血病的几率较高，因而实验室血清学检测对 ABO 新生儿溶血病的诊治具有重要作用[25]。当前，对新生儿 ABO 溶血病的诊断包括红细胞抗体释放试验、直接抗人球蛋白试验、血清游离抗体试验等[26]。在新生儿红细胞或血清中查出对抗其自身红细胞的血型抗体是诊断新生儿 ABO 溶血病的重要实验根据。微柱凝胶卡法较传统试管法对新生儿溶血病检测的灵敏度更高，结果更加客观，并且能够满足大批量标本同时检测的临床需要[27]。放散试验主要为检测红细胞上致敏的抗体，但由于其所用的红细胞表面上的血型抗原比较多，因此其灵敏度很高。有研究显示放散试验所使用的红细胞比直抗试验多 200 倍左右，有可能达到较高的敏感度，可以直接反映新生儿溶血病是否发生[28]。

本研究中，冷冻复融放散试验诊断新生儿 ABO 溶血病的敏感性和特异性为 73.8 %和 95.5 %，ROC 曲线面积 0.775；改良热放散试验诊断为新生儿 ABO 溶血病的敏感性和特异性为 100 %和 95.2 %，ROC 曲线面积 0.853；二者联合诊断新生儿 ABO 溶血病的敏感性和特异性为 90.0 %和 97.85 %，ROC 曲线面积 0.872，联合诊断的特异性优于改良热放散试验检诊和冷冻复融放散试验诊断，且改良热放散试验诊断的敏感性优于冷冻复融放散试验诊断，又不影响诊断的特异性。从机制上分析，冷冻复融放散试验原理主要是依靠低温冷冻和 37℃水浴复融的物理方法，导致红细胞膜机械性破坏，使红细胞上结合的抗体放散，导致微柱凝胶卡的检测结果不易观察，易出现假阳性结果，且在检测中比较耗费人力[29]。改良热放散试验将振摇时间缩短为 1 min，其是利用木瓜蛋白酶处理红细胞加强凝集反应，能破坏多种抗原，可通过分子筛效应协助抗人球蛋白捕捉微量致敏红细胞或抗原抗体复合物，从而具有较高的诊断敏感性，二者联合诊断的特异性优于改良热放散试验检诊和冷冻复融放散试验诊断。也有研究显示对于新生儿 ABO 溶血病，血清学检测血样应该在出生 7 d 内采集并完成试验，采集时间的不同可能会影响检测结果[30]。

总之，相对于冷冻复融放散试验，改良热放散试验对新生儿 ABO 溶血病的诊断敏感性更高，且不影响诊断特异性，两种放散方法联合检测具有更好的应用价值。本研究也存在一定的不足，样本数量较少，如果只选择单一放散试验进行新生儿 ABO 溶血病的诊断，会增加假阳性的概率。

参 考 文 献(References)

[1] Claes V, Peyrard T, Deleers M, et al. Acute hemolytic transfusion reaction associated with anti-Mt (a) : case report and review of the literature[J]. Transfusion, 2019, 59(11): 3314-3318

[2] Crispin P, Sliwinski K, Wilson C, et al. Cold reacting anti-M causing delayed hemolytic disease of the newborn [J]. Transfusion, 2019, 59 (12): 3575-3579

[3] Moinuddin I, Fletcher C, Millward P. Prevalence and specificity of clinically significant red cell alloantibodies in pregnant women - a study from a tertiary care hospital in Southeast Michigan [J]. J Blood Med, 2019, 10(8): 283-289

[4] Sanchez-Duran MA, Higueras MT, Halajdian-Madrid C, et al. Management and outcome of pregnancies in women with red cell isoimmunization: a 15-year observational study from a tertiary care university hospital[J]. BMC Pregnancy Childbirth, 2019, 19(1): e356

[5] Sun J B. The prenatal intervention of pregnancy complicated with anti-Kell isoimmunization: a review [J]. J Matern Fetal Neonatal Med, 2019, 9(13): 1-7

[6] Takahashi K, Migita O, Sasaki A, et al. Amplicon Sequencing-Based Noninvasive Fetal Genotyping for RHD-Positive D Antigen-Negative Alleles[J]. Clin Chem, 2019, 65(10): 1307-1316

[7] Zhu XJ, Wei J K, Zhang CM. Evaluation of endothelial microparticles as a prognostic marker in hemolytic disease of the newborn in China [J]. J Int Med Res, 2019, 47(11): 5732-5739

[8] Bachofner A, Rufli T, Holbro A, et al. The Remarkable Journey of a Low-Frequency Alloantibody [J]. Transfus Med Hemother, 2019, 46 (5): 384-385

[9] Bel Hadj I, Boukhris R, Khalsi F, et al. ABO hemolytic disease of newborn : Does newborn's blood group a risk factor?[J]. Tunis Med, 2019, 97(3): 455-460

[10] Blumberg N, Cholette JM, Cahill C, et al. Transfusion medicine: A research agenda for the coming years[J]. Transfus Apher Sci, 2019, 58 (5): 698-700

[11] Guarente J, Harach M, Gould J, et al. Dilution is not the solution: acute hemolytic transfusion reaction after ABO-incompatible pooled platelet transfusion[J]. Immunohematology, 2019, 35(3): 91-94

[12] Moinuddin I, Fletcher C, Millward P. Prevalence and specificity of clinically significant red cell alloantibodies in pregnant women - a study from a tertiary care hospital in Southeast Michigan [J]. J Blood Med, 2019, 10(9): 283-289

[13] Adebiyi MG, Zhao Z, Ye Y, et al. Circadian period 2: a missing beneficial factor in sickle cell disease by lowering pulmonary inflamma-

tion, iron overload, and mortality [J]. Faseb J, 2019, 33 (9): 10528-10537

[14] Dvorak CC, Higham C, Shimano KA. Transplant-Associated Thrombotic Microangiopathy in Pediatric Hematopoietic Cell Transplant Recipients: A Practical Approach to Diagnosis and Management [J]. Front Pediatr, 2019, 7(18): e133

[15] Eryilmaz M, Acar Soykut E, Cetin D, et al. SERS-based rapid assay for sensitive detection of Group A Streptococcus by evaluation of the swab sampling technique[J]. Analyst, 2019, 144(11): 3573-3580

[16] Huang Y, Liu X, Chen F, et al. Prediction of thrombosis risk in patients with paroxysmal nocturnal hemoglobinuria [J]. Ann Hematol, 2019, 98(10): 2283-2291

[17] Neves F PG, Marlow MA, Rezende-Pereira G, et al. Differences in gram-positive bacterial colonization and antimicrobial resistance among children in a high income inequality setting [J]. BMC Infect Dis, 2019, 19(1): e478

[18] Nishino A, Katsumata Y, Kawasumi H, et al. Usefulness of soluble CD163 as a biomarker for macrophage activation syndrome associated with systemic lupus erythematosus[J]. Lupus, 2019, 28(8): 986-994

[19] Al-Lawama M, Badran E, Elrimawi A, et al. Intravenous Immunoglobulins as Adjunct Treatment to Phototherapy in Isoimmune Hemolytic Disease of the Newborn: A Retrospective Case-Control Study[J]. J Clin Med Res, 2019, 11(11): 760-763

[20] Al-Lawama M, Badran E, Elrimawi A, et al. Intravenous Immunoglobulins as Adjunct Treatment to Phototherapy in Isoimmune Hemolytic Disease of the Newborn: A Retrospective Case-Control Study[J]. J Clin Med Res, 2019, 11(11): 760-763

[21] Altahan R, Al Mugairi A. The unusual abundance of a rare finding! [J]. Clin Case Rep, 2019, 7(9): 1809-1810

[22] Bi S H, Jiang LL, Dai LY, et al. Rh-incompatible hemolytic disease of the newborn in Hefei [J]. World J Clin Cases, 2019, 7 (20): 3202-3207

[23] Sawada T, Kurano M, Shirai H, et al. Serum phosphatidylserine-specific phospholipase A1 as a novel biomarker for monitoring systemic lupus erythematosus disease activity [J]. Int J Rheum Dis, 2019, 22 (11): 2059-2066

[24] Sundell K, Landor L, Nicolas P, et al. Phenotypic and Genetic Predictors of Pathogenicity and Virulence in Flavobacterium psychrophilum [J]. Front Microbiol, 2019, 10(8): e1711

[25] Uddin S MM, Haq A, Haq Z, et al. Case Report: Rare comorbidity of celiac disease and Evans syndrome: The rare correlation of Celiac and Evans syndrome[J]. F1000Res, 2019, 8(13): e181

[26] Zemsky CJ, Sherman SW, Schubert HD, et al. Case Report: Management of Corneal Clouding from Lecithin: Cholesterol Acyltransferase Deficiency[J]. Optom Vis Sci, 2019, 96(2): 137-141

[27] Shahverdi E, Moghaddam M, Hajbeigi B, et al. The First Comprehensive Study of H-Deficient Phenotypes in Iran [J]. Transfus Med Hemother, 2019, 46(5): 376-380

[28] Tasaki M, Saito K, Nakagawa Y, et al. Analysis of the prevalence of systemic de novo thrombotic microangiopathy after ABO-incompatible kidney transplantation and the associated risk factors [J]. Int J Urol, 2019, 26(12): 1128-1137

[29] Tynuv M, Flegel WA. Quality improvement with platelet additive solution for safer out-of-group platelet transfusions[J]. Immunohematology, 2019, 35(3): 108-115

[30] Zhu XJ, Wei JK, Zhang CM. Evaluation of endothelial microparticles as a prognostic marker in hemolytic disease of the newborn in China [J]. J Int Med Res, 2019, 47(11): 5732-5739

（上接第 3769 页）

[28] Gunasekaran K, Amladi A, Mathew SK, et al. A case of septicaemic melioidosis: Utility of therapeutic drug monitoring and high-dose meropenem in successful management [J] .Indian J Med Microbiol, 2018, 36(4): 597-599

[29] Perdigão Neto LV, Oliveira MS, Martins RCR, et al. Fosfomycin in severe infections due to genetically distinct pan-drug-resistant Gram-negative microorganisms: synergy with meropenem [J]. J Antimicrob Chemother, 2019, 74(1): 177-181

[30] García-Rodríguez JF, Bardán-García B, Peña-Rodríguez MF, et al. Meropenem antimicrobial stewardship program: clinical, economic, and antibiotic resistance impact [J]. Eur J Clin Microbiol Infect Dis, 2019, 38(1): 161-170