UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
INSTITUTO DE CIÊNCIAS BÁSICAS DA SAÚDE
CURSO DE ESPECIALIZAÇÃO EM MICROBIOLOGIA CLÍNICA

Josiane Fatima de Paula

COMPARAÇÃO DE DESEMPENHO ENTRE A METODOLOGIA ASPERGILLUS POR ENSAIO DE FLUXO LATERAL E ELISA PARA DETECTAR O ANTÍGENO GALACTOMANNAN NO DIAGNÓSTICO DE ASPERGILOSE INVASIVA

Porto Alegre
2023

Josiane Fatima de Paula

COMPARAÇÃO DE DESEMPENHO ENTRE A METODOLOGIA ASPERGILLUS POR ENSAIO DE FLUXO LATERAL E ELISA PARA DETECTAR O ANTÍGENO GALACTOMANNAN NO DIAGNÓSTICO DE ASPERGILOSE INVASIVA

Trabalho de conclusão de curso de especialização apresentado ao Instituto de Ciências Básicas da Saúde da Universidade Federal do Rio Grande do Sul como requisito parcial para a obtenção do título de Especialista em Microbiologia Clínica.

Orientador: Prof. Dr. Valério Rodrigues Aquino

Porto Alegre

2023

de Paula, Josiane Fatima
COMPARAÇÃO DE DESEMPENHO ENTRE A METODOLOGIA ASPERGILLUS POR ENSAIO DE FLUXO LATERAL E ELISA PARA DETECTAR O ANTÍGENO GALACTOMANNAN NO DIAGNÓSTICO DE ASPERGILOSE INVASIVA / Josiane Fatima de Paula. -- 2023.
43 f.
Orientador: Valério Rodrigues Aquino.

Trabalho de conclusão de curso (Especialização) -- Universidade Federal do Rio Grande do Sul, Instituto de Ciências Básicas da Saúde, Especialização em Microbiologia Clínica, Porto Alegre, BR-RS, 2023.

1. Metodologia diagnóstica para Aspergilose Invasiva. 2. Antígeno Galactomannan. 3. Ensaio de Fluxo Lateral. 4. Elisa. I. Aquino, Valério Rodrigues, orient. II. Título.

RESUMO

A Aspergilose Invasiva (AI) é uma doença infecciosa oportunista, causada pelo fungo do gênero *Aspergilllus* spp., o qual acomete principalmente pacientes imunocomprometidos. É responsável por elevada taxa de morbimortalidade nesses indivíduos, se não for diagnosticada o mais breve possível. Por quanto, a capacidade de tratar essas infecções depende diretamente do diagnóstico precoce, bem como da identificação das espécies presentes em cada hospedeiro. Entretanto, os métodos diagnósticos clássicos estão longe de ser adequados. Visto que, requer testes invasivos em pacientes gravemente enfermos, o que muitas vezes é inviável. O desenvolvimento de ensaios para detectar os biomarcadores do antígeno Galactomannan (GM) de pacientes com risco de AI melhorou significativamente o manejo dela. No entanto, o teste convencional imunoenzimático tem um alto custo e tempo de resposta. Devido a esses fatores tem sido desenvolvido metodologias menos laboriosas, como o teste de Fluxo Lateral (LFA – GM) para o diagnóstico AI. Diante do exposto o objetivo do presente trabalho, com base na literatura, foi avaliar o desempenho da metodologia de Fluxo Lateral (LFA - GM) e comparar com o teste ELISA – GM, usualmente utilizado para detecção do antígeno Galactomannan e contrapor com dados analisados do laboratório de microbiologia do Hospital de Clínicas de Porto Alegre. Por conseguinte, a metodologia GM-LFA mostrou excelente desempenho para o diagnóstico de IA em pacientes pré-dispostos a doença e pode ser uma opção confiável em ambientes onde o teste ELISA - GM não é viável.

Palavras-chave: Galactomannan, Fluxo lateral, Aspegilose invasiva, ELISA GM.

ABSTRACT

Invasive Aspergillosis (IA) is an opportunistic infectious disease caused by the fungus of the genus Aspergilllus spp. It is responsible for a high rate of morbidity and mortality in these individuals, if not diagnosed as soon as possible. Therefore, the ability to treat these infections depends directly on early diagnosis, as well as on the identification of the species present in each host. However, classical diagnostic methods are far from adequate. Since it requires invasive testing in severely ill patients, this is often not feasible. The development of assays to detect the galactomannan (GM) antigen biomarkers of patients at risk of IA has significantly improved the management of IA. However, the conventional enzyme immunoassay has a high cost and turnaround time. Due to these factors less laborious methodologies have been developed, such as the Lateral Flow Assay (LFA-GM) for IA diagnosis. The objective of this study, based on the literature, was to evaluate the performance of the LFA-GM methodology and compare it with the ELISA-GM test usually used to detect the galactomannan antigen and compare it with data analyzed in the microbiology laboratory of the Hospital de Clínicas de Porto Alegre. Therefore, the GM-LFA methodology showed excellent performance for AI diagnosis in patients pre-disposed to the disease and may be a reliable option in settings where the ELISA - GM test is not feasible.

Keywords: Galactomannan, lateral flow, Invasive aspegillosis, GM ELISA.

SUMÁRIO

1 INTRODUÇÃO

A Aspergilose Invasiva (AI) é uma doença fúngica invasiva (DFI) causada por fungos filamentosos do gênero *Aspergillus* spp. que acomete principalmente pacientes imunocomprometidos, sendo o principal fator de risco é a neutropenia prolongada.[1]

A doença é causada pelo microrganismo do gênero Aspergillus, os quais são caracterizados como fungos filamentosos, hialinos, septados. Estão presentes no ambiente, no solo, onde há matéria orgânica em decomposição. Reproduzem-se assexuadamente através da produção de conídios, estruturas esféricas de camada externa hidrofóbica e tamanho relativamente pequeno com facilidade de dispersão no ar.[2] Estas estruturas são produzidas em grandes quantidades e os humanos podem inalar centenas destas diariamente. A infecção em humanos se inicia pelo trato respiratório, pela inalação dos seus esporos presentes no ar. Além disso, há evidencias que fatores relacionados ao clima favorece a permanência do fungo no local e a sua relação hospedeiro parasita.[3,4]

Este gênero apresenta mais de 250 espécies, divididos em subgêneros ou complexos de espécies, no entanto apenas algumas são patogênicas ao homem, em destaque: *Aspergillus fumigatus,* o qual é responsável pela maioria das infecções, seguido por *A. flavus, A. niger e A. terreus*, há ainda evidências de outras espécies, que também tem destaque em pacientes imunodeprimidos.[3,5]

Eles têm a capacidade de causar uma variedade de doenças aos humanos, variando desde alergias até formas mais graves e invasivas. Esta última é definida como Aspergilose Invasiva, sendo a mais grave a Aspergilose Pulmonar Invasiva (API), a qual está relacionada a elevada taxa de morbidade e a mortalidade, que varia de 70 a 90% nesses pacientes.[6] No entanto a sua a gravidade dependerá da resposta imunológica do indivíduo ao patógeno, visto que, ela afeta principalmente pacientes imunocomprometidos.[7]

A Aspergilose Invasiva acomete principalmente pacientes Hematológicos, pós transplantados halogênicos de células tronco, transplantados de órgãos sólidos, indivíduos com alguma patologia pré-existente, com tumores sólidos, distúrbios autoimunes, imunodeficiência congênita ou doenças pulmonares crônicas, assim como, aqueles em tratamento com imunossupressores ou quimioterápicos. Entretanto, há também relatos na literatura do acometimento de pessoas fora do grupo de risco, mas que estão gravemente enfermos, internados em unidade de terapia intensiva.[3,4,7]

Além disso, recentemente AI tem acometido e agravado o prognóstico de pacientes internados em centro de terapia intensiva com influenza grave e infecção por síndrome

respiratória aguda grave coronavírus 2 (SARS-CoV2). A mortalidade nesses indivíduos pode chegar a 50%.[8]

Por conseguinte, o prognóstico não favorável da API é consequência tanto da imunossupressão do paciente quanto da inexatidão do diagnóstico clínico, visto que, a doença não apresenta sinais e sintomas específicos. Logo, devido a esses fatores, ocorre um atraso no início do tratamento, o que resulta no agravamento do quadro ou até mesmo a morte do paciente. Portanto, o diagnóstico precoce e específico é um fator fundamental para a diminuição da mortalidade. No entanto, devido a limitação da identificação do fungo, existe uma busca constante de exames que possam indicar a presença de *Aspergillus* spp. no paciente imunodeprimido.[9]

Por quanto, a capacidade de tratar essas infecções depende diretamente do diagnóstico precoce, bem como da identificação das espécies presentes em cada hospedeiro.

1.1 DIAGNÓSTICO DA ASPERGILOSE INVASIVA E A DETECÇÃO DO ANTÍGENO GALACTOMANNAN (GM)

Em relação ao diagnóstico da Aspergilose Invasiva existe uma grande dificuldade para se chegar a um resultado específico e exato. Para o diagnóstico definitivo é necessário a visualização de elementos fúngicos nos tecidos obtidos por biópsia ou punção aspirativa com agulha do sítio de infecção, aliados com achados radiológicos e micológicos de evidência clínica.[10.11] No entanto, exames histológicos requerem procedimentos invasivos e frequentemente são excluídos, uma vez que os pacientes suspeitos são indivíduos imunodeprimidos, principalmente aqueles neutropênicos, os quais são submetidos a tratamentos quimioterápicos e aqueles pós transplantes de células tronco.[12,13]

Já a cultura a partir de amostras biológicas possui baixo valor preditivo positivo, visto que, nem sempre pode ser diferenciado se um resultado positivo é referente à doença invasiva, ou contaminação.[14] No entanto, novas abordagens diagnósticas têm se baseado na detecção de marcadores circulantes, antígenos ou constituintes da parede celular fúngica.

Estes biomarcadores foram incluídos como critério micológico em consenso sobre doenças fúngicas invasivas (DFI) elaborado pela European Organization for Research and Treatment of Cancer/ Invasive Fungal Infection Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG).[15] Este consenso foi projetado para pesquisa clínica e estudos epidemiológicos. Ademais, eles foram adotados por

agências reguladoras para avaliação de antifúngicos e para avaliação de testes diagnósticos, todavia essas definições não são indicadas para direcionar ou guiar o atendimento ao paciente.[16]

O consenso elaborado pelo EORTC/MSG propõe definições padronizadas para o diagnóstico da DFI baseadas em fatores do hospedeiro, critérios clínicos e evidência micológica, dos quais faz parte a detecção do antígeno Galactomannan (GM) em plasma e no líquido cefalorraquidiano como critério comprovado para o diagnóstico da Aspergilose Pulmonar Invasiva. Os níveis de probabilidade atribuídos são: DFI "comprovada", "provável" em pacientes com câncer e transplantados de células tronco hematopoiéticas ou transplantes de órgãos sólidos.[15]

O desenvolvimento de ensaios para detectar os biomarcadores de antígeno GM de pacientes com risco de AI melhorou significativamente o manejo dela. Ademais, estudos recentes apontaram que a negatividade persistente da reação em cadeia da polimerase (PCR de GM) e detecção do antígeno Galactomannan por ELISA (GM-ELISA) é suficiente para excluir a infecção e suspender ou interromper a terapia antifúngica sem afetar negativamente o prognóstico do paciente.[11] No entanto, para a realização da PCR-GM é necessário validação de ensaios e equipamentos de laboratório molecular, os quais estão disponíveis somente em grandes centros laboratoriais, assim como existe uma limitação da disponibilidade de testes GM-ELISA para pequenos centros diagnósticos.[17]

O diagnóstico definitivo é realizado através da combinação de achados clínicos, juntamente com métodos laboratoriais e estudos de imagem. Além disso, mesmo apresentando baixa sensibilidade e recuperação fúngica baixa, a cultura fúngica continua sendo o padrão-ouro diagnóstico e, se positiva, permite guiar a terapia através do teste de suscetibilidade, quando necessário.[18]

1.1.1 Detecção do antígeno Galactomannan por ELISA - GM ELISA

O Galactomannan (GM) é um heteropolissacarídeo termoestável que está presente na parede do *Aspergillus* spp. sendo liberada durante o crescimento da hifa e germinação de conídios no tecido que é infectado. A molécula imunogênica com sítios imunorreativos contém unidades de galactofuranose.[19,20] Cada espécie fúngica possui GM com propriedades químicas diferentes entre si. A GM é um biomarcador que contribui para diagnóstico da AI, uma vez que o antígeno é liberado na circulação sanguínea durante o crescimento das hifas nos tecidos do hospedeiro. Ainda, por ser hidrossolúvel, o antígeno pode ser encontrado em diferentes

amostras clínicas, como no soro, urina, líquido cefalorraquidiano e no lavado bronco alveolar (BALF).[11,20-22]

A metodologia mais utilizada é realizada por ensaios imunoenzimáticos do tipo Elisa sanduíche, no qual é utilizado o anticorpo monoclonal de rato EBA-2 dirigido contra Aspergillus galactomannan. O antígeno é ligado aos poços da microplaca, a qual é revestida com o anticorpo EBA-2, o resultado, então, pode ser detectado por uma reação colorimétrica medida por densidade óptica.[23]

O desempenho do teste apresenta sensibilidade e especificidade variada, a depender do tipo de amostra, no soro e no líquido do lavado brônquico alveolar.[24] No entanto, em amostras de lavado bronco alveolar mostrou sensibilidade e especificidade próximas de 95 %, o que sugere boa precisão diagnóstica.[8.23] Ademais, as diretrizes europeias recomendam, atualmente, o uso de Galactomannan no lavado brônquio alveolar como um critério micológico para diagnóstico da AI.[25]

Entretanto, o teste pode apresentar reações cruzadas com outros fungos, mesmo sendo específico para *Aspergillus spp*, essas reações podem ocorrer com os microorganismos da família Trichocomaceae, *Fusarium spp. e Histoplasma capsulatum*.[23]

Além disso, o teste GM possui algumas limitações, pois apesenta resultados falsos positivos em pacientes com infeções bacterianas, em tratamento com antibióticos B lactmâmicos, em transfusões de sangue, e Hemodiálise, já os resultados falsos negativos estão relacionados a profilaxia antifúngica e a doença não invasiva.[6,11,23]

A cinética de liberação da GM ainda não é bem conhecida, o que se sabe é que fatores como o estado imunológico do hospedeiro, sítio da infecção, fase de crescimento do fungo, podem influenciar na concentração de GM liberada. Assim, quanto mais GM é detectada no tecido infectado, maior é o crescimento fúngico, mesmo que o paciente não tenha sinais clínicos da infecção.[6]

1.1.2 Ensaio de Fluxo Lateral para detecção de Galactomannan - (GM-LFA)

O Ensaio de Fluxo Lateral Galactomanana (GM-LFA) é um teste imunocromatográfico sanduíche para a detecção qualitativa e quantitativa de *Aspergillus* spp. a partir de amostras de soro e BAL. A metodologia é semelhante ao teste de gravidez amplamente utilizado, eliminando a necessidade de equipamentos avançados de laboratório, pela simplicidade de uso, é conhecido como teste Point Of Care, ou popularmente: como teste rápido.[26-28]

O princípio metodológico do Fluxo Lateral utiliza anticorpo monoclonal específicos de GM conjugados com ouro nano coloidal, os quais se ligam aos epítopos do antígeno GM, se estiver presente na amostra, à medida que acontece a corrida nas duas zonas testes da tira por fluxo capilar, o resultado positivo resulta na formação de uma linha de teste visível. O controle do teste se dá pelos anticorpos conjugados com ouro que fluem junto com a amostra, os quais são capturados pelos anticorpos presentes na linha de controle.[29]

Para realizar o teste são necessários em média 300 µl amostra, BALF ou soro, a qual é pré tratada para que ocorra a ligação eficaz dos anticorpos de detecção. A amostra, então, é desnaturada por aquecimento para minimizar a interferência das proteínas presentes, assim como para liberar o GM para a detecção, em seguida é centrifugada e acrescentada ao tampão de corrida. Após o tratamento as tiras testes são inseridas nessa mistura, que após 30 minutos os resultados já podem ser interpretados manualmente, como também através de leitor digital, o qual fornece um valor quantitativo, que corresponde aos títulos de GM presente na amostra.[22]

O teste apresenta reação cruzada com a cultura positiva para outros fungos que produzem galactofuranose, como por exemplo *Paracoccidiodes brasiliensis, Coccidioides* spp*., Histoplasma* spp., *Fusarium* spp*. e Candida* spp., no entanto não está claro a relevância clínica e se é verídica essa reatividade ou se esses pacientes estão coinfectados com os fungos relacionados acima.[30]

Estudos recentes encontraram uma sensibilidade e especificidade do GM-LFA para AI comprovada ou provável variando de 80% a 90% na leitura visual, o que pode ser uma alternativa confiante ao ELISA-GM para confirmar ou excluir um diagnóstico de AI.[27] Ainda, quando testado em amostras de BALF mostrou-se mais sensível e específico do que a amostra sorológica.[17]

Além do mais, quando utilizado a leitura automatizada o teste apresentou boa acurácia diagnóstica e uma boa concordância ao teste ELISA -GM, visto que remove a subjetividade do operador, como também fornece um valor quantitativo, o que permite a comparação direta com o GM-ELISA, logo, pode ser usado com confiança para monitorar a resposta à terapia ou determinar prognóstico do paciente.[17,26]

O teste GM-LFA apresenta bom desempenho diagnóstico, além de ser rápido e de fácil manuseio, pode superar a limitação do tempo de realização do teste convencional GM-ELISA, o que pode facilitar ainda mais o diagnóstico de AI no local de atendimento. Como também, é clinicamente relevante para direcionar a terapia precoce do paciente, o que pode determinar um bom prognóstico.[8,18,20,26,27]

1.2 OBJETIVOS

1.2.1 Objetivo geral

O trabalho visa comparar duas metodologias para detecção de antígenos do *Aspergillus* spp. no diagnóstico de Aspergilose Invasiva: Galactomannan pelo método de Elisa (GM Elisa) e por imunocromatografia GM-LFA (Ensaio de Fluxo Lateral Galactomannan).

1.2.2 Objetivos específicos

a) Revisar a literatura sobre a Aspergilose Invasiva;
b) Avaliar o perfil de pacientes para os quais são solicitados os exames de Galactomana no HCPA;
c) Revisar a metodologia diagnóstica não cultural para Aspergilose Invasiva;
d) Comparar o método ELISA- GM com o GM Lateral Flow para o diagnóstico;
e) Avaliar o desempenho da metodologia GM-LFA.

3 CONCLUSÃO E PERSPECTIVAS

A metodologia de LFA mostra-se promissora para o diagnóstico da Aspergilose Invasiva, a fim de diminuir a dificuldade para o estabelecimento da doença, visto que, o diagnóstico definitivo é feito através de procedimentos invasivos, o que muitas vezes é limitante, devido ao perfil de pacientes acometidos. Além do mais, o teste padrão GM – ELISA é demorado e necessita de lotes de amostras para o ensaio diagnóstico, também como de laboriosos equipamentos de laboratório, o que dificulta o diagnóstico, e consequentemente, o início do tratamento ao paciente.

Diante do exposto faz-se necessária a abordagem de metodologias simples e rápidas para o diagnóstico da Aspergilose Invasiva e que possam detectar marcadores da doença antes das suas manifestações clínicas desta. Além disso, o diagnóstico rápido e preciso visa adequar o tratamento desses pacientes aumentando sua sobrevida.

Portanto, o presente trabalho conclui que o teste GM-LFA apresenta bom desempenho diagnóstico, além de ser rápido e de fácil manuseio, não só supera a limitação do tempo de realização do teste convencional GM-ELISA, como também pode facilitar ainda mais o diagnóstico de AI no local de atendimento, pois não necessita de grandes equipamentos laboratoriais. Além disso, o menor tempo do ensaio é clinicamente relevante para direcionar a terapia precoce do paciente, o que pode determinar um bom prognóstico.[8,18,20,26,27]

No entanto há poucos estudos que abordam outros pacientes, que não sejam hematológicos que foram submetidos ao diagnóstico pelas metodologias acima mencionadas, o que sugere a realização de outros estudos, com pacientes de outros grupos de risco à Aspergilose Invasiva.

REFERÊNCIAS

1. Blanchard E, Gabriel F, Jeanne-Leroyer C, Servant V, Dumas PY. Aspergillose pulmonaire invasive. Rev Mal Respir [Internet]. Fev 2018;35(2):171–87. Disponível em: https://doi.org/10.1016/j.rmr.2018.01.002.

2. Park SJ, Mehrad B. Innate Immunity to *Aspergillus* Species. Clin Microbiol Rev [Internet]. Out 2009 [citado 9 de março de 2023];22(4):535–51. Disponível em: https://doi.org/10.1128/CMR.00014-09.

3. Cadena J, Thompson GR, Patterson TF. Aspergillosis. Infect Dis Clin North Am [Internet]. Jun 2021 [citado 31 de janeiro de 2023];35(2):415–34. Disponível em: https://doi.org/10.1016/j.idc.2021.03.008.

4. Townsend L, Martin-Loeches I. Invasive Aspergillosis in the Intensive Care Unit. Diagnostics [Internet]. Nov 2022 [citado 9 de março de 2023];12(11):2712. Disponível em: https://doi.org/10.3390/diagnostics12112712.

5. Cadena J, Thompson GR, Patterson TF. Invasive Aspergillosis: Current Strategies for Diagnosis and Management. Infect Dis Clin North Am. Mar 2016;30(1):125–42. Disponível em: http://doi.org/10.1016/j.idc.2015.10.015.

6. Mesquita-Rocha S. Teste de galactomanana para o diagnóstico de aspergilose invasiva: uma revisão. R Inst Adolfo Lutz [Internet]. 2018 [citado 9 de março de 2023];e1749–e1749. Disponível em: http://www.ial.sp.gov.br/resources/insituto-adolfo-lutz/publicacoes/rial/10/rial77_completa/1749_final_05_12_2019.pdf.

7. Arastehfar A, Carvalho A, Houbraken J, Lombardi L, Garcia-Rubio R, Jenks JD, et al. Aspergillus fumigatus and aspergillosis: From basics to clinics. Stud Mycol [Internet]. Set 2021;100:100115. Disponível em: http://doi.org/10.1016/j.simyco.2021.100115.

8. Jenks JD, Nam HH, Hoenigl M. Invasive aspergillosis in critically ill patients: Review of definitions and diagnostic approaches. Mycoses [Internet]. Set 2021a [citado 9 de março de 2023];64(9):1002–14. Disponível em: https://doi.org/10.1111/myc.13274.

9. Bassetti M, Giacobbe DR, Grecchi C, Rebuffi C, Zuccaro V, Scudeller L, et al. Performance of existing definitions and tests for the diagnosis of invasive aspergillosis in critically ill, adult patients: A systematic review with qualitative evidence synthesis. J Infect. July 2020;81(1):131–46. Disponível em: http://doi.org/10.3390/jof7030176.

10. Metan G, Keklik M, Dinç G, Pala Ç, Yıldırım A, Saraymen B, et al. Performance of Galactomannan Antigen, Beta-d-Glucan, and Aspergillus-Lateral-Flow Device for the Diagnosis of Invasive Aspergillosis. Indian J Hematol Blood Transfus [Internet]. Mar 2017 [citado 9 de março de 2023];33(1):87–92. Disponível em: https://doi.org/10.1007/s12288-016-0653-3.

11. Jenks JD, Nam HH, Hoenigl M. Invasive aspergillosis in critically ill patients: Review of definitions and diagnostic approaches. Mycoses [Internet]. Set 2021b [citado 9 de março de 2023];64(9):1002–14. Disponível em: https://doi.org/10.1111/myc.13274.

12. Heldt S, Hoenigl M. Lateral Flow Assays for the Diagnosis of Invasive Aspergillosis: Current Status. Curr Fungal Infect Rep [Internet]. Jun 2017 [citado 9 de março de 2023];11(2):45–51. Disponível em: http://link.springer.com/10.1007/s12281-017-0275-8.

13. Tejerina EE, Abril E, Padilla R, Rodríguez Ruíz C, Ballen A, Frutos-Vivar F, et al. Invasive aspergillosis in critically ill patients: An autopsy study. Mycoses [Internet]. Ago 2019 [citado 31 de janeiro de 2023];62(8):673–9. Disponível em: https://doi.org/10.1111/myc.12927.

14. Aquino V. Aspergilose invasiva em pacientes com doença pulmonar obstrutiva crônica internados em unidade de terapia intensiva. [tese]. Porto Alegre: Universidade Federal do Rio Grande do Sul, 2011. Disponível em: https://lume.ufrgs.br/handle/10183/37498.

15. Donnelly JP, Chen SC, Kauffman CA, Steinbach WJ, Baddley JW, Verweij PE, et al. Revision and Update of the Consensus Definitions of Invasive Fungal Disease From the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. Clin Infect Dis [Internet]. Set 2020 [citado 3 de março de 2023];71(6):1367–76. Disponível em: https://doi.org/10.1093/cid/ciz1008

16. Sherif R, Segal BH. Pulmonary aspergillosis: clinical presentation, diagnostic tests, management and complications. Curr Opin Pulm Med. May 2010;16(3):242–50. Disponível em: http://doi.org/10.1097/MCP.0b013e328337d6de.

17. White PL, Price JS, Posso R, Cutlan-Vaughan M, Vale L, Backx M. Evaluation of the Performance of the IMMY sona *Aspergillus* Galactomannan Lateral Flow Assay When Testing Serum To Aid in Diagnosis of Invasive Aspergillosis. Hanson KE, organizador. J Clin Microbiol [Internet]. May 2020 [citado 31 de janeiro de 2023];58(6):e00053-20. Disponível em: https://doi.org/10.1128/JCM.00053-20.

18. Jani K, McMillen T, Morjaria S, Babady NE. Performance of the sōna *Aspergillus* Galactomannan Lateral Flow Assay in a Cancer Patient Population. Hanson KE, organizador. J Clin Microbiol [Internet]. Ago 2021 [citado 31 de janeiro de 2023];59(9):e00598-21. Disponível em: https://doi.org/10.1128/JCM.00598-21.

19. Duarte RF, Sánchez-Ortega I, Cuesta I, Arnan M, Patiño B, Fernández de Sevilla A, et al. Serum galactomannan-based early detection of invasive aspergillosis in hematology patients receiving effective antimold prophylaxis. Clin Infect Dis Off Publ Infect Dis Soc Am. Dez 2014;59(12):1696–702. Disponível em: http://doi.org/10.1093/cid/ciu673.

20. Jenks JD, Mehta SR, Taplitz R, Law N, Reed SL, Hoenigl M. Bronchoalveolar lavage Aspergillus Galactomannan lateral flow assay versus Aspergillus-specific lateral flow device test for diagnosis of invasive pulmonary Aspergillosis in patients with hematological

malignancies. J Infect [Internet]. Mar 2019 [citado 31 de janeiro de 2023];78(3):249–59. Disponível em: https://doi.org/10.1016/j.jinf.2018.10.014.

21. Sales M da PU. Capítulo 5 - Aspergilose: do diagnóstico ao tratamento. J Bras Pneumol [Internet]. Dez 2009 [citado 9 de março de 2023];35:1238–44. Disponível em: https://doi.org/10.1590/S1806-37132009001200012.

22. Jenks JD, Miceli MH, Prattes J, Mercier T, Hoenigl M. The Aspergillus Lateral Flow Assay for the Diagnosis of Invasive Aspergillosis: an Update. Curr Fungal Infect Rep [Internet]. Dez 2020a [citado 31 de janeiro de 2023];14(4):378–83. Disponível em: https://doi.org/10.1007/s12281-020-00409-z.

23. Lamoth F. Galactomannan and 1,3-β-d-Glucan Testing for the Diagnosis of Invasive Aspergillosis. J Fungi [Internet]. July 2016 [citado 9 de março de 2023];2(3):22. Disponível em: https://doi.org/10.3390/jof2030022.

24. Takazono T, Izumikawa K. Recent Advances in Diagnosing Chronic Pulmonary Aspergillosis. Front Microbiol [Internet]. Ago 2018 [citado 9 de março de 2023];9:1810. Disponível em: http://doi.org/10.3389/fmicb.2018.01810.

25. Imbert S, Meyer I, Palous M, Brossas JY, Uzunov M, Touafek F, et al. Aspergillus PCR in Bronchoalveolar Lavage Fluid for the Diagnosis and Prognosis of Aspergillosis in Patients With Hematological and Non-hematological Conditions. Front Microbiol [Internet]. 2018 [citado 9 de março de 2023];9. Disponível em: http://doi.org/0.3389/fmicb.2018.01877.

26. Autier B, Prattes J, White PL, Valerio M, Machado M, Price J, et al. Aspergillus Lateral Flow Assay with Digital Reader for the Diagnosis of COVID-19-Associated Pulmonary Aspergillosis (CAPA): a Multicenter Study. Hanson KE, organizador. J Clin Microbiol [Internet]. Jan 2022 [citado 31 de janeiro de 2023];60(1):e01689-21. Disponível em: https://journals.asm.org/doi/10.1128/JCM.01689-21.

27. Jenks JD, Miceli MH, Prattes J, Mercier T, Hoenigl M. The Aspergillus Lateral Flow Assay for the Diagnosis of Invasive Aspergillosis: an Update. Curr Fungal Infect Rep [Internet]. Dez 2020b [citado 31 de janeiro de 2023];14(4):378–83. Disponível em: https://doi.org/10.1007/s12281-020-00409-z.

28. Sabino R, Veríssimo C. Novel Clinical and Laboratorial Challenges in Aspergillosis. Microorganisms [Internet]. Jan 2022 [citado 9 de março de 2023];10(2):259. Disponível em: https://doi.org/10.3390/microorganisms10020259.

29. Scharmann U, Verhasselt HL, Kirchhoff L, Buer J, Rath P, Steinmann J, et al. Evaluation of two lateral flow assays in BAL fluids for the detection of invasive pulmonary aspergillosis: A retrospective two-centre study. Mycoses [Internet]. Dez 2020 [citado 31 de janeiro de 2023];63(12):1362–7. Disponível em: https://doi.org/10.1111/myc.13176.

30. Lass-Flörl C, Lo Cascio G, Nucci M, Camargo dos Santos M, Colombo AL, Vossen M, et al. Respiratory specimens and the diagnostic accuracy of Aspergillus lateral flow assays

(LFA-IMMY^{TM}): real-life data from a multicentre study. Clin Microbiol Infect [Internet]. Dez 2019 [citado 9 de março de 2023];25(12):1563.e1-1563.e3. Disponível em: https://doi.org/10.1016/j.cmi.2019.08.009.

ANEXO A – NORMAS DE PUBLICAÇÃO DO BRAZILIAN JOURNAL OF INFECTIOUS DISEASES

ELSEVIER

THE BRAZILIAN JOURNAL OF INFECTIOUS DISEASES

Official publication of the Brazilian Society of Infectious Diseases

AUTHOR INFORMATION PACK

TABLE OF CONTENTS

ISSN: 1413-8670

DESCRIPTION

The Brazilian Journal of Infectious Diseases is the official publication of the Brazilian Society of Infectious Diseases (SBI). It aims to publish relevant articles in the broadest sense on all aspects of microbiology, infectious diseases and immune response to infectious agents.

The *BJID* is a bimonthly publication and one of the most influential journals in its field in Brazil and Latin America with a high impact factor, since its inception it has garnered a growing share of the publishing market.

AUDIENCE

Infectious Disease specialists

IMPACT FACTOR

2019: 1.971 © Clarivate Analytics Journal Citation Reports 2020

ABSTRACTING AND INDEXING

Science Citation Index Expanded
Scopus
Directory of Open Access Journals (DOAJ)
PubMed/Medline
PubMed/Medline
SciELO - Scientific Electronic Library Online

EDITORIAL BOARD

Editor-in-Chief

Luciano Goldani, Department of Infectious Diseases, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil

Area of expertise: AIDS and Opportunistic Infections; Antifungicals; Infections by Paracoccidioides brasiliensis, Histoplasma, Cryptococcus, Rhodotorula, and Other Emerging Fungi

Associate Editors

Alberto Chebabo, Medical Division, Hospital Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil
Area of expertise: Hospital Infections; Microbiology; Bacterial and Viral Infections

Ana Gales, Department of Infectious Diseases, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil
Area of expertise: Antimicrobial Resistance

Angelica E. Miranda, Department of Social Medicine, Faculdade de Medicina, Universidade Federal do Espirito Santo, Vitória, ES, Brazil
Area of expertise: Infectious Diseases in Gynecology and Obstetrics; HIV and STI

Helio Sader, Department of Infectious Diseases, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil
Area of expertise: Clinical Microbiology Laboratory; Antimicrobial Resistance; Hospital Epidemiology; New Drug Development

Maria Cássia Mendes-Corrêa, Department of Infectious and Parasitic Diseases, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil
Area of expertise: Viral Hepatitis; Hospital Infections

Editorial Board

Adauto Castelo, Núcleo de Patologias Infecciosas da Gestação (NUPAIG), Faculdade de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil
Area of expertise: HIV/AIDS; Viral Hepatitis; HPV; Tuberculosis

Alberto Duarte, Department of Pathology, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil
Area of expertise: Experimental Immunomodulation; Immunopathology

Alessandro Pasqualotto, Department of Clinical Medicine, Faculdade de Medicina, Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, RS, Brazil
Area of expertise: Fungal infections

Alexandre Zavascki, Infectious Diseases Service, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil
Area of expertise: Antimicrobial Resistance, Hospital Infections

Aluisio Augusto Cotrim Segurado, Department of Infectious Diseases, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil
Area of expertise: Retrovirology; Tropical Medicine; Global Health

Andre Lyra, Department of Infectious Diseases, Faculdade de Medicina, Universidade Federal da Bahia, Salvador, BA, Brazil
Area of expertise: Hepatitis; Stem-cells; Advanced chronic Liver Disease

Antonio Barone, Department of Infectious Diseases, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil
Area of expertise: Tropical Medicine

Arnaldo Colombo, Department of Infectious Diseases, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil
Area of expertise: Clinical Mycology

Beatriz Grinsztein, Instituto Nacional de Infectologia Evandro Chagas, Instituto Oswaldo Cruz, Fundação Oswaldo Cruz, Rio de Janeiro, RJ, Brazil
Area of expertise: HIV/AIDS; STIs; Tuberculosis

Boris Renjifo, Division of Medical Sciences, T.H. Chan School of Public Health, Harvard University, Atlanta, GA, United States
Area of expertise: HIV/AIDS

Carlos Graeff-Teixeira, Department of Parasitology, Faculdade de Medicina, Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre, RS, Brazil
Area of expertise: Human Helminthology

Cristiana Carvalho, Department of Pediatrics, Faculdade de Medicina, Universidade Federal da Bahia, Salvador, BA, Brazil
Area of expertise: Pediatric Infectious Diseases; Mother and Child Health

Edgard Carvalho, Department of Parasitology, Faculdade de Medicina, Universidade Federal da Bahia, Salvador, BA, Brazil
Area of expertise:Immunology and Immunotherapy of Leishmaniasis; Allergy and Infections by Helminths; Immunopathogenesis of HIV Infection

Edson Duarte Moreira Junior, Department of Healthcare Biotechnology and Investigative Medicine, Instituto Gonçalo Moniz, Fundação Oswaldo Cruz, Rio de Janeiro, BA, Brazil
Area of expertise: HPV; Rotavirus; Antimicrobial Resistance; Leishmaniasis

Eduardo Gotuzzo, Department of Medicine, Institute of Tropical Medicine and Infectious Diseases, Universidad Peruana Cayetano Heredia, Lima, Peru
Area of expertise: Emerging diseases; TB; HTLV-1; Free-living Amoebas; Brucellosis; Typhoid Fever; Cholera; Leptospirosis; Parasites
Eduardo Netto, Laboratório de Pesquisa em Infectologia, Hospital Univ. Prof. Edgard Santos, Universidade Federal da Bahia, Salvador, BA, Brazil
Area of expertise: Infectious Diseases; Epidemiology
Eduardo Sprinz, Infectious Diseases Service, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil
Area of expertise: HIV/AIDS
Erico Arruda, Department of Infectious Diseases, Centro de Ciências da Saúde, Universidade Estadual do Ceará, Fortaleza, CE, Brazil
Area of expertise: HIV/AIDS
Esper Kallas, Department of Infectious Diseases, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil
Area of expertise: HIV/AIDS; Immunology of Infectious Diseases; Vaccines
Evaldo Araujo, Department of Infectious and Parasitic Diseases, Hospital das Clínicas, Universidade de São Paulo, São Paulo, SP, Brazil
Area of expertise: Viral Hepatitis; Hospital Infections; Public Health
Felipe Tuon, Department of Infectious Diseases, Faculdade de Medicina, Universidade Federal do Paraná, Curitiba, PR, Brazil
Area of expertise: Hospital Infections; Microbiology
Guido Levi, Department of Health, Comissão Permanente Assessora em Imunizações da Secretaria de Estado da Saúde de S. Paulo, Instituto de Infectologia Emílio Ribas, São Paulo, SP, Brazil
Area of expertise: Infectious Diseases; Vaccines
Jan Felix Drexler, Institute of Virology, University of Bonn Medical Centre, German Center for Infectious Diseases Research, Bonn, Germany
Area of expertise: Emerging Infections
Jeffrey Jon Shaw, Department of Infectious Diseases, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil
Area of expertise: Medical Entomology; Tropical Diseases
Jorge Pinto, Department of Pediatrics, Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil
Area of expertise: Mother-to-child Transmission of HIV; Primary Immunodeficiencies
Julio Croda, Department of Infectious Diseases, Faculdade de Medicina, Universidade Federal do Mato Grosso do Sul, Campo Grande, MS, Brazil
Area of expertise: TB in Populations Deprived of Liberty; Arbovirosis; COVID-19
Kleber Luz, Department of Infectious Diseases, Faculdade de Medicina, Universidade Federal do Rio Grande do Norte, Natal, RN, Brazil
Area of expertise: Tropical Diseases — Visceral Leishmaniasis, Dengue and Viral Hepatitis
Kleper Almeida, Infectious Diseases Division, JFK Medical Center, Palm Beach County, FL, United States
Area of expertise: General infectious Diseases; Transplant-related Infections; Cardiac Device-related Infections; Diagnostic Tests Evaluation
Marcelo Ferreira, Department of Infectious Diseases, Faculdade de Medicina, Universidade Federal de Uberlândia, Uberlândia, MG, Brazil
Area of expertise: HIV/AIDS
Maria Lima, Department of Infectious Diseases, Faculdade de Medicina, Pontifícia Universidade Católica de Campinas, Campinas, SP, Brazil
Area of expertise: Vertical Transmission of Infectious Diseases; Hospital Infections; Antiviral Therapy (HIV, HBV, and HCV)
Maria Yasuda, Department of Infectious Diseases, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil
Area of expertise: Paracoccidioidomycosis; Fungal Infections in Immunosuppressed Patients
Mauro Schechter, Department of Infectious Diseases, Faculdade de Medicina, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil
Area of expertise: HIV/AIDS; TB; Hepatitis
Mitermayer Galvão, Molecular Biology Laboratory, Instituto Gonçalo Muniz, Fundação Oswaldo Cruz, Salvador, BA, Brazil
Area of expertise: Pathology; Infectious and Parasitic Diseases; Tropical Medicine
Reinaldo Salomão, Department of Infectious Diseases, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil
Area of expertise: Pathogenesis of Infectious Diseases — Sepsis
Renato Grinbaum, Department of Infectious Diseases, Faculdade de Medicina, Universidade Cidade de São Paulo, São Paulo, SP, Brazil

Area of expertise: Hospital Infections; Antimicrobial Agents

Ricardo Diaz, Infectious Diseases Division, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, São Paulo, Brazil

Area of expertise: HIV/AIDS

Richard Guerrant, Division of Infectious Diseases & International Health, School of Medicine, University of Virginia, Charlottesville, VA, United States

Area of expertise: Recognition, Diagnosis, Pathogenesis, Impact, Treatment and Prevention of Enteric Infections; Global Health; Tropical Infectious Diseases

Robert Schooley, Division of Infectious Diseases & Global Public Health, School of Medicine, University of California, Oakland, CA, United States

Area of expertise: HIV/AIDS; Hepatitis

Roberto Focaccia, Department of Infectious Diseases, Postgraduate Coordination, Instituto de Infectologia Emílio Ribas, São Paulo, Brazil

Area of expertise: Viral Hepatitis, COVID-19

Sergio Cimerman, Department of Infectious Diseases, Hospital Emilio Ribas, Instituto de Infectologia Emílio Ribas, São Paulo, SP, Brazil

Area of expertise: HIV/AIDS; Intestinal Parasitosis

Sylvia L Hinrichsen, Department of Infectious Diseases, Faculdade de Medicina,, Recife, PE, Brazil

Area of expertise: Travel-associated Infections and Prevention

Zilton Andrade, Department of Infectious Diseases, Instituto Gonçalo Moniz, Fundação Oswaldo Cruz, Salvador, BA, Brazil

Area of expertise: Hepatic Fibrosis; Cirrhosis; Chagas Disease

GUIDE FOR AUTHORS

Introduction

The Brazilian Journal of Infectious Diseases is the official publication of the Brazilian Society of Infectious Diseases (SBI). It aims to publish relevant articles in the broadest sense on all aspects of microbiology, infectious diseases and immune response to infectious agents. The BJID is a bimonthly publication and one of the most influential journals in its field in Brazil and Latin America with a high impact factor, since its inception it has garnered a growing share of the publishing market.

The article publishing charge (APC) that authors, their institutions or funding bodies pay, covers all expenses needed to support the publication process.

For articles submitted from 16th July 2018, the APC to publish a paper in the Brazilian Journal of Infectious Diseases is USD 1,500 for original and review articles, and USD 600 for case reports, short communications and letters.

Once the manuscript has been approved, the corresponding author will receive the instructions for the payment of the publication fee.

Types of article

Manuscripts may be submitted within designated categories of communication, including:
- Original basic or clinical investigation (original papers);
- Brief reports of new methods or observations (brief communications);
- State-of-the-art presentations or reviews (review or mini review papers);
- Case presentation and discussion (case reports);
- Clinical infectious diseases images;
- Letters to the editor concerning previous publications;
- Editor's corner, containing ideas, hypotheses and comments (Editorial).

Original articles

It is the most important section of the Journal. Original articles present new data about researches, issues and matters in the field of infectious diseases. These articles should conform strictly to the rules of publication, containing the following sections: abstract, objective or hypothesis, experimental design and methods used (statistical data), essential features of any interventions, main outcome measures, main results of the study, discussion and conclusion. An Original Paper should contain:
- An abstract of no more than 300 words;
- No more than 7 keywords;
- The text should be divided into separate sections (Introduction, Material and Methods, Results, Discussion, References);
- No more than 50 references;
- Number of authors should not exceed 10;
- Authors should state in the cover letter that the manuscript is intended to be an original paper.

Brief communications

A brief communication is focused in a single subject, which should be concise and a new point of view presentation of the subject. The scope of this section is intended to be wide and methods, results and discussion should be in the same text. A brief communication should contain:
- An abstract of no more than 200 words;
- No more than 4 keywords;
- Text should not exceed 12 double-spaced typed pages of 23 lines each;
- A maximum of 2 figures or tables (or one of each);
- No more than 20 references;
- The text should not be divided into separate sections;
- Authors should state in the cover letter that the manuscript is intended to be a brief communication;
- Number of authors should not exceed 5.

Review article

This section is for an updated presentation on a specific topic. This section should contain critical analysis and a new point of view of a relevant area and not a chronological description of the literature. This section aims to raise discussion among readers about controversial issues and the development

of concepts in Infectious Diseases. A review article has to bring the new point of view of the focus of the subject. A minireview is focused on a restricted part of a subject. A minireview and review article should contain:
• An abstract of no more than 300 words;
• No more than 7 keywords;
• No more than 80 references;
• The text may be divided into sections with appropriate titles and subtitles;
• Number of authors should not exceed 5;
• Authors should state in the cover letter that the manuscript is intended to be a review or mini review article.

Case reports
Reports of clinical cases must contain a brief introduction about the nature of the case diagnosis, whose focus is the importance of the subject. The case has to be described with data and reports of examinations, treatment and prognosis of the case, discussion about the importance of the findings and presentation of the case in relation to literature. A case report should have a special interest to the clinical research community or it has to be a rare case; or to present a new diagnostic method; or new or modified treatment. A case report article should contain:
• An abstract of no more than 150 words;
• No more than 4 keywords;
• No more than 20 references;
• The text may be divided into sections: brief introduction with a review of literature, case reports, and conclusion;
• Number of authors should not exceed 5;
• Authors should state in the cover letter that the manuscript is intended to be a case report article.

Clinical infectious diseases images
For submission to Clinical Infectious Diseases Images, which is not intended as a vehicle for case reports, all text should contain:
• A minimum of references (no more than 4);
• No abstract;
• The text should be uniform and contain no more than 300 words;
• Number of authors should not exceed 5.

Letters to the editor
Letters may be written in response to previous content published in The Brazilian Journal of Infectious Diseases (BJID) or on any topic of general interest or concern. In the first case, the letter must emphasize the main message of the author of the article, focusing the contribution of that scientific article in the medical practice, drawing attention to the reference and impact it had on the community. The Letter to the Editor should contain:
• Title and the text with no more than 23 line pages;
• No more than 5 references;
• Number of authors should not exceed 5.

Contact details for submission
To submit an article to the journal: https://www.editorialmanager.com/bjid/default.aspx If you have problems with sending or reviewing manuscripts, please contact us by email (spanish-support@elsevier.com) or by phone (+34 932 406 176) Monday through Friday, from 9:30 to 18:00 (GMT +1).

Submission checklist
You can use this list to carry out a final check of your submission before you send it to the journal for review. Please check the relevant section in this Guide for Authors for more details.

Ensure that the following items are present:

One author has been designated as the corresponding author with contact details:
• E-mail address
• Full postal address

All necessary files have been uploaded:
Manuscript:

• Include keywords
• All figures (include relevant captions)
• All tables (including titles, description, footnotes)
• Ensure all figure and table citations in the text match the files provided
• Indicate clearly if color should be used for any figures in print
Graphical Abstracts / Highlights files (where applicable)
Supplemental files (where applicable)

Further considerations
• Manuscript has been 'spell checked' and 'grammar checked'
• All references mentioned in the Reference List are cited in the text, and vice versa
• Permission has been obtained for use of copyrighted material from other sources (including the Internet)
• A competing interests statement is provided, even if the authors have no competing interests to declare
• Journal policies detailed in this guide have been reviewed
• Referee suggestions and contact details provided, based on journal requirements

For further information, visit our Support Center.

BEFORE YOU BEGIN

Ethics in publishing

Please see our information pages on Ethics in publishing and Ethical guidelines for journal publication.

Studies in humans and animals

If the work involves the use of human subjects, the author should ensure that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The manuscript should be in line with the Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals and aim for the inclusion of representative human populations (sex, age and ethnicity) as per those recommendations. The terms sex and gender should be used correctly.

Authors should include a statement in the manuscript that informed consent was obtained for experimentation with human subjects. The privacy rights of human subjects must always be observed.

All animal experiments should comply with the ARRIVE guidelines and should be carried out in accordance with the U.K. Animals (Scientific Procedures) Act, 1986 and associated guidelines, EU Directive 2010/63/EU for animal experiments, or the National Institutes of Health guide for the care and use of Laboratory animals (NIH Publications No. 8023, revised 1978) and the authors should clearly indicate in the manuscript that such guidelines have been followed. The sex of animals must be indicated, and where appropriate, the influence (or association) of sex on the results of the study.

Declaration of interest

All authors must disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential competing interests include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding. Authors must disclose any interests in two places: 1. A summary declaration of interest statement in the title page file (if double-blind) or the manuscript file (if single-blind). If there are no interests to declare then please state this: 'Declarations of interest: none'. This summary statement will be ultimately published if the article is accepted. 2. Detailed disclosures as part of a separate Declaration of Interest form, which forms part of the journal's official records. It is important for potential interests to be declared in both places and that the information matches. More information.

Submission declaration and verification

Submission of an article implies that the work described has not been published previously (except in the form of an abstract, a published lecture or academic thesis, see 'Multiple, redundant or concurrent publication' for more information), that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in

English or in any other language, including electronically without the written consent of the copyright-holder. To verify originality, your article may be checked by the originality detection service Crossref Similarity Check.

Preprints
Please note that preprints can be shared anywhere at any time, in line with Elsevier's sharing policy. Sharing your preprints e.g. on a preprint server will not count as prior publication (see 'Multiple, redundant or concurrent publication' for more information).

Use of inclusive language

Inclusive language acknowledges diversity, conveys respect to all people, is sensitive to differences, and promotes equal opportunities. Content should make no assumptions about the beliefs or commitments of any reader; contain nothing which might imply that one individual is superior to another on the grounds of age, gender, race, ethnicity, culture, sexual orientation, disability or health condition; and use inclusive language throughout. Authors should ensure that writing is free from bias, stereotypes, slang, reference to dominant culture and/or cultural assumptions. We advise to seek gender neutrality by using plural nouns ("clinicians, patients/clients") as default/wherever possible to avoid using "he, she," or "he/she." We recommend avoiding the use of descriptors that refer to personal attributes such as age, gender, race, ethnicity, culture, sexual orientation, disability or health condition unless they are relevant and valid. These guidelines are meant as a point of reference to help identify appropriate language but are by no means exhaustive or definitive.

Changes to authorship

Authors are expected to consider carefully the list and order of authors **before** submitting their manuscript and provide the definitive list of authors at the time of the original submission. Any addition, deletion or rearrangement of author names in the authorship list should be made only **before** the manuscript has been accepted and only if approved by the journal Editor. To request such a change, the Editor must receive the following from the **corresponding author**: (a) the reason for the change in author list and (b) written confirmation (e-mail, letter) from all authors that they agree with the addition, removal or rearrangement. In the case of addition or removal of authors, this includes confirmation from the author being added or removed.
Only in exceptional circumstances will the Editor consider the addition, deletion or rearrangement of authors **after** the manuscript has been accepted. While the Editor considers the request, publication of the manuscript will be suspended. If the manuscript has already been published in an online issue, any requests approved by the Editor will result in a corrigendum.

Clinical trials registry

Clinical trials must be registered according to WHO recommendation at http://www.who.int/ictrp/en. The definition of clinical trial include preliminary trials (phase I): any study with prospective recruiting of subjects to undergo any health-related intervention (drugs, surgical procedures, equipment, behavioral therapies, food regimen, changes in health care) to evaluate the effects on clinical outcomes (any biomedical or health-related parameter, including pharmacokinetics measurements and adverse reactions).
The Journal has the right not to publish trials not complying with these and other legal and ethical standards determined by international guidelines.

Copyright

Upon acceptance of an article, authors will be asked to complete a 'Journal Publishing Agreement' to assign to the society the copyright in the manuscript and any tables, illustrations or other material submitted for publication as part of the manuscript (the "Article") in all forms and media (whether now known or later developed), throughout the world, in all languages, for the full term of copyright, effective when the Article is accepted for publication.

Author rights

As an author you (or your employer or institution) have certain rights to reuse your work. For more information on author rights please see https://www.elsevier.com/copyright.

Elsevier supports responsible sharing
Find out how you can share your research published in Elsevier journals.

Role of the funding source
You are requested to identify who provided financial support for the conduct of the research and/or preparation of the article and to briefly describe the role of the sponsor(s), if any, in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. If the funding source(s) had no such involvement then this should be stated.

Role of the Funding Source
Authors: please indicate any financial support in the cover letter.

Open access
Please visit our Open Access page for more information.

Language
Please write your text in good English (American or British usage is accepted, but not a mixture of these).

Informed consent and patient details
Studies on patients or volunteers require ethics committee approval and informed consent, which should be documented in the paper. Appropriate consents, permissions and releases must be obtained where an author wishes to include case details or other personal information or images of patients and any other individuals in an Elsevier publication. Written consents must be retained by the author but copies should not be provided to the journal. Only if specifically requested by the journal in exceptional circumstances (for example if a legal issue arises) the author must provide copies of the consents or evidence that such consents have been obtained. For more information, please review the Elsevier Policy on the Use of Images or Personal Information of Patients or other Individuals. Unless you have written permission from the patient (or, where applicable, the next of kin), the personal details of any patient included in any part of the article and in any supplementary materials (including all illustrations and videos) must be removed before submission.

Submission
Our online submission system guides you stepwise through the process of entering your article details and uploading your files. The system converts your article files to a single PDF file used in the peer-review process. Editable files (e.g., Word, LaTeX) are required to typeset your article for final publication. All correspondence, including notification of the Editor's decision and requests for revision, is sent by e-mail.

Submit your article
Please submit your article via https://www.editorialmanager.com/bjid/default.aspx.

Referees
Please submit the names and institutional e-mail addresses of several potential referees. For more details, visit our Support site. Note that the editor retains the sole right to decide whether or not the suggested reviewers are used.

Additional information
Additional information
All papers must be submitted in English.

PREPARATION

Peer review
This journal operates a double anonymized review process. All contributions will be initially assessed by the editor for suitability for the journal. Papers deemed suitable are then typically sent to a minimum of two independent expert reviewers to assess the scientific quality of the paper. The Editor is responsible for the final decision regarding acceptance or rejection of articles. The Editor's decision is final. Editors are not involved in decisions about papers which they have written themselves or have been written by family members or colleagues or which relate to products or services in which the editor has an interest. Any such submission is subject to all of the journal's usual procedures, with peer review handled independently of the relevant editor and their research groups. More information on types of peer review.

Double anonymized review

This journal uses double anonymized review, which means the identities of the authors are concealed from the reviewers, and vice versa. More information is available on our website. To facilitate this, please include the following separately:

Title page (with author details): This should include the title, authors' names, affiliations, acknowledgements and any Declaration of Interest statement, and a complete address for the corresponding author including an e-mail address.

Blinded manuscript (no author details): The main body of the paper (including the references, figures, tables and any acknowledgements) should not include any identifying information, such as the authors' names or affiliations.

Use of word processing software

It is important that the file be saved in the native format of the word processor used. The text should be in single-column format. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. In particular, do not use the word processor's options to justify text or to hyphenate words. However, do use bold face, italics, subscripts, superscripts etc. When preparing tables, if you are using a table grid, use only one grid for each individual table and not a grid for each row. If no grid is used, use tabs, not spaces, to align columns. The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the Guide to Publishing with Elsevier). Note that source files of figures, tables and text graphics will be required whether or not you embed your figures in the text. See also the section on Electronic artwork.

To avoid unnecessary errors you are strongly advised to use the 'spell-check' and 'grammar-check' functions of your word processor.

Article structure

Introduction

State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

Material and methods

- This section should be subdivided by short underscore headings referring to methods used;
- This section cannot contain figures or tables;
- The material and methods used must be carefully described to allow the study repetition and to determine if the results were possible and correct;
- Papers with statistical testing should state the name of the test, the name for each analysis, the comparisons of interest, a justification of that test, the alpha level for all tests, whether the tests were over two-tailes, and the actual p-value for each test;
- Data sets should be summarized with descriptive statistics, which should include then for each data set, a clearly labeled measure of centre (such as the mean or median), and a clearly labeled measure of variability (such as the standard deviation or range).

Theory/calculation

A Theory section should extend, not repeat, the background to the article already dealt with in the Introduction and lay the foundation for further work. In contrast, a Calculation section represents a practical development from a theoretical basis.

Results

Results should be clear and concise.

Discussion

The discussion presents the results comparing and evaluating them to literature and the existing knowledge. References to other studies should appear in the Discussion to compare the data obtained in the methods and results of the paper.

Conclusions

The main conclusions of the study may be presented in a short Conclusions section, which may stand alone or form a subsection of a Discussion or Results and Discussion section.

Appendices

If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations in appendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix, Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc.

Essential title page information

• ***Title.*** Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible.

• ***Author names and affiliations, including ORCID ID.*** Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author. Author affiliations should be presented in decreasing hierarchical order (e.g. Harvard University, Harvard Business School, Boston, USA) and should be written as established in its own language (e.g. Universite Paris-Sorbonne; Harvard University, Universidade de São Paulo). The **ORCID ID** of the corresponding author must be inserted in the submission system. If you don't have an ORCID ID, it can be registered at https://orcid.org/register.

• ***Corresponding author.*** Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. **Ensure that the e-mail address is given and that contact details are kept up to date by the corresponding author.**

• ***Present/permanent address.*** If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the work must be retained as the main, affiliation address. Superscript Arabic numerals are used for such footnotes.

Abstract

A concise and factual abstract is required. The abstract should state briefly the purpose of the research, the principal results and major conclusions. An abstract is often presented separately from the article, so it must be able to stand alone. For this reason, references should be avoided. Also, non-standard or uncommon abbreviations should be avoided, but if essential they must be defined at their first mention in the abstract itself.

Keywords

Immediately after the abstract, provide the keywords, avoiding general and plural terms and multiple concepts (avoid, for example, 'and', 'of'). Be sparing with abbreviations: only abbreviations firmly established in the field may be eligible. These keywords will be used for indexing purposes. Please consider the manuscript formats to verify the number of keywords.

Abbreviations

• Do not abbreviate institutions;

• Abbreviations must follow the format of the National Library of Medicine (USA) as in Index Medicus.

Acknowledgements

Collate acknowledgements in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.).

Formatting of funding sources

List funding sources in this standard way to facilitate compliance to funder's requirements:

Funding: This work was supported by the National Institutes of Health [grant numbers xxxx, yyyy]; the Bill & Melinda Gates Foundation, Seattle, WA [grant number zzzz]; and the United States Institutes of Peace [grant number aaaa].

It is not necessary to include detailed descriptions on the program or type of grants and awards. When funding is from a block grant or other resources available to a university, college, or other research institution, submit the name of the institute or organization that provided the funding.

If no funding has been provided for the research, please include the following sentence:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Units

Follow internationally accepted rules and conventions: use the international system of units (SI). If other units are mentioned, please give their equivalent in SI.

Math formulae
Please submit math equations as editable text and not as images. Present simple formulae in line with normal text where possible and use the solidus (/) instead of a horizontal line for small fractional terms, e.g., X/Y. In principle, variables are to be presented in italics. Powers of e are often more conveniently denoted by exp. Number consecutively any equations that have to be displayed separately from the text (if referred to explicitly in the text).

Footnotes
Footnotes should be used sparingly. Number them consecutively throughout the article. Many word processors can build footnotes into the text, and this feature may be used. Otherwise, please indicate the position of footnotes in the text and list the footnotes themselves separately at the end of the article. Do not include footnotes in the Reference list.

Artwork

Electronic artwork
General points
- Make sure you use uniform lettering and sizing of your original artwork.
- Embed the used fonts if the application provides that option.
- Aim to use the following fonts in your illustrations: Arial, Courier, Times New Roman, Symbol, or use fonts that look similar.
- Number the illustrations according to their sequence in the text.
- Use a logical naming convention for your artwork files.
- Provide captions to illustrations separately.
- Size the illustrations close to the desired dimensions of the published version.
- Submit each illustration as a separate file.
- Ensure that color images are accessible to all, including those with impaired color vision.

A detailed guide on electronic artwork is available.
You are urged to visit this site; some excerpts from the detailed information are given here.
Formats
If your electronic artwork is created in a Microsoft Office application (Word, PowerPoint, Excel) then please supply 'as is' in the native document format.
Regardless of the application used other than Microsoft Office, when your electronic artwork is finalized, please 'Save as' or convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):
EPS (or PDF): Vector drawings, embed all used fonts.
TIFF (or JPEG): Color or grayscale photographs (halftones), keep to a minimum of 300 dpi.
TIFF (or JPEG): Bitmapped (pure black & white pixels) line drawings, keep to a minimum of 1000 dpi.
TIFF (or JPEG): Combinations bitmapped line/half-tone (color or grayscale), keep to a minimum of 500 dpi.
Please do not:
- Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); these typically have a low number of pixels and limited set of colors;
- Supply files that are too low in resolution;
- Submit graphics that are disproportionately large for the content.

Color artwork
Please make sure that artwork files are in an acceptable format (TIFF (or JPEG), EPS (or PDF), or MS Office files) and with the correct resolution. If, together with your accepted article, you submit usable color figures then Elsevier will ensure, at no additional charge, that these figures will appear in color online (e.g., ScienceDirect and other sites) regardless of whether or not these illustrations are reproduced in color in the printed version. **For color reproduction in print, you will receive information regarding the costs from Elsevier after receipt of your accepted article.** Please indicate your preference for color: in print or online only. Further information on the preparation of electronic artwork.

Illustration services
Elsevier's Author Services offers Illustration Services to authors preparing to submit a manuscript but concerned about the quality of the images accompanying their article. Elsevier's expert illustrators can produce scientific, technical and medical-style images, as well as a full range of charts, tables and graphs. Image 'polishing' is also available, where our illustrators take your image(s) and improve them to a professional standard. Please visit the website to find out more.

Figure captions
Ensure that each illustration has a caption. Supply captions separately, not attached to the figure. A caption should comprise a brief title (**not** on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used.

Tables

- The data presented in this section have to be oriented by universal units;
- Tables should be clear enough to the readers do not need the text to understand them;
- Tables should be presented on separate pages, portrait orientation, and upright on the page;
- Tables should present a short one-line title in bold;
- Tables have to be numbered consecutively with Arabic numerals in the text;
- Symbols and abbreviations are defined immediately below the table;
- More information about the table should be below the symbols and abbreviations;
- If the table is from another source, the authors must indicate the source and send the permission to the Journal.

References

Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.

Reference links
Increased discoverability of research and high quality peer review are ensured by online links to the sources cited. In order to allow us to create links to abstracting and indexing services, such as Scopus, CrossRef and PubMed, please ensure that data provided in the references are correct. Please note that incorrect surnames, journal/book titles, publication year and pagination may prevent link creation. When copying references, please be careful as they may already contain errors. Use of the DOI is highly encouraged.

A DOI is guaranteed never to change, so you can use it as a permanent link to any electronic article. An example of a citation using DOI for an article not yet in an issue is: VanDecar J.C., Russo R.M., James D.E., Ambeh W.B., Franke M. (2003). Aseismic continuation of the Lesser Antilles slab beneath northeastern Venezuela. Journal of Geophysical Research, https://doi.org/10.1029/2001JB000884. Please note the format of such citations should be in the same style as all other references in the paper.

Web references
As a minimum, the full URL should be given and the date when the reference was last accessed. Any further information, if known (DOI, author names, dates, reference to a source publication, etc.), should also be given. Web references can be listed separately (e.g., after the reference list) under a different heading if desired, or can be included in the reference list.

Data references
This journal encourages you to cite underlying or relevant datasets in your manuscript by citing them in your text and including a data reference in your Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and global persistent identifier. Add [dataset] immediately before the reference so we can properly identify it as a data reference. The [dataset] identifier will not appear in your published article.

References in a special issue
Please ensure that the words 'this issue' are added to any references in the list (and any citations in the text) to other articles in the same Special Issue.

Reference management software
Most Elsevier journals have their reference template available in many of the most popular reference management software products. These include all products that support Citation Style Language styles, such as Mendeley. Using citation plug-ins from these products, authors only need to select the appropriate journal template when preparing their article, after which citations and bibliographies will be automatically formatted in the journal's style. If no template is yet available for this journal, please follow the format of the sample references and citations as shown in this Guide. If you use

reference management software, please ensure that you remove all field codes before submitting the electronic manuscript. More information on how to remove field codes from different reference management software.

If you manage your research with Mendeley Desktop, you can easily install the reference style for this journal by clicking the link below:
http://open.mendeley.com/use-citation-style/brazilian-journal-of-infectious-diseases
When preparing your manuscript, you will then be able to select this style using the Mendeley plug-ins for Microsoft Word or LibreOffice. For more information about the Citation Style Language, visit http://citationstyles.org.

Reference style
Please quote all the authors in works with until six authors; after six authors, quote the first three followed by the expression et al. Reference Manager or Endnote programs are strongly recommended for use adopting the "Vancouver" style.
Examples for reference citation are presented below. Authors should consult NLM's Citing Medicine for additional information on the reference formats.

Article
Turner SW, Young S, Goldblatt J, Landau LI, Le Souëf PN. Child hood asthma and increased airway responsiveness a relationship that begins in infancy. Am J Respir Crit Care Med. 2009;179:98-104.
Chang ML, Yang CW, Chen JC, et al. Disproportional exaggerated arpartate transaminase is a useful prognostic parameter in late leptospirosis. World J Gastroenterol. 2005;11:5553-6.

Book chapter
Taylor DM, Personnet J. Epidemiology and natural history of Helicobacter pylori infection. In: Blaser MJ, Smith PD, Ravdin J eds. Infections of the gastrointestinal tract. New York: Raven Press, 1994.

Book
Polak JM, Van Noordan S. An introduction to immunochemistry: current techniques and problems. Oxford, UK: Oxford University Press, 1987.

Abstract
Blatt SP, Butzin CA, Lucey DR, Melcher GP, Hendrix CR. Anergy status and CD4 CD29 memory T-cells predict progression to AIDS (abstract PoB 3480). In: Program and abstracts: VIII International Conference on AIDS (Amsterdam). Amsterdam: CONGREX Holland, 1992.

Journal abbreviations source
Journal names should be abbreviated according to the List of Title Word Abbreviations.

Video
Elsevier accepts video material and animation sequences to support and enhance your scientific research. Authors who have video or animation files that they wish to submit with their article are strongly encouraged to include links to these within the body of the article. This can be done in the same way as a figure or table by referring to the video or animation content and noting in the body text where it should be placed. All submitted files should be properly labeled so that they directly relate to the video file's content. In order to ensure that your video or animation material is directly usable, please provide the file in one of our recommended file formats with a preferred maximum size of 150 MB per file, 1 GB in total. Video and animation files supplied will be published online in the electronic version of your article in Elsevier Web products, including ScienceDirect. Please supply 'stills' with your files: you can choose any frame from the video or animation or make a separate image. These will be used instead of standard icons and will personalize the link to your video data. For more detailed instructions please visit our video instruction pages. Note: since video and animation cannot be embedded in the print version of the journal, please provide text for both the electronic and the print version for the portions of the article that refer to this content.

Supplementary material
Supplementary material such as applications, images and sound clips, can be published with your article to enhance it. Submitted supplementary items are published exactly as they are received (Excel or PowerPoint files will appear as such online). Please submit your material together with the article and supply a concise, descriptive caption for each supplementary file. If you wish to make changes to

supplementary material during any stage of the process, please make sure to provide an updated file. Do not annotate any corrections on a previous version. Please switch off the 'Track Changes' option in Microsoft Office files as these will appear in the published version.

Research data

This journal encourages and enables you to share data that supports your research publication where appropriate, and enables you to interlink the data with your published articles. Research data refers to the results of observations or experimentation that validate research findings. To facilitate reproducibility and data reuse, this journal also encourages you to share your software, code, models, algorithms, protocols, methods and other useful materials related to the project.

Below are a number of ways in which you can associate data with your article or make a statement about the availability of your data when submitting your manuscript. If you are sharing data in one of these ways, you are encouraged to cite the data in your manuscript and reference list. Please refer to the "References" section for more information about data citation. For more information on depositing, sharing and using research data and other relevant research materials, visit the research data page.

Data linking

If you have made your research data available in a data repository, you can link your article directly to the dataset. Elsevier collaborates with a number of repositories to link articles on ScienceDirect with relevant repositories, giving readers access to underlying data that gives them a better understanding of the research described.

There are different ways to link your datasets to your article. When available, you can directly link your dataset to your article by providing the relevant information in the submission system. For more information, visit the database linking page.

For supported data repositories a repository banner will automatically appear next to your published article on ScienceDirect.

In addition, you can link to relevant data or entities through identifiers within the text of your manuscript, using the following format: Database: xxxx (e.g., TAIR: AT1G01020; CCDC: 734053; PDB: 1XFN).

Mendeley Data

This journal supports Mendeley Data, enabling you to deposit any research data (including raw and processed data, video, code, software, algorithms, protocols, and methods) associated with your manuscript in a free-to-use, open access repository. During the submission process, after uploading your manuscript, you will have the opportunity to upload your relevant datasets directly to *Mendeley Data*. The datasets will be listed and directly accessible to readers next to your published article online.

For more information, visit the Mendeley Data for journals page.

Data statement

To foster transparency, we encourage you to state the availability of your data in your submission. This may be a requirement of your funding body or institution. If your data is unavailable to access or unsuitable to post, you will have the opportunity to indicate why during the submission process, for example by stating that the research data is confidential. The statement will appear with your published article on ScienceDirect. For more information, visit the Data Statement page.

AFTER ACCEPTANCE

Proofs

One set of page proofs (as PDF files) will be sent by e-mail to the corresponding author (if we do not have an e-mail address then paper proofs will be sent by post) or a link will be provided in the e-mail so that authors can download the files themselves. To ensure a fast publication process of the article, we kindly ask authors to provide us with their proof corrections within two days. Elsevier now provides authors with PDF proofs which can be annotated; for this you will need to download the free Adobe Reader, version 9 (or higher). Instructions on how to annotate PDF files will accompany the proofs (also given online). The exact system requirements are given at the Adobe site.
If you do not wish to use the PDF annotations function, you may list the corrections (including replies to the Query Form) and return them to Elsevier in an e-mail. Please list your corrections quoting line number. If, for any reason, this is not possible, then mark the corrections and any other comments

(including replies to the Query Form) on a printout of your proof and scan the pages and return via e-mail. Please use this proof only for checking the typesetting, editing, completeness and correctness of the text, tables and figures. Significant changes to the article as accepted for publication will only be considered at this stage with permission from the Editor. We will do everything possible to get your article published quickly and accurately. It is important to ensure that all corrections are sent back to us in one communication: please check carefully before replying, as inclusion of any subsequent corrections cannot be guaranteed. Proofreading is solely your responsibility.

AUTHOR INQUIRIES

Visit the Elsevier Support Center to find the answers you need. Here you will find everything from Frequently Asked Questions to ways to get in touch.
You can also check the status of your submitted article or find out when your accepted article will be published.

© Copyright 2018 Elsevier | https://www.elsevier.com