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**EDITORIAL**

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MGUS: Proposal for outpatient management

Savini P, Marano G, Lanzi A, Castagnari B, Musardo G, Molinari A, Cellini C, Stefanini GF

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AIM AND SCOPE *World Journal of Hematology* (*World J Hematol*, *WJH*, online ISSN 2218-6204, DOI: 10.5315) is a bimonthly peer-reviewed, online, open-access (OA), journal supported by an editorial board consisting of 102 experts in hematology from 26 countries.
The aim of *WJH* is to report rapidly new theories, methods and techniques for prevention, diagnosis, treatment, rehabilitation and nursing in the field of hematology. *WJH* covers experimental, clinical, oncological and transplant hematology, transfusion science, hemostasis and thrombosis, traditional medicine, integrated Chinese and Western medicine, evidence-based medicine, epidemiology and nursing. The journal also publishes original articles and reviews that report the results of applied and basic research in fields related to hematology, such as immunology, physiopathology, cell biology, pharmacology, medical genetics, and pharmacology of Chinese herbs.

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MGUS: Proposal for outpatient management

Paolo Savini, Giorgio Marano, Arianna Lanzi, Barbara Castagnari, Giuseppe Musardo, Annalia Molinari, Claudia Cellini, Giuseppe Francesco Stefanini

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< 10 g/L if IgA or IgM, without end-organ damage and without signs and symptoms of LPD. However, a hematological evaluation is recommended for patients with M-protein IgG > 15 g/L, or M-protein IgA > 10 g/L, or IgM > 10 g/L, or any M-protein with end-organ damage (not attributable to any others causes) or with signs and symptoms of LPD, or rapidly increasing M-protein (> 5 g/L per year).

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Key words: Monoclonal gammopathy; Multiple myeloma; Macroglobulinaemia; End-organ damage; Serum protein electrophoresis

Peer reviewer: Raymond HS Liang, Professor, Department of Medicine, Hong Kong Sanatorium and Hospital, 2 Village Road, Hong Kong, China

Abstract

The term monoclonal gammopathy of undetermined significance (MGUS) indicates the presence of a monoclonal protein (M-protein) without features of multiple myeloma, Waldenström's macroglobulinemia, primary amyloidosis or malignant lymphoproliferative disorders (LPD). While several guidelines on the treatment of LPD exist, many doubts and perplexities still exist on who should treat a MGUS, when and how. Even where MGUS does not require any therapy, the risk of progression to a LPD is 1% per year. This risk does not diminish over time and persists even in patients (pts) whose condition has remained stable for decades, and a prolonged follow up is, therefore, recommended. We met primary care doctors to share and agree on criteria for the management of outpatients with MGUS. Our aim is to draw up guidelines or, at least, suggestions that may help to determine which MGUS pts could be cared for by the primary care doctor and which should be followed by the hematologist. We suggest that once a MGUS is diagnosed, the primary care physician will attend patients with M-protein < 15 g/L if IgG and pts with M-protein

Savini P, Marano G, Lanzi A, Castagnari B, Musardo G, Molinari A, Cellini C, Stefanini GF. MGUS: Proposal for outpatient management. *World J Hematol* 2012; 1(2): 5-7 Available from: URL: <http://www.wjgnet.com/2218-6204/full/v1/i2/5.htm>
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MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE

The term monoclonal gammopathy of undetermined significance (MGUS) indicates the presence of a monoclonal protein (M-protein) without features of multiple myeloma (MM), Waldenström's macroglobulinemia, primary amyloidosis or other malignant lymphoproliferative disorder (LPD). The MGUS represents a large portion of the total M-protein. The overall prevalence of MGUS in people older than 50 years is 3.2% in a predominantly white population. The prevalence increases with age and in black people.

Even where MGUS does not require any therapy, the

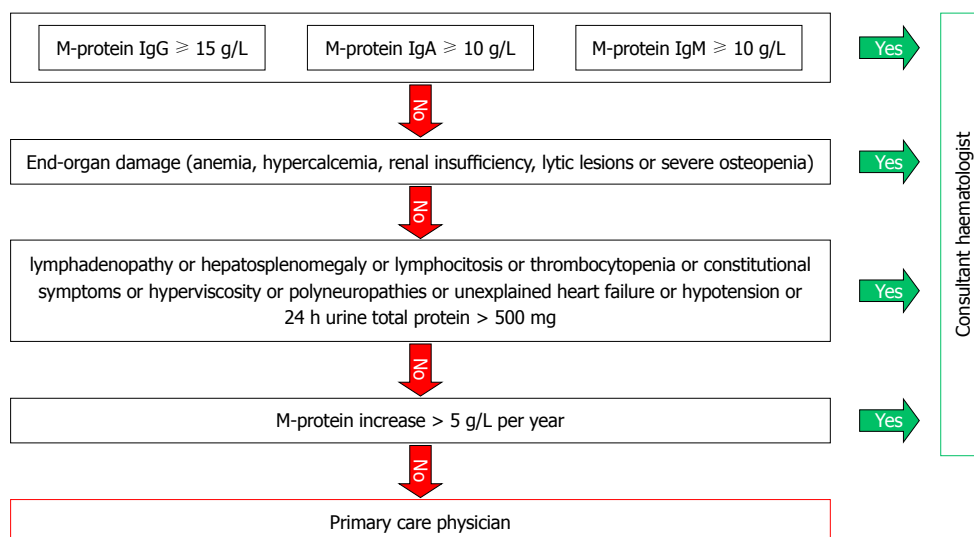


Figure 1 An easy reference guide for primary care physicians and other clinicians.

risk of progression to a LPD is 1% per year. This risk does not diminish over time and persists even in patients (pts) whose condition has remained stable for decades, and a prolonged follow up is, therefore, recommended^[1].

At the present there are no formal guidelines regarding follow-up for patients with MGUS. Clinical trials have provided very little evidence to inform the guidelines published; most of the recommendations are based on the outcomes of large observational studies and evidence from expert committee reports and/or clinical experiences of respected authorities and are therefore grade C, level IV^[2].

We met the primary care physicians to share criteria for classification and to agree on criteria for the management MGUS.

Our aim is to draw up guidelines or, at least, suggestions that may help to determine which MGUS pts could be cared for by the primary care doctor and which should be referred to the specialist.

MGUS is characterized by a serum M-protein < 30 g/L, plasma cells in the bone marrow < 10% and absence of end-organ damage: anemia (normochromic, normocytic with a haemoglobin value of > 2 g/dL below the lower limit of normal or a hemoglobin value < 10 g/dL), renal failure (creatinine > 2 mg/dL or estimated creatinine clearance < 40 mL/min), hypercalcemia (serum calcium > 11.5 mg/dL), bone lesions (lytic lesions or osteoporosis with compression fractures)^[3].

Agarose gel serum protein electrophoresis and immunofixation allow detection, quantification and to typing of the M-protein.

Once M-protein is detected the primary care physician needs full blood count, serum creatinine, serum calcium, 24 h urine total protein (easily quantifiable, can reveal a nephrosic syndrome, due to myeloma or amyloidosis, unlike Bence Jones proteinuria that does not predict progression).

Clinical attention should be addressed to the pres-

ence of constitutional symptoms (night sweats, fever, and weight loss), bone pain, lymphadenopathy and splenomegaly.

At this point β -2 microglobulin, serum quantitative immunoglobulins, urine protein electrophoresis, Bence Jones proteinuria are not necessary.

In the absence of end-organ damage, and with M-protein < 30 g/L, MGUS can be discriminated from asymptomatic myeloma only with bone marrow biopsy. In any case, since the latter does not require any therapy, this discrimination is not essential.

Once a MGUS is diagnosed the primary care physician will attend patients with M-protein < 15 g/L if IgG and pts with M-protein < 10 g/L if IgA or IgM, without end-organ damage and without signs and symptoms of LPD (lymphocytosis, thrombocytopenia, lymphadenopathy, hepatosplenomegaly, constitutional symptoms, hyperviscosity, unexplained heart failure, polyneuropathy).

Six-month follow-up testing is suggested. This should include full blood count, serum creatinine, serum calcium, serum protein electrophoresis and 24 h urine total protein.

However, hematological evaluation is recommended for patients with M-protein IgG > 15 g/L, or M-protein IgA > 10 g/L, or IgM > 10 g/L, or any M-protein with end-organ damage (not attributable to any others causes) or with signs and symptoms of LPD, or showing rapid increase in M-protein (> 5 g/L per year).

DISCUSSION

Prediction of which MGUS will remain stable and which will progress to LPD is very difficult at the time of diagnosis of MGUS. Risk factors for transformation of MGUS to malignant conditions have been addressed in several studies. A major shortcoming of most of these studies has been their relative small size and the inclusion of patients who today would be classified as asymptomatic MM. The data are conflicting but the initial con-

centration of M-protein^[4,5] and the type of M-protein, IgA or IgM, are consistent risk factors for progression^[5-7].

In other hand, the risk of progression in patients with abnormal free light chain ratio was found to be significantly higher than in patients with a normal ratio, and was independent of the size and the type of serum M-protein so the authors proposed a risk stratification model based on concentration of the serum M-protein, the type of immunoglobulin and the presence of an abnormal free light chain ratio^[4]. However these findings need to be confirmed by other studies before this model can be recommended for all the patients.

The risk of progression to LPD does not diminish over time and persists even in patients whose condition has remained stable for decades, so a prolonged follow up is recommended. There is no published evidence on which to base recommendations for the frequency of follow-up so guidance is, of necessity, pragmatic.

Even if a patient is seen by the physician at 3-monthly or even shorter intervals, symptoms may rapidly develop in the meantime. The patient is the best person to be aware of the onset of relevant symptoms. It is essential therefore that patients are fully aware of important symptoms and they should encouraged to report these if they occur outside appointment visits.

These recommendations have been summarised in an algorithm (Figure 1) intended as an easy reference guide for primary care physicians and other clinicians to use when deciding whether referral to a consultant haematologist is necessary.

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Events Calendar 2012

March 18-19, 2013

3rd Annual International Conference on Advances in Biotechnology (BioTech 2013)
Singapore

April 23-26, 2012

The 11th International Jordanian Conference in Internal Medicine
Amman, Jordan

April 25-28, 2012

34th World Congress Of The International Society Of Hematology 2012
Quintana Roo, Mexico

May 8-11, 2013

12th International Symposium on Myelodysplastic Syndrome
Berlin, Germany

May 9-12, 2012

American Society of Pediatric Hematology/oncology 25th Annual Meeting 2012
New Orleans, United States

June 27-30, 2012

SSC 2012 - 58th Scientific and Standardization Committee meeting of the ISTH
Liverpool, United Kingdom

June 28-30, 2012

MASCC/ISOO 2012 - International Symposium--International Symposium on Supportive Care in Cancer
New York, NY, United States

August 8-10, 2012

Coagulation Testing Quality Conference and Wet Workshop
Rochester, MI, United States

August 23-26, 2012

ISEH - Society for Hematology and Stem Cells Annual Scientific Meeting
41st Annual Scientific Meeting
Amsterdam, Netherlands

September 6-8, 2012

COHEM - The 2nd World Congress on Controversies in Hematology
Barcelona, Spain



GENERAL INFORMATION

World Journal of Hematology (*World J Hematol*, *WJH*, online ISSN 2218-6204, DOI: 10.5315) is a bimonthly peer-reviewed, online, open-access (OA), journal supported by an editorial board consisting of 102 experts in hematology from 26 countries.

The biggest advantage of the OA model is that it provides free, full-text articles in PDF and other formats for experts and the public without registration, which eliminates the obstacle that traditional journals possess and usually delays the speed of the propagation and communication of scientific research results. The open access model has been proven to be a true approach that may achieve the ultimate goal of the journals, i.e. the maximization of the value to the readers, authors and society.

Maximization of personal benefits

The role of academic journals is to exhibit the scientific levels of a country, a university, a center, a department, and even a scientist, and build an important bridge for communication between scientists and the public. As we all know, the significance of the publication of scientific articles lies not only in disseminating and communicating innovative scientific achievements and academic views, as well as promoting the application of scientific achievements, but also in formally recognizing the "priority" and "copyright" of innovative achievements published, as well as evaluating research performance and academic levels. So, to realize these desired attributes of *WJH* and create a well-recognized journal, the following four types of personal benefits should be maximized. The maximization of personal benefits refers to the pursuit of the maximum personal benefits in a well-considered optimal manner without violation of the laws, ethical rules and the benefits of others. (1) Maximization of the benefits of editorial board members: The primary task of editorial board members is to give a peer review of an unpublished scientific article *via* online office system to evaluate its innovativeness, scientific and practical values and determine whether it should be published or not. During peer review, editorial board members can also obtain cutting-edge information in that field at first hand. As leaders in their field, they have priority to be invited to write articles and publish commentary articles. We will put peer reviewers' names and affiliations along with the article they reviewed in the journal to acknowledge their contribution; (2) Maximization of the benefits of authors: Since *WJH* is an OA journal, readers around the world can immediately download and read, free of charge, high-quality, peer-reviewed articles from *WJH* official website, thereby realizing the goals and significance of the communication between authors and peers as well as public reading; (3) Maximization of the benefits of readers: Readers can read or use, free of charge, high-quality peer-reviewed articles without any limits, and cite the arguments, viewpoints, concepts, theories, methods, results, conclusion or facts and data of pertinent literature so as to validate the innovativeness, scientific and practical values of their own research achievements, thus ensuring that their articles have novel arguments or viewpoints, solid evidence and correct conclusion; and (4) Maximization of the benefits of employees: It is an iron law that a first-class journal is unable to exist without first-class editors, and only first-class editors can create a first-class academic journal. We insist on strengthening our team cultivation and construction so that every employee, in an open, fair and transparent environment, could contribute their wis-

dom to edit and publish high-quality articles, thereby realizing the maximization of the personal benefits of editorial board members, authors and readers, and yielding the greatest social and economic benefits.

Aims and scope

The aim of *WJH* is to report rapidly new theories, methods and techniques for prevention, diagnosis, treatment, rehabilitation and nursing in the field of hematology. *WJH* covers experimental, clinical, oncological and transplant hematology, transfusion science, hemostasis and thrombosis, traditional medicine, integrated Chinese and Western medicine, evidence-based medicine, epidemiology and nursing. The journal also publishes original articles and reviews that report the results of applied and basic research in fields related to hematology, such as immunology, physiopathology, cell biology, pharmacology, medical genetics, and pharmacology of Chinese herbs.

Columns

The columns in the issues of *WJH* will include: (1) Editorial: To introduce and comment on the substantial advance and its importance in the fast-developing areas; (2) Frontier: To review the most representative achievements and comment on the current research status in the important fields, and propose directions for the future research; (3) Topic Highlight: This column consists of three formats, including (A) 10 invited review articles on a hot topic, (B) a commentary on common issues of this hot topic, and (C) a commentary on the 10 individual articles; (4) Observation: To update the development of old and new questions, highlight unsolved problems, and provide strategies on how to solve the questions; (5) Guidelines for Clinical Practice: To provide guidelines for clinical diagnosis and treatment; (6) Review: To systemically review the most representative progress and unsolved problems in the major scientific disciplines, comment on the current research status, and make suggestions on the future work; (7) Original Articles: To originally report the innovative and valuable findings in hematology; (8) Brief Articles: To briefly report the novel and innovative findings in hematology; (9) Case Report: To report a rare or typical case; (10) Letters to the Editor: To discuss and make reply to the contributions published in *WJH*, or to introduce and comment on a controversial issue of general interest; (11) Book Reviews: To introduce and comment on quality monographs of hematology; and (12) Guidelines: To introduce consensus and guidelines reached by international and national academic authorities worldwide on the research in hematology.

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- 3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA*

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- 4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 PMCID:2516377 DOI:10.1161/01.HYP.00000035706.28494.09]

Both personal authors and an organization as author

- 5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

No author given

- 6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

Volume with supplement

- 7 **Geraud G**, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002; **42** Suppl 2: S93-99 [PMID: 12028325 DOI:10.1046/j.1526-4610.42.s2.7.x]

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No volume or issue

- 9 Outreach: Bringing HIV-positive individuals into care. *HRS: A Careaction* 2002; 1-6 [PMID: 12154804]

Books

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- 10 **Sherlock S**, Dooley J. Diseases of the liver and biliary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

Chapter in a book (list all authors)

- 11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

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- 12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wiczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

Conference proceedings

- 13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

Conference paper

- 14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

Electronic journal (list all authors)

- 15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: <http://www.cdc.gov/ncidod/eid/index.htm>

Patent (list all authors)

- 16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

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Write as mean \pm SD or mean \pm SE.

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