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# On the path to evidence-based reporting of serum protein electrophoresis patterns in the absence of a discernible monoclonal protein – A critical review of literature and practice suggestions

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## 1. Introduction

Serum protein electrophoresis (SPE) is a commonly deployed clinical laboratory technique that separates serum proteins into 5 or 6 major fractions or zones (Fig. 1), and is used primarily to detect and quantify monoclonal immunoglobulin(s) or its components (M-protein). However, the reporting of serum protein patterns with narrative comments pertaining to pattern-implied and presumed clinical conditions that may or may not be related to monoclonal gammopathy (MG), particularly in the absence of a discernible M-protein, is controversial. A recent Canada-wide practice survey [1] sanctioned by the Monoclonal Gammopathy Interest Group (MGIG) of the Canadian Society of Clinical Chemists showed that the SPE reporting practice remained highly variable, despite the availability of instructional monographs [2–5] and general guidelines [6,7]. These guiding documents are, unfortunately, mostly opinion-based and do not provide the necessary framework for developing a unified reporting practice. The MGIG believes that the move towards evidence-based reporting is a critical step towards practice standardization and harmonization. Thus, a working group of the MGIG led by the authors sought evidence to support these SPE reporting practices through literature search, laboratory audits and practice reviews. The current report summarizes findings of this working group so far and reflects the Canadian perspective on the reporting of SPE patterns in the absence of a readily discernible M-protein.

## 2. Preamble

### 2.1. SPE report components

As laboratories may serve different patient populations and choose to provide different information in a patient report depending on local needs and preferences e.g. comment only when M-protein is detected, the breadth and depth of information contained in an SPE report can vary significantly [1]. In this report, we assume the following components are present in an SPE patient report (Fig. 1 C):

(i) The amount of protein represented in each of the 5 or 6 SPE fractions and their corresponding reference intervals (RIs);
(ii) An independently reported estimate of M-protein concentration(s), if present; and
(iii) A narrative comment to aid interpretation where applicable.

*Abbreviations:* MG, Monoclonal gammopathy; M-protein, Monoclonal immunoglobulin protein; IFE, Immunofixation electrophoresis; AGE, Agarose gel electrophoresis; CZE, Capillary zone electrophoresis; RI, Reference interval; CI, Confidence interval; A1AT, Alpha1 antitrypsin; A1AG, Alpha1 acid glycoprotein; SPE, Serum protein electrophoresis; Alb, Albumin; A1G, Alpha1 globulin; A2G, Alpha2 globulin; BG, Beta globulin; B1G, Beta1 globulin; B2G, Beta2 globulin; GG, Gamma globulin; ↓, decreases; ↑, increases; MGIG, Monoclonal Gammopathy Interest Group, Canadian Society of Clinical Chemists

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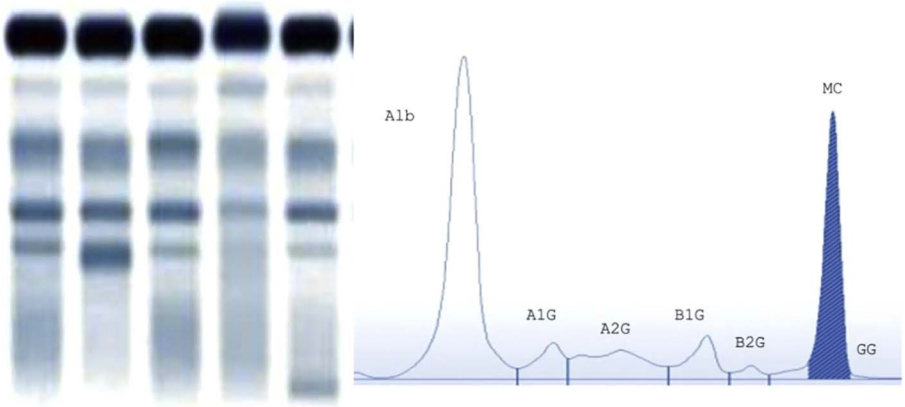
**(A) AGE of SPE**

**(B) Electrophoretogram showing 6 fractions**

M-protein is labeled "MC" and is included in the gamma "GG" fraction.




**(C) A typical SPE patient report**

| Fraction | g/L | Ref. Interval g/L |
|---|---|---|
| **Albumin** | **35** | **34-53** |
| **Alpha1 globulin** | **4** | **2-4** |
| **Alpha2 globulin** | **7** | **4-9** |
| **Beta1 globulin** | **4** | **3-6** |
| **Beta2 globulin** | **1** | **2-5** |
| **Gamma globulin** | **34** | **7-17** |
| **M-protein** | **30** | |
| **Comment: A discrete band in gamma region. IFE recommended.** | | |

**Fig. 1.** (A) Image of an agarose gel SPE with each lane representing a serum sample, (B) SPE tracing of one lane/sample showing 6 protein fractions, and (C) the fraction values and corresponding reference intervals, an estimated M-protein concentration and a narrative comment. Note that both (A) and (B) are generally not included in an SPE patient report although exceptions exist.

### *2.2. Considerations for interpretive commenting*

An SPE narrative text comment is no different from any other interpretative comment appearing on clinical laboratory reports. These interpretive comments should be concise, relevant and provide additional information or emphasis that is not already conveyed by numeric results on the same report. Particular attention should be paid to the clinical utility of the information conveyed, and how it might be interpreted and acted upon. General considerations and guidance in best practice for providing interpretative comments have been discussed elsewhere [8,9] and may include considerations of, but not limited to, the following:

(i) Utility in aiding diagnosis, management and/or further investigation;
(ii) Accuracy and added clinical value;
(iii) Relevance to the investigation and clinical context;
(iv) Use of precise, unambiguous and simple-to-understand language;
(v) Recipient-oriented e.g. primary and tertiary care physicians may expect different amount of information;
(vi) Restating the clinical question and obvious findings already contained elsewhere in the report unnecessarily;
(vii) Avoidance of instructing physicians how to do his/her job or suggest invasive investigations without due consideration of the complete clinical picture;
(viii) Avoidance of extensive listing of diagnostic and management possibilities.

### *2.3. Use of SPE*

An SPE narrative comment should be user/recipient-oriented and relevant to its use in the particular clinical investigation. For example, in a follow-up investigation of a known M-protein, the focus should be placed on the concentration of, and perhaps, the change in amount or isotype of the M-protein. If the estimation of the M-protein concentration is significantly confounded by background proteins, the increased measurement uncertainty should be highlighted in the narrative comment. The reporting of other SPE patterns for the sake of improving M-protein detection e.g. increased beta fraction may become irrelevant. On the other hand, if SPE is used as a first time investigation for diagnostic purposes, narrative comments on patterns associated with an increased likelihood of M-protein would be much warranted e.g. commenting on an increased beta fraction which relates to a possible masked or co-migrating M-protein. Under the diagnostic scenario, the simultaneous use of other tests such as serum free light chain assays (sFLC), immunofixation electrophoresis (IFE), urine electrophoresis, etc., with SPE in a "screening" panel will also play an important role in determining the extent of SPE commenting required. For example, when a simultaneous IFE detects an M-protein in the beta region, there is little value and potentially confusing to comment that the presence of an M-protein is a possibility in light of the increased SPE beta fraction. Alternatively, if internal protocol calls for IFE only on a positive SPE finding, then an SPE comment on an increased beta fraction provides a clear explanation of the follow-up testing. Physician users should be encouraged to consult identified personnel from the laboratory for