matory markers were within reference intervals. Arterial blood gas measurement revealed hypoxemia and hyper-car-pnia. Serum protein capillary zone electrophoresis results are shown in Fig. 1.

QUESTIONS
1. What finding does this protein electrophoresis gel demonstrate?
2. What could be the diagnosis for this pattern?
3. How can the diagnosis be established?

The answers are below.

ANSWERS

The patient’s serum α1 globulins were reduced at 1.3 g/L (reference interval, 2.1–3.5 g/L). Potential causes include malnutrition, excessive excretion, decreased production, and α1-antitrypsin (A1AT) deficiency. The clinical history was consistent with A1AT deficiency (1–3). The diagnosis should be confirmed by direct quantification of circulating A1AT by immunoassay and confirmation of the presence of A1AT disease alleles by isoelectrofocusing and/or genotyping (2–4). In this case, A1AT was not detectable and a Z/Z homozygote phenotype was found.

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References

News & Views

Realities of Observational Study Registration

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Interest in registration of observational studies is growing. Observational studies (OSs) of human subjects represent a large fraction of published scientific reports and may be considered closer to bedside than clinical trials (CTs), yet the majority are unregistered in prospective study registries. A recent article by Dal-Re et al. in Science Translational Medicine (1) provides commentary on the ethical and scientific rationale supporting prospective registration of OSs. To briefly illustrate their point, the authors performed a literature search of PubMed articles from 2011 and observed that the number of publications from OSs outnumbered those from randomized controlled trials (RCTs) almost 300,000 to 20,000. Although approximately 20% of RCT reports were accompanied by a registration num-
ber, the registration of OSs was uncommon and more likely to occur if the OS used data from an RCT. In those cases, the OS was not registered as a separate protocol but rather used the registration number of the RCT, thus providing no additional information on the OS design or data. The authors suggested that much of the ethical and scientific rationale that led to systematic registration of CTs also applies to OSs.

Registration of CTs was introduced as a way to discover and reduce selective reporting and publication of positive results. Nonpublication of entire studies, misinterpreting data, and other selective reporting practices introduce significant bias and compromise validity through overestimation of effectiveness in both CTs and OSs.

Beyond transparency that facilitates reporting of the total evidence base and enables detection of protocol deviations, there are other benefits to systematically registering all OSs. These include increased awareness by potential subjects, researchers, and funding agencies that could enhance recruitment, identify gaps, promote collaboration, and prevent duplication of efforts in research. Registration of an OS also supports ethical obligations to human subjects, particularly those related to the release of study findings for advancement of medical knowledge. Additionally, OS registration could promote public data sharing and standardization among similar types of registries.

Some individuals caution that registration of OSs may hinder new idea generation and reduce availability for analyses of endpoints that were not prespecified. Proponents counter that high-quality research is based on a priori delineation of hypotheses and statistical plans. Others wonder if the existing infrastructure for RCT registries is applicable for OS registration owing to the heterogeneity of purpose and methods in OSs.

Deborah A. Zarin, Director of ClinicalTrials.gov, reported that, as of July 24, 2013, OSs comprised 19% (n = 27 666) of all (n = 148 607) studies and 6% (n = 603) of all (n = 9471) results registered at ClinicalTrials.gov (2). Despite the perceived challenges inherent to OSs, this is one example where the largest existing registry is accommodating OS protocols and data. Several of the registries in the WHO’s Registry Network also indicate that they accept OSs.

If systematic registration of OSs is to become a reality, influential stakeholders must support the idea and provide incentives to encourage OS registry submission. These stakeholders include institutional review boards, medical journal editors, international medical professional associations, and regulatory and funding agencies. Researchers can make this a reality now by deciding to prospectively register their OSs.

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