The International Normalized Ratio (INR) is simple to use once it is understood, and its application to the monitoring of oral anticoagulant therapy of patients who are international travelers and to the publishing of studies from different parts of the world seems an obvious conclusion.

On the other hand, there are a number of logical medical doctors (LMDs) who have been happily following their patients for years on coumarin derivatives using the prothrombin time (PT) as it is actually measured (in seconds) and who, now that the doses of coumarin have been decreased to prevent the bleeding complications so prevalent in the 1960s and 70s are quite successful in this mode.

In recent months, there has been a furor raised regarding lack of use of INR in America as commercial interests on both sides of the Atlantic attempt to sell coagulation analyzers and reagents on the basis of the reporting of INR and measuring the PT with more sensitive thromboplastins.

Even the College of American Pathologists (CAP) has been stimulated to produce a survey of laboratories to determine the state of mind of coagulation laboratory directors and clinicians regarding the INR. The CAP, led by a distinguished group of specialists, has tended, with the proficiency testing programs, to drive laboratories toward instruments and reagents that provide short PTs and narrow coefficients of variation (CVs). Proponents of the INR point out that more sensitive reagents are needed for studies of low dose coumadin effects. The rub comes when the claims of better control of coumarin dose and better outcomes become exaggerated and when it is suggested that only the INR should be reported to force clinicians to learn it and to use it.

There are settings in which the INR may not be necessary if the patient is not in a study and is being followed by one laboratory or by a group of laboratories using thromboplastins with the same International Sensitivity Index (ISI). The ISI is what throws gasoline on the smoldering fire! In the 1970s, even the International Council on Standardization in Hematology and the International Council on Thrombosis and Hemorrhage (ICSH/ICTH) could not agree on determining the ISI, a number which is supposed to equate each manufacturer's thromboplastin to a standard thromboplastin approved by the World Health Organization (WHO). By 1985, standardization was much improved but cumbersome and expensive using 20 normal plasmas and 60 plasmas from patients on stable doses of coumarin. There is still some dissent voiced, even in England, where for years the PTs in all the hospitals have been standardized on the "Manchester Reagent."

Now, manufacturers of reagents have begun to offer thromboplastins with a variety of ISIs from 1.2 (most sensitive) to 2.6 (least sensitive). Laboratories can have the best of both worlds using low sensitivity (ISI 2.6) thromboplastins for short PTs and small CVs for CAP proficiency tests and for diagnosis, and high sensitivity (ISI 1.2) thromboplastins for monitoring low dose coumadin treatment.

Of course, great care will have to be taken to avoid confusion if thromboplastins of different ISI are used in the same laboratory.
Recently, results were reported of introducing the INR in a University Hospital setting. The Cardiology Clinic and the Hematology Clinic physicians (6) were quick to order the INR for 36 patients they were following. The remaining physicians (34) from General Medical and Surgical Clinics and from Vascular and Orthopedic Clinics (15) continued to use seconds in the usual way. No differences were found in level of PT or variation in PT whether the patients were followed by INR or by seconds; the only complications found by surveying the clinicians were two patients in the Cardiology Clinic who had recurrent thrombotic episodes while on low dose coumadin.

More work is necessary to separate the effects of (1) close monitoring (inpatient daily versus outpatient monthly), (2) dose (low dose, low PT versus high dose, high PT), and (3) uncontrolled factors\(^2\),\(^12\) (compliance, concurrent medications, dietary changes, liver disease), any or all of which may play an important role in control of anticoagulant therapy. There is much yet to be learned. Let us not allow our passions to dissuade us from good sense and cautious experimentation.

References


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EDWARD E. MORSE, M.D.,
Director of Hematology,
Department of Laboratory Medicine,
University of Connecticut School of Medicine,
Farmington, CT 06030