OBJECTIVES: Our laboratory has developed a new method for studying blood coagulation that monitors light reflected from whole blood as it clots. Preliminary measurements suggest that this method probes aspects of coagulation that are not assessed by standard clinical tests and that it may distinguish some disease states. The long-term goal of this project is to validate this method as a standard clinical test and to determine its range of usefulness. The immediate goal is to elucidate the mechanism by which clotting affects scattered light.

RESEARCH DESIGN: Numerous external factors influence clotting and the initial approach will be to examine the effect of known factors, such as surface activation, aspirin, and anticoagulant, on reflected light.

METHODOLOGY: The primary experimental method will involve the following procedure. When phlebotomy is to be performed for some medically indicated reason, an extra tube will be drawn into the anticoagulant of interest. An aliquot of blood will be placed in a glass cuvette thermostated at body temperature and illuminated with broadband light. Clotting will be initiated by reversing the anticoagulant, usually by recalcification. Light backscattered from the incident beam will be measured by a diode array spectrometer. The time course over twenty minutes will be digitized and stored in a computer workstation. Alternatively, blood drawn from the patient may be placed immediately in the cuvette without anticoagulant and allowed to clot.

FINDINGS: Preliminary studies reveal that at least four processes are detected by this method. The first process will be fit by a double exponential function; the second by a logit function; the third by a straight line. The fourth process corresponds to clot retraction and is highly irregular. This generates four parameters that constitute the measurement. Initial studies show that the erythrocyte membrane, in particular band 3 protein, plays a major role in the first two processes. This finding raises the possibility that this new method may detect the abnormalities of band 3 noted in Alzheimer's disease and be useful in diagnosis. Ex vivo experiments suggest that this method can also distinguish a procoagulant effect of inhibitors of cyclo-oxygenase 2 (COX2), whereas aspirin, naproxyen and indomethacin demonstrate an anticoagulant effect. Although epidemiological data have raised concern that the widely used COX2 inhibitors may increase the risk of thrombotic events, no standard coagulation test demonstrates a procoagulant effect. Similarly, no standard coagulation test can detect the involvement of the red cell membrane in clotting. The preliminary findings thus lead to the conclusion that this new method may be a useful supplement to the standard coagulation profile. Furthermore, in so far as it may contribute to our understanding of Alzheimer's disease and thrombosis, it will improve the medical care given to elderly patients and, therefore, especially to those served by the VA.

In the past year we have presented our findings at the 4th International Conference on Arteriology, Thrombosis and Vascular Biology (Greco, FA: An effect intrinsic to blood of COX2 inhibitors on coagulation. Arterioscler Thromb Vase Biol. 2003;23:a21.) and have published the first manuscript (Greco, FA: Reflectance spectroscopy of clotting blood: A description of the time-dependent behavior. Arch Path Lab Med. 2004;128:173-180.). The technique has been improved by the addition of standardized mixing before measuring light scattering and by the addition of a simultaneous measurement of electrical impedance as a non-optical probe of clotting.