New clinical study will help doctors assess abnormal bleeding

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How do you know if you bleed normally? Scientists at The Rockefeller University Hospital's Center for Clinical and Translational Science (CCTS) aim to answer that question more definitively with the launch of an assessment tool designed to help physicians and researchers more accurately determine what is inside and outside the normal range of bleeding symptoms. The Phenotype Recording and Analysis Tool (PRAT), a Web-based questionnaire designed by Physician in Chief Barry S. Coller, Clinical Scholar Andreas C. Mauer and their colleagues, is the subject of a new pilot study that may change the way we diagnose and deal with bleeding disorders.

Mauer, principal investigator on the study and instructor in clinical investigation in Coller's Allen and Frances Adler Laboratory of Blood and Vascular Biology, is currently recruiting 500 participants with no known bleeding-related disease and no recent use of medication with anti-coagulant or anti-platelet properties. Participants will answer an hour-long questionnaire detailing their history of everyday bleeding symptoms — e.g., shaving nicks, nosebleeds and menstruation — and uncommon ones — unexplained bruises, coughing blood or bleeding in joints or muscles.

The primary aim of the study is to extrapolate characteristics and ranges of bleeding symptoms for normal individuals, parameters that could eventually be used as a tool in diagnosing bleeding disorders and improving screening standards for assessing preoperative risk. "Many subtle bleeding diatheses manifest only after an individual is exposed to

a hemostatic challenge such as surgery, when a problem occurs," says Mauer. The study carries implications for research as well, as the results may allow investigators to draw correlations between lab results or genetic analyses and bleeding symptoms, which will in turn allow them to identify patients who may have genetic or environmental factors that influence their bleeding symptoms.

Mauer and his colleagues, including Ed Barbour, Nickolay Khazanov, Natasha Levenkova and Shamim Mollah of the CCTS's informatics department, will also break down the range of what's normal for subgroups classified by age, sex, medication use, race, ethnicity and history of trauma or surgeries — factors that may affect the bleeding score. Further delineation of "normal" bleeding will assist the team with its secondary aim of validating and refining the questionnaire.

Screening for bleeding symptoms is hardly a new thing, but PRAT is an improvement on standard tests and questionnaires in a number of ways. Certain questions — have you ever had a skin disorder that manifests in little red dots, for example — are much easier to get across with the aid of photographs, which PRAT's Web-based interface allows for. Participants complete the survey with the assistance of a physician or nurse practitioner, who helps properly interpret all questions. The questions themselves are highly specific and cover a comprehensive gamut of symptomology. "What we're applying here is something that pollsters are very familiar with, that how you ask the question makes a big difference in the answer," says Mauer.

Being a Web-based, open-source, HTML-coded interface, the questionnaire can also be administered at sites outside The Rockefeller University Hospital. "Our ultimate vision is that researchers worldwide will be interested in using our tool and downloading their data into our database, which will then be available to all investigators," says Coller, who is also director of the CCTS, established in 2006 by an inaugural

Clinical and Translational Science Award from the National Institutes of Health. "By standardizing the way clinical information is collected and organized on large numbers of patients, the correlations with genetic and biochemical data will be much clearer."

The current study will be followed next year by a study involving patients with diagnosed bleeding disorders. "We'll then be able to test out various scoring combinations in order to evaluate which scoring cutoffs are optimal for the purposes of separating the normal population from the population of individuals with a bleeding disorder," says Mauer. "This will make it more likely that only those individuals who are likely to have a disorder undergo the inconvenience and expense of further evaluation."

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