PLATELET THROMBOPLASTIC FUNCTION

A technique for its measurement and its uses.

By


A thesis for the degree of Doctor of Medicine of the University of Adelaide, based on work conducted at the Institute of Medical and Veterinary Science, Adelaide.

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PREFACE

I. Indications for the Study.

The gravity of diseases characterized by a tendency to abnormal haemorrhage based upon a defect of blood coagulation has never been minimized. Recent years have seen spectacular and rewarding progress in the understanding of blood coagulation and its disorders. Many of the advances have had their beginning in the publication of qualitative techniques which have made it possible to study effectively various phases of normal blood coagulation and thereafter to distinguish if not isolate individual factors and to implicate specific deficiencies as the causative defects in various haemorrhagic diatheses. Side by side with progress in diagnosis, advances in treatment have demanded the development of appropriate quantitative techniques whereby not only the character of a bleeding tendency might be uncovered but its initial severity and subsequent response to therapy gauged.

The long delayed recognition of blood platelets as an integral part of normal intrinsic blood coagulation had provided a background for the interest in haemorrhagic diseases dependent on platelet abnormalities, (especially of their thromboplastin component) existing in the laboratory wherein the work contained in this thesis was undertaken. Leading this work, Dr. J.A. Bennin had modified the thromboplastin generation test described by Biggs and Douglas in 1953, to quantitate platelet thromboplastin factor. In a series of papers, published or in preparation when this present work was undertaken, Bennin was able to provide an essential clue whereby discrepancies between platelet numbers and the severity of haemorrhage in diseases affecting platelets began to be resolved.
Briefly his work suggested that haemorrhage was related to the
degree of impairment of platelet thromboplastic function and,
equally, quite unrelated to platelet numbers. This suggestion
was more than a possible solution to an academic problem for it
found an important clinical application in the assessment and
management of the haemorrhagic state in diseases affecting blood
platelets. It was realized, however, that, despite its practical
importance, this work would probably find limited routine adoption
for the technical difficulties inherent in the thromboplastin
generation test and the attendant need for skilled and experienced
staff mitigated against its use in laboratories other than those
able to undertake the more complex coagulation investigations. So,
too, with increasing local experience it was accepted that the
thromboplastin generation test, modified to quantitate platelet
thromboplastic function, presented certain disadvantages which
rendered it less than ideal for this purpose. Accordingly it was
considered worthwhile to seek an alternative method, the aim being,
if possible, to develop a less complicated procedure than the
modified thromboplastin generation test and, thus, one likely to
find wider acceptance and greater clinical application along lines
suggested by earlier studies published from the Institute of Medical
and Veterinary Science.

For the most part this thesis describes the development of a
new method to quantitate platelet thromboplastic function together
with a thorough investigation of the factors participating in the
reaction. A further section illustrates the uses of the
established technique as applied in a series of appropriate cases in
which haemorrhage is a common if not the dominant feature. More-
ever while this work was in progress it was realized that, while the
technique to be described was primarily a reliable means of
detecting and assessing platelet thromboplastic dysfunction, it
would almost certainly be possible to adapt the basic reaction to
serve other uses. Further sections describe preliminary experiments
modifying the reaction to assay factor X, and others in which the
reaction is displayed as a means to study the behaviour of plasma
and serum anti-thromboplastic activity. In accordance with the regulations, the original content of this thesis is introduced with an historical review of relevant antecedent work.

2. **Acknowledgements.**

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