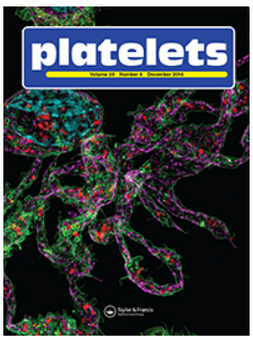

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SPECIAL REVIEW: GUS BORN

Personal reflections on the early contributions of Gus Born to platelet research

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ABSTRACT

Professor GVR Born, Gus to his friends, was one of the great pioneers of platelet research. My early memories of him have enabled me to look back at his early years in Oxford and London. A brilliant and generous man with always the time to discuss and advise he was instrumental in deciphering the principle stages of the aggregation of blood platelets by ADP, a path aided by his development and use of the platelet aggregometer. He applied his knowledge to the real time analysis of platelet and leukocyte involvement in thrombus formation in animal models and to the development of atherosclerosis and thrombosis and their pharmacological inhibition. What follows is a personal account of the major steps in this early work and of the actors involved.

KEYWORDS

Professor GVR Born, a pioneer of platelet research, atherosclerosis and thrombosis

History

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Professor GVR Born was born in Göttingen in Germany in 1921, the youngest of three children of Max Born (later to receive the Nobel prize for Physics) and his mother, Hedwig. Of Jewish nationality, the rise of anti-Semitism in Germany prompted his family to move to Britain and to establish a home in Edinburgh where Gus studied medicine graduating in 1938. Serving in the Royal Army Medical corps during the war, he was among the first to witness the horrors of the atomic bomb blast in Hiroshima, memories of which changed his life. He attributed the severe bleeding experienced by many of the Hiroshima victims to a lack of platelets and so started his lifelong interest in platelet biology and pharmacology. After his return to the United Kingdom, Gus made the first significant steps in his research career in Oxford University working both in the then Nuffield Institute for Medical Research (associated with the Radcliffe hospital) and the Sir William Dunn School of Pathology in South Parks road (Figure 1).

The Oxford Years

One of the first colleagues of Gus in Oxford was John Vane (later to become Sir John Vane and to receive the Nobel Prize in partnership with Bengt Samuelsson and Sune Bergström for studies on prostaglandins and other biologically active substances). Their first paper together described the quantitative determination of free histamine in blood [1]. They put together a procedure involving an initial dialysis of blood against saline followed by separation of the histamine by paper chromatography. It is fascinating nearly 70 years on to read the paper written by the two then young researchers. These studies, performed on blood from cats, were followed by a series of manuscripts again using animal models in which Gus looked at the physiological effects of histamine and other amines in blood. Included was a paper on acute edema in the isolated, perfused lungs of rabbits; surprisingly, histamine and adrenaline had no direct effect whereas 2,4-dinitrophenol caused a slow edema associated with ATP breakdown contrasting with the rapid edema induced by mercury compounds [2]. This early stage of his career also included studies on smooth muscle and interestingly on the role of arterial O_2 saturation and/or the release of sympathetic amines on the constriction of the ductus arteriosus in newly born lambs [3]. This is a subject of much recent interest as the molecular mechanisms and platelet involvement in the separation of the blood vascular and lymphatic systems are now elucidated [4,5]. The work on ductus arteriosus from Gus was one of the several papers published with Geoffrey Dawes, Director of the Nuffield Institute for Medical Research in Oxford. Despite his passing interest in the fetal circulation, Gus's passion for platelets gradually took priority over his other early pharmacological research.

A series of short communications on the storage and metabolism of ATP, 5-hydroxytryptamine (5-HT), and adrenaline in platelets established the benchmarks for his future research. He was fascinated by the relationship between ATP and 5-HT in platelets and quantified the reduction in ATP in platelets during clotting [6]. He showed that this breakdown involved the loss of one or two of its phosphorus residues with formation of ADP or adenosine monophosphate (AMP). By performing chloroform/methanol extractions of the clot, he was able to compare changes both in phospholipid phosphorus and protein-bound phosphorus hypothesizing a link between the degradation of platelet ATP and the formation of "thromboplastin" a newly recognized essential cellular component of coagulation. Gus had many discussions in Oxford with Professor R.G. Macfarlane who in the Sir William Dunn School was laying the basis of the coagulation cascade while mention should also be made of Professor Rosemary Biggs who at the then Churchill Hospital in Oxford made valuable contributions to the early understanding of the molecular basis of hemophilia [7,8]. Notwithstanding the "coagulation theme" of Oxford at the time, Gus continued with his interest in platelet biology beginning with the mechanisms behind the

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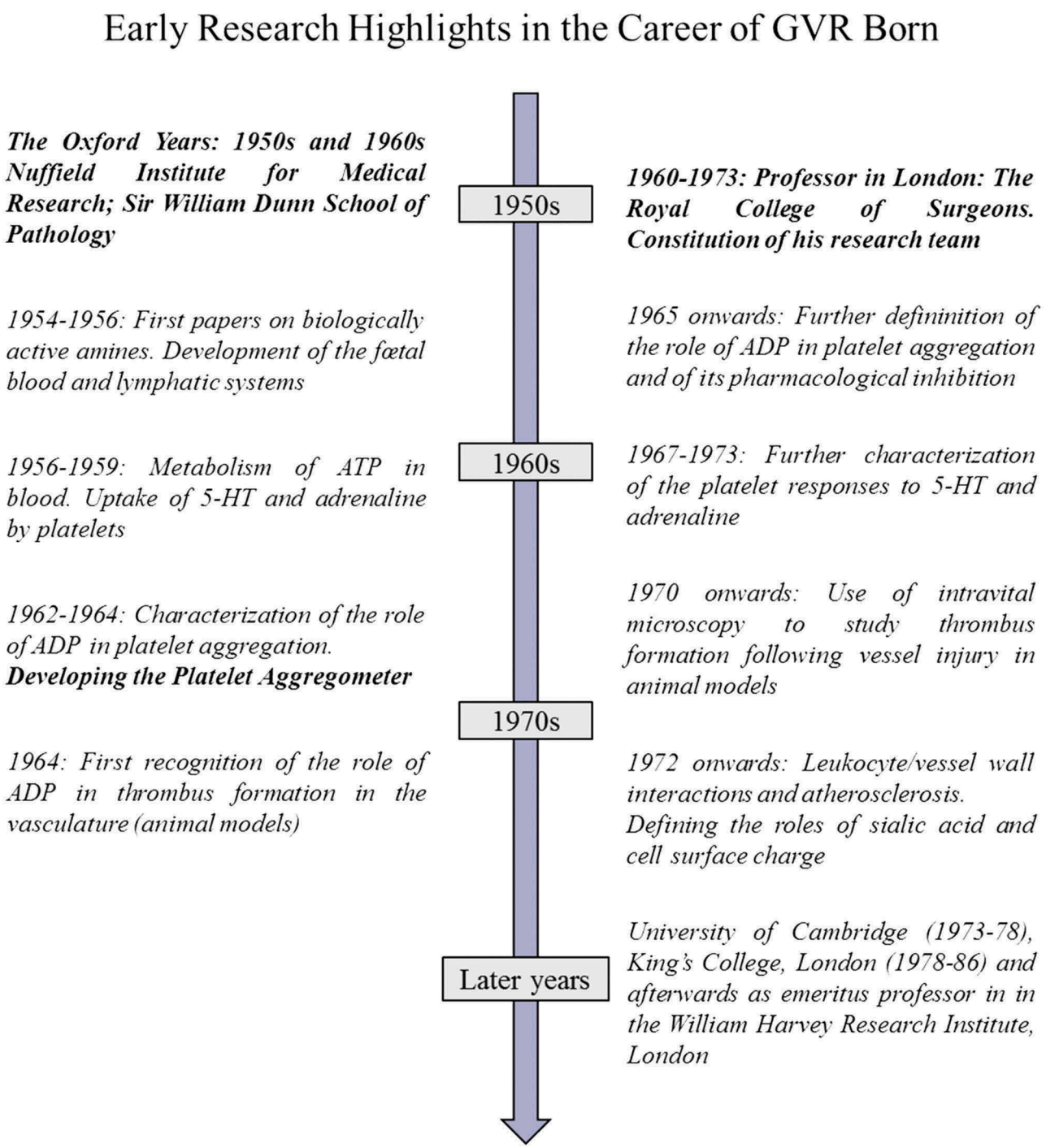

Figure 1. Synopsis of the early career of Gustav Born featuring highlights discussed in this review.

storage of 5-HT [9]. He was fascinated by the extraordinary capacity of platelets to take up and store 5-HT, necessarily by an active process, speculating that 5-HT was stored as an ionic complex with ATP; with hindsight, we now know that both 5-HT and other amines are stored with ATP, ADP, and pyrophosphate at high density in dense granules.

For a time, Gus was based in the Sir William Dunn School of Pathology where I believe he studied for his Ph.D. although he was reticent to talk about a thesis director for whom he had little respect. Much more positive was the close relationship he established with Howard Florey (another Nobel Prize winner). Although Gus had long left when I walked through the doors of the Sir William Dunn School for the first time in 1968 to begin my own research career, I can confirm the aura of this Department of Oxford University largely established by Florey's war-time work showing the therapeutic value of penicillin. Although Florey (1898–1968) was now deceased, many of the people who worked with him were still active including Norman Heatley (a kind quiet spoken man), Margaret Jennings, and EP Abrahams (a biochemist) although Ernst Chain (1906–1979), another major player in the penicillin work, had moved elsewhere. Significantly, Howard Florey late in his career had developed an interest in the vessel wall and particularly in the endothelial cell working on the development of atherosclerosis with John Poole and the then Reader in Pathology, John French [10,11]. It was in the context of this unique Oxford scientific environment that Gus

developed his interests in atherosclerosis and platelet–vessel interactions.

London and the Royal College of Surgeons

Moving to the Royal College of Surgeons where he became Professor of Pharmacology gave Gus the much-needed freedom to develop what is for me "the golden age" of his research. A recent report had described that ADP released from red cells was a powerful inducer of platelet aggregation [12]. Gus quickly turned his attention to ADP thinking that platelets themselves could also be a source (from degraded ATP). His first article in *Nature* characterized in detail the unique ability of ADP to aggregate platelets [13]. It is anecdotal but shows the scientific importance of this epoch that this manuscript was accompanied in the same volume of *Nature* by an article by Max Perutz (another Nobel Prize winner) on the structure of hemoglobin [14]. In this prelude to a series of *Nature* papers, Gus added ADP to citrated platelet-rich plasma and followed optical density changes in a commercial spectrophotometer as the platelets aggregated in the stirred suspension. This was a prototype to the development of the platelet aggregometer that marks the career of Gus and which will be covered elsewhere in this special edition of *Platelets* (see manuscript by R. Flower). Remarkably, ADP was the only 1 of 22 nucleotides tested able to induce platelet aggregation and while the response to low amounts of ADP was reversible, the aggregate failed to disperse at high concentrations. Gus attributed the reversibility at low concentrations to the breakdown of the ADP to AMP an inhibitor of aggregation but he also predicted that a further degradation of AMP might release other inhibitors – a forecast that proved correct for adenosine. He additionally confirmed that ATP itself was an inhibitor. Of major importance was his recognition of ADP as an essential element in the formation of the hemostatic plug and as a key factor in thrombosis.

A follow-up paper in *Nature* showed that when ADP was infused into the circulation of cats, the platelet count fell presumably due to the formation of aggregates although the cause of the fall was not fully established [15]. Further studies with Michael Cross again using animal models identified calcium as a major cofactor of platelet aggregation while the competitive nature of the inhibition of the effects of ADP by adenosine and ATP was again underlined [16,17]. Their first hypothesis was that calcium formed bridges between ADP bound to the surface of adjacent platelets. However, in the second of these papers, the authors looked at the effect of washing the platelets and concluded that a protein cofactor was also necessary. This was present in a euglobulin fraction of plasma; fibrinogen (Fg) and/or FVIII were proposed as candidates. Gus noted that the resistance of 2-chloroadenosine to degradation by adenosine deaminase meant that its inhibitory activity was maintained for longer in whole blood at 37°C [18]. Sites of major or minor injury were mechanically inflicted on arteries in rabbits and the *in vivo* inhibitory effects of adenosine and 2-chloroadenosine on thrombus formation were thus compared [19]. While infusion of adenosine before major injury did not result in bleeding, the formation of platelet-rich white bodies protruding into the vessel lumen was much reduced. White body formation was restored with time but the inhibitory effect of 2-chloroadenosine lasted for longer. When added after the formation of the thrombi, both inhibitors increased the rate and extent of embolization. Significantly, in a back-to-back paper in the same volume of *Nature*, Richard Haslam working at the Radcliffe hospital in Oxford showed a role for ADP in the aggregation of blood platelets by thrombin and fatty acids [20]. Others had shown that ADP was an essential cofactor in the aggregation of platelets by collagen as was nicely reviewed by Marjorie Zucker [21]. These were the key early steps in identifying the universal role of ADP as a stimulus in the platelet response to vessel injury and its importance for hemostasis was now unambiguously established. His work also formed the early experimental basis for the successful development of drugs inhibiting arterial thrombosis by blocking the action of ADP on platelets and for their use in clinic.

(1) **Putting together his research team**. In the following years at the Royal College of Surgeons, Gus further defined the platelet response to ADP and its inhibition by adenosine derivatives both *in vitro* and in animal models with regular articles in *Nature* and other journals. Significantly, Gus progressively established a dynamic group of mostly young researchers around him. As a young graduate student in Oxford, I was invited to London on several occasions and met many of these researchers who are now recalled. There is no doubt that Gus was an outstanding mentor. Many of his research team featured in his publications and went on to establish themselves after leaving London and setting up research groups of their own. With Hans Baumgartner, he studied the uptake of 5-HT by platelets and its ability to stimulate platelet aggregation and to desensitize them [22,23]. Hans was to become a leading international authority on the platelet–vessel wall interaction working with F. Hoffmann-La Roche in Basle, Switzerland. David Mills and J Bryan Smith helped Gus to unravel the pharmacology of the inhibition of platelet aggregation by adenosine and of the potential of platelets to uptake, metabolize, and release adrenaline [24–26]. David and Bryan were senior members of Gus's group and endlessly debated the mechanisms whereby ADP activated platelets. Richard Haslam also collaborated with Gus on adenosine analogues and on adenylate kinase while working in industry with Imperial Chemical Industries, Macclesfield, UK [27,28]. After Richard moved to McMaster University in Canada, he became a leading expert on platelet signaling mechanisms showing, as two examples, the central roles of adenylate cyclase and plekstrin [29,30]. David Mills and J Bryan Smith took up positions in Temple University in Philadelphia where Bryan continued his interest on the signaling mechanisms of platelets working on inositol 1,4,5-triphosphate and also several biologically active lipid derivatives [31,32]. In contrast, David continued to work on the ADP receptor of platelets – in fact he identified it as a 43 kDa protein using a novel photoaffinity labeling approach with a P^{32}-labeled ADP derivative [33]. This protein linked to adenylate cyclase showed all the characteristics of the P2Y12 receptor later identified by Hollopeter et al. [34] who with the progress of time had the advantage of gene cloning technology.

Returning to Gus's group in the Royal College of Surgeons in the 1970s, David Mills was joined by Donald MacFarlane and later by Noel Cusack who in fact introduced the concept of using photolysable 2-azido analogues of adenosine, AMP, and ATP in characterizing their interaction with platelets [35]. Donald MacFarlane is still active, now heading a clinical department in the University of Iowa specializing in hemophilia. In parallel, with the above biochemical approaches, Gus turned his attention more and more toward understanding the role of ADP in intravascular thrombus formation and mention should be made of another young postgraduate student, Nicola Begent, who quantified the growth of platelet thrombi in vessels and specifically looked at the effect of histamine in venules [36,37]. Nicola later turned her attention to the use of aspirin but this will be the object of another chapter in this special edition of *Platelets*. Anne Atherton was interested in how leukocytes interacted with blood vessel walls under flow [38,39]. Nicola and Anne were with Gus pioneers in intravital microscopy. I clearly remember seeing blood flowing through capillaries in the cheek pouch of anaesthetized hamsters for the first time with Gus in his laboratory. Not to be forgotten is Frank Michel who

studied in fine detail platelet shape change using the platelet aggregometer [40]. Finally, a key figure in Gus's group was the now elderly Helen Payling-Wright with a lifelong experience of a wide range of medical problems including vascular diseases and thrombosis. With Gus, she studied the role of platelets in scurvy and later she became interested in multiple sclerosis [41,42]. Yet, her main focus in the Royal College of Surgeons was the vasculature and especially endothelial cells [43]. I remember spending hours with her as she explained her work; she was a kind and remarkable lady. One cannot help but speculate what would have happened if this group in its ensemble could have stayed together longer under Gus's direction.

(2) Surface charge on platelets and endothelial cells. As time went by, Gus became more involved in studies on atherosclerosis. He questioned the role of the surface charge of platelets and endothelial cells and particularly on how sialic acid influenced the interactions of platelets and leukocytes with the vessel wall. Gus's lasting influence in the Sir William Dunn School of Pathology became apparent to me on my very first day in 1968. Recruited in the group headed by John French, I was told that my research project was to identify those surface components of platelets and vascular cells contributing to their surface charge. John French was an electron microscopist; he was also influenced by the work of Olav Behnke who had visualized the platelet glycocalyx by combining histochemical procedures with electron microscopy [44]. We obtained platelets from porcine and bovine blood while endothelial cells were stripped from the dorsal aorta of pigs and cows during early morning visits to the local Oxford abattoir. The procedure involved over-layering the washed open blood vessel with cellulose acetate paper [45]. This work much interested Gus and I gave my first talk in his department in 1970 describing the clear differences that we had found in the oligosaccharide composition of platelets and aorta endothelial cells and also between species; pig platelets for example had mostly *N*-glycolylneuraminic acid contrasting with the *N*-acetylneuraminic acid of cow (and human) platelets [46]. Gus was by now collaborating with a group in France to examine how changes in the surface charge of platelets influenced the functional response [47]. Enzymatically enriching platelets in sialic acid diminished aggregation to ADP whereas that induced by 5-HT was enhanced. Interestingly, increasing the sialic acid of platelets favored both their incorporation of K^+ and of 5-HT [47,48].

By now, the concept that sialic acid was a major contributor to the surface charge of platelets was gathering strength worldwide. Duncan Pepper and Graham Jamieson in Washington, USA, reported the oligosaccharide composition of sialic acid-containing glycopeptides released from human platelets by proteases showing the presence of mucin-like structures [49,50]. For the lipid-based gangliosides, the early pioneer was Aaron Marcus in New York [51]. Gus and Anne Atherton (see above) looked at the effects of enzymatic removal of sialic acid by neuraminidase on the adhesion of circulating granulocytes and platelets in venules. They did this by intravital microscopy timing the appearance of thrombi following the iontophoretic application of ADP [52]. Interestingly, enzymatic removal of sialic acid with neuraminidase affected granulocyte adhesion (and granulocyte number) more than platelets although the degree of loss of sialic acid from the platelets in their plasma environment was not measured. Later, Fraser Mustard's group in Canada confirmed that while loss of sialic acid had only small affects on the aggregation of rabbit platelets, its cleavage led to the rapid removal of platelets from the circulation [53]. It had now been established that much of the platelet surface charge on platelets was contributed by sialic acid on glycocalicin, a macroglycopeptide representing the major extracellular domain of GPI (later to become known as GPIb), one of four major surface GPs known at the time, reviewed by Nurden et al. [54]. By promoting studies on sialic acid and surface charge, Gus was also helping the thrust that eventually defined the molecular mechanisms of platelet adhesion.

From a personal point of view, Gus was instrumental in1970 of finding me a position in the Nuffield Institute of Comparative Medicine in Regents Park in London. He lived in Hampstead Heath just to the north and on occasion, he would walk across Primrose Hill and see what I was doing. London was a great place to be for platelets in the early 1970s with Gus the leader, always ready to talk and advise.

Conclusions

I have tried to provide insight into Gus's early work ranging from his work in Oxford in the early 1960s to the early 1970s in London. This is the period during which my personal contacts allowed me to get to know him and to appreciate just how he changed the platelet field. His early work on ADP and thrombus formation was inspirational and gave rise to many Nature papers. He sustained international collaborations during this period including that with Jacques Caen in Paris who remained a competitive but lifelong friend. Each year in the 1960s, the two laboratories met and exchanged views on their research topics. Gus was a kind and gentle man with a great enthusiasm. Inspired by his father, Max Born, he thought deeply about his work constantly trying to unravel how atherosclerosis developed and how arterial thrombosis could be combatted pharmacologically. This is perhaps why so many of his early papers were single author. He loved talking about his work and meeting with young researchers and students. He was both a scientist and a philosopher, made you feel important, and the ideas flowed. He loved giving lectures and was invited all over the world. After I moved to Paris, my contact with him diminished although he always had a kind word when we met. My last image of him rests in my memory. Gus was by now living mostly in the Cotswolds in England, a beautiful country area not far from Oxford and Stratford-on-Avon. I was driving through the picturesque town of Chipping Campden when suddenly I saw Gus who was walking slowly through the town with his wife, Faith, pausing to look into one of the many antique shops that line the streets. I hope that he found peace in his final years, I am sure that he did.

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References

1. Born GVR, Vane JR. The quantitative determination of diffusible histamine in blood. Br J Pharmacol Chemother 1952;7:293–303.
2. Born GV. Acute oedema in the isolated, perfused lungs of rabbits. J Physiol 1954;124:502–514.
3. Born GV, Dawes GS, Mott JC, Rennick BR. The constriction of the ductus arteriosus caused by oxygen and by asphyxia in newborn lambs. J Physiol 1956;132:304–342.
4. Bertozzi CC, Hess PR, Kahn ML. Platelets: covert regulators of lymphatic development. Arterioscler Thromb Vasc Biol 2010;30:2368–2371.
5. Navarro-Nunez L, Langan SA, Nash GB, Watson SP. The physiologiocal and pathophysiological roles of platelet CLEC-2. Thromb Haemost 2013;109:991–998.
6. Born GVR. Changes in the distribution of phosphorus in platelet-rich plasma during clotting. Biochem J 1958;68:695–704.
7. Macfarlane RG. Blood coagulation with particular reference to the early stages. Physiol Rev 1956;36:479–502.
8. Biggs R, Macfarlane RG. Haemophilia and related conditions: a survey of 187 cases. Br J Haematol 1958;4:1–27.
9. Born GVR, Gillson RE. Studies on the uptake of 5-hydroxytryptamine by blood platelets. J Physiol 1959;140:472–491.
10. Poole JC, Florey HW. Changes in the endothelium of the aorta and the behaviour of macrophages in experimental atheroma of rabbits. J Pathol Bacteriol 1958;75:245–251.

11. French JE, Jennings MA, Florey HW. Morphological studies on atherosclerosis in swine. Ann NY Acad Sci 1965;127:780–799.
12. Gaarder A, Jonson J, Laland S, Hellem A, Owren PA. Adenosine diphosphate in red cells as a factor in the adhesiveness of human blood platelets. Nature 1961;192:531–532.
13. Born GV. Aggregation of blood platelets by adenosine diphosphate and its reversal. Nature 1962;194:927–929.
14. Perutz MF. Relation between structure and sequence of haemoglobin. Nature 1962;194:914–917.
15. Born GV, Cross MJ. Effect of adenosine diphosphate on the concentration of platelets in circulating blood. Nature 1963;197:974–976.
16. Clayton S, Born GV, Cross MJ. Inhibition of the aggregation of blood platelets by nucleosides. Nature 1963;200:138–139.
17. Born GVR, Cross MJ. Effect of inorganic ions and of plasma proteins on the aggregation of blood platelets by adenosine diphosphate. J Physiol 1964;170:397–414.
18. Born GVR. Strong inhibition by 2-chloroadenosine of the aggregation of blood platelets by adenosine diphosphate. Nature 1964;202:95–96.
19. Born GVR, Honour AJ, Mitchell JRA. Inhibition by adenosine and by 2-chloroadenosine of the formation and embolization of platelet thrombi. Nature 1964;202:761–762.
20. Haslam RJ. Role of adenosine diphosphate in the aggregation of blood platelets by thrombin and by fatty acids. Nature 1964;202:765–768.
21. Zucker MB. ADP- and collagen-induced platelet aggregation in vivo and in vitro? Thromb Diath Haemorrh Suppl 1967;26:175–184.
22. Baumgartner HR, Born GV. Effects of 5-hydroxytryptamine on platelet aggregation. Nature 1968;218:137–141.
23. Baumgartner HR, Born GV. The relation between the 5-hydroxytryptamine content and aggregation of rabbit platelets. J Physiol 1969;201:397–408.
24. Born GV, Mills DC, Roberts GC. Potentiation of platelet aggregation by adrenaline. J Physiol 1967;191:43P–44P.
25. Born GV, Smith JB. Uptake, metabolism and release of (3H)-adrenaline by human platelets. Br J Pharmacol 1970;39:765–778.
26. Born GV, Mills DC, Smith JB. Pharmacology of the inhibition of platelet aggregation. Bull Schweiz Akad Med Wiss 1973;29:215–222.
27. Born GV, Haslam RJ, Goldman M. Comparative effectiveness of adenosine analogues as inhibitors of blood-platelet aggregation and as vasodilators in man. Nature 1965;205:678–680.
28. Haslam RJ, Mills DC. The adenylate kinase of human plasma, erythrocytes and platelets in relation to the degradation of adenosine diphosphate in plasma. Biochem J 1967;103:773–784.
29. Haslam RJ, Davidson MM, Desjardins JV. Inhibition of adenylate cyclase by adenosine analogues in preparations of broken and intact human platelets. Evidence for the unidirectional control of platelet function by cyclic AMP. Biochem J 1978;176:83–95.
30. Haslam RJ, Kode HB, Hemmings BA. Pleckstrin homology domain. Nature 1993;363:309–310.
31. Daniel JL, Dangelmeier CA, Smith JB. Calcium modulates the generation of inositol 1,3,4-triphosphate in human platelets by the activation of inositol 1,4,5-triphosphate 3-kinase. Biochem J 1988;253:789–794.
32. Selak MA, Smith JB. Platelet-activating factor-induced calcium mobilization in human platelets and neutrophils: effects of PAF-acether antagonists. J Lipid Mediat 1989;1:125–137.
33. Cristalli G, Mills DC. Identification of a receptor for ADP on blood platelets by photoaffinity labelling. Biochem J 1993;291:875–881.
34. Hollopeter G, Jantzen HM, Vincent D, Li G, England L, Ramakrishnan V, Yang RB, Nurden P, Nurden A, Julius D, et al. Identification of the platelet ADP receptor targeted by antithrombotic drugs. Nature 2001;409:202–207.
35. Cusack NJ, Born GV. Effect of photolysable 2-azido analogues of adenosine, AMP and ADP on human platelets. Proc R Soc Lond B Biol Sci 1977;197:515–520.
36. Begent N, Born GV. Growth rate in vivo of platelet thrombi, produced by iontophoresis of ADP, as a function of mean blood flow velocity. Nature 1970;227:926–930.
37. Begent NA, Born GV, Sharp DE. The initiation of platelet thrombi in normal venules and its acceleration by histamine. J Physiol 1972;223:229–242.
38. Atherton A, Born GV. Quantitative investigations of the adhesiveness of circulating polymorphonuclear leucocytes to blood vessel walls. J Physiol 1972;222:447–474.
39. Atherton A, Born GV. Relationship between the velocity of rolling granulocytes and that of the blood flow in venules. J Physiol 1973;233:157–165.
40. Michal F, Born GV. Effect of the rapid shape change of platelets on the transmission and scattering of light through plasma. Nat New Biol 1971;231:220–222.
41. Born GV, Wright HP. Diminished platelet aggregation in experimental scurvy. J Physiol 1968;197:27P–28P.
42. Gul S, Smith AD, Thompson RH, Wright HP, Zilkha KJ. Fatty acid composition of phospholipids from platelets and erythrocytes in multiple sclerosis. J Neurol Neurosurg Psychiatry 1970;33:506–510.
43. Wright HP. Endothelial mitosis around aortic branches in normal guinea pigs. Nature 1968;220:78–79.
44. Behnke O. Electron microscopical observations on the surface coating of human blood platelets. J Ultrastruct Res 1968;24:412–433.
45. Nurden AT. Platelet membrane glycoproteins: A historical review. Semin Thromb Hemost 2014;12:1562–1569.
46. Adams EP, Nurden AT, French JE. A comparative study of the bound carbohydrates in platelets, plasma and endothelium. Symp Zool Soc Lond 1970;27:91–98.
47. Mester L, Szabados L, Born GV, Michal F. Changes in the aggregation response of platelets enriched in sialic acid. Nat New Biol 1972;236:213–214.
48. Michal F, Born GVR, Mester L, Szabados L. Effect of 5-hydroxytryptamine on the potassium ion exchange of human platelets enriched in sialic acid. Biochem J 1972;129:977–978.
49. Szabados L, Mester L, Michal F, Born GV. Accelerated uptake of 5-hydroxytryptamine by human platelets enriched in a sialic acid. Biochem J 1975;148:335–336.
50. Pepper DS, Jamieson GA. Sudies on glycoproteins. 3. Isolation of sialylglycopeptides from human platelet membranes. Biochemistry 1969;8:3362–3369.
51. Pepper DS, Jamieson GA. Isolation of a macroglycopeptide from human platelets. Biochemistry 1970;9:3706–3713.
52. Marcus AJ, Ullman HL, Safier LB. Studies on human platelet gangliosides. J Clin Invest 1972;51:2602–2612.
53. Greenberg J, Packham MA, Cazenave JP, Reimers HJ, Mustard JF. Effects on platelet function of removal of platelet sialic acid by neuraminidase. Lab Invest 1975;32:476–484.
54. Nurden AT, Phillips DR, George JN. Platelet membrane glycoproteins: Historical perspectives. J Thromb Haemost 2006;4:3–9.