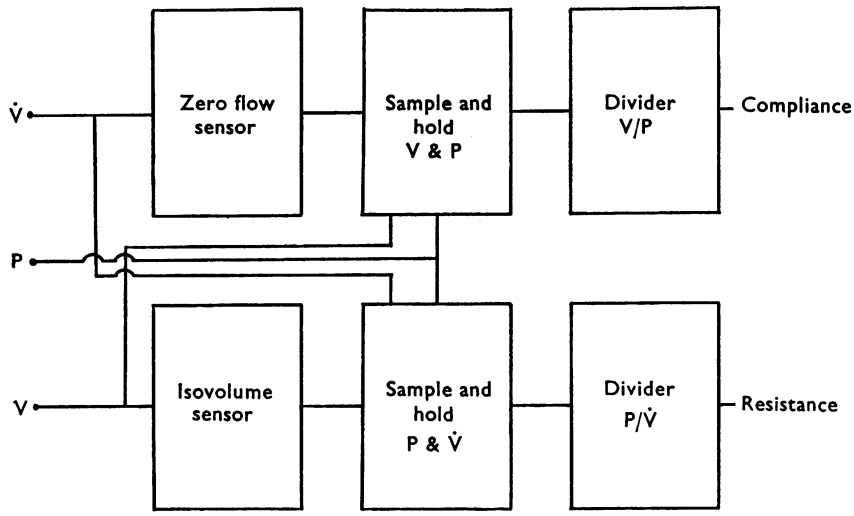

and pressure signals. Values of airways resistance are computed for each breath at isovolume points from instantaneous pressure and flow signals.

Tape-recorded signals of V̇, V & P from experimental animals will be used to demonstrate the computer.

REFERENCES

DENNIS, M. W., DOUGLAS, J. S., CASBY, J. U., STOLWICK, J. A. J. & BOUHUYS, A. (1969). On-line analog computer for dynamic lung compliance and pulmonary resistance. *J. appl. Physiol.*, **26**, 248–252.

DOUGLAS, J. S., DENNIS, M. W., RIDGEWAY, P. & BOUHUYS, A. (1972). Airway dilation and constriction in spontaneously breathing guinea-pigs. *J. Pharmac, exp. Ther.*, **180**, 98–109.

GILES, R. E., FINKEL, M. P. & MAZUROWSKI, J. (1971). Use of an analog on-line computer for the evaluation of pulmonary resistance and dynamic compliance in the anaesthetized dog. *Arch. int. Pharmacodyn.*, **194**, 213–222.

The role of adenosine diphosphate (ADP) in collagen-induced platelet aggregation

BARBARA NUNN (introduced by R. S. STACEY)

Pharmacology Laboratory, The Wellcome Research Laboratories, Beckenham, Kent

When a suspension of collagen is added to citrated platelet-rich-plasma (PRP), aggregation (Zucker & Borrelli, 1962) and a release of ADP (Hovig, 1963) occurs. On the evidence that adenosine monophosphate, an inhibitor of ADP-induced aggregation (Born, 1962), antagonized collagen-induced aggregation but not collagen-induced release, Hovig proposed that the liberated ADP mediated the aggregation seen after addition of collagen. This explanation has found general acceptance (Mustard & Packham, 1970). The present work demonstrates two aspects of collagen-induced aggregation that are not compatible with this concept.

Human citrated PRP was gently mixed with 0·1 volumes 1 mM ADP and left to stand at room temperature for 3·5–4 h. The responsiveness of this ADP-treated PRP to ADP and to collagen (prepared as described by Holmsen, Day & Storm,

1969) was compared at 37° with that of untreated PRP using a turbidometric technique. ADP-treated PRP was found to be insensitive to even very high concentrations of ADP, yet it retained its sensitivity to collagen (see Figure 1).

The poor responsiveness to ADP of platelets resuspended in salt solutions is well established. Packham, Warrior, Glynn, Senyi & Mustard (1967) found that collagen aggregated washed pig platelets whereas ADP could not. Platelets, sedimented from human blood with acid-citrate-dextrose anticoagulant and resuspended in a Tris-buffered medium (Haslam, 1964) were similarly found to aggregate in response

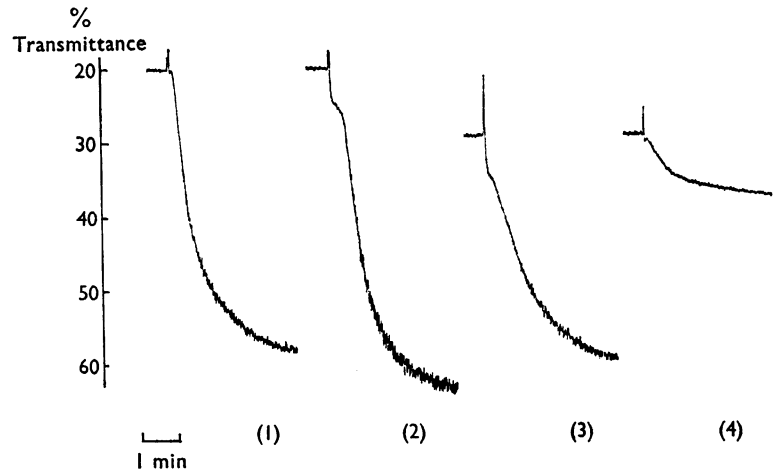

FIG. 1. Changes in the optical density of human PRP in response to 118 μM ADP (final concentration) (1 and 4) or to 0·3 ml collagen suspension (2 and 3). Samples 3 and 4 had been incubated with 100 μM ADP.

to collagen but not to ADP (1 μM–1 mM). However, ADP (10 μM) added 1 min before collagen led to considerable enhancement of the aggregating effect of collagen.

These experiments indicate that human platelets, unresponsive to exogenous ADP, will aggregate when exposed to collagen, and that ADP and collagen have a synergistic action. It seems reasonable to conclude that if collagen-induced aggregation is mediated by ADP, then the latter does not act at the outer surface of the membrane. Alternatively, collagen may have a direct action, or some other endogenous substance may be responsible for the observed aggregation.

REFERENCES

BORN, G. V. R. (1962). Aggregation of blood platelets by adenosine diphosphate and its reversal. *Nature, Lond.*, **194**, 927–929.

HASLAM, R. J. (1964). Role of adenosine diphosphate in the aggregation of human blood platelets by thrombin and by fatty acids. *Nature, Lond.*, **202**, 765–768.

HOLMSEN, H., DAY, H. J. & STORM, E. (1969). Adenine nucleotide metabolism of blood platelets. VI. Subcellular localization of nucleotide pools with different functions in the platelet release reaction. *Biochim. Biophys. Acta*, **186**, 254–266.

HOVIG, T. (1963). Release of a platelet aggregating substance (adenosine diphosphate) from rabbit blood platelets induced by saline 'extract' of tendons. *Thromb. Diath. Haemorrh.*, **9**, 264–278.

MUSTARD, J. F. & PACKHAM, M. A. (1970). Factors influencing platelet function: adhesion, release and aggregation. *Pharmac. Rev.*, **22**, 97–187.

PACKHAM, M. A., WARRIOR, E. S., GLYNN, M. F., SENYI, A. S. & MUSTARD, J. F. (1967). Alteration of the response of platelets to surface stimuli by pyrazole compounds. *J. exp. Med.*, **126**, 171–188.

ZUCKER, M. B. & BORRELI, J. (1962). Platelet clumping produced by connective tissue suspensions and by collagen. *Proc. Soc. exp. Biol. Med.*, **109**, 779–787.