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PARTICULATE CONTAMINATION OF DRUGS: THEIR EFFECT ON PLATELET KINETICS AND THE PULMONARY CIRCULATION. CM Backhouse, DAJ Galvin, RA Harper, AC Meek, CN McCollum. Department of Surgery, Charing Cross & Westminster Medical School, London, UK.

More than  $10^7$  particulate contaminants  $>2\mu\text{m}$  and many more  $<2\mu\text{m}$  are infused daily in parenteral medications to intensive care patients. They may form emboli with aggregated platelets and damage pulmonary vasculature [1], perhaps contributing to alveolar fibrosis in very premature babies. We studied this possibility in neonatal pigs.

Nineteen newborn pigs were randomised to either daily  $0.2\mu\text{m}$  filtered saline as controls, or infusions of particles similar to drug contaminants at  $10\times$  greater than the patient equivalent dose/kg given via subcutaneous injection portals with tunnelled central venous catheters. Four weeks later, autologous platelets were labelled with  $^{111}\text{In}$  and arterial and Swann Ganz catheters inserted under general anaesthesia. Before particle or filtered saline infusion and at 5 and 20 minutes later platelet count, lung platelet uptake, mean arterial pressure (BP), pulmonary vascular resistance, pulmonary shunt and alveolar-arterial  $\text{PO}_2$  difference were measured.

Initially, there were no significant differences between the groups indicating no measureable effect from chronic particle dosing over 4 weeks. Within 30 sec of bolus particle injection BP fell from a mean ( $\pm$  sem) of  $68.9 \pm 2.1\text{mmHg}$  to  $61.0 \pm 2.1$  ( $p < 0.01$ , paired t-test) but returned to normal within 5 minutes. This was not seen with controls or particle injections given over 5 minutes. Platelet counts fell in the particle group from  $660 \pm 43$  ( $\times 10^9/\text{L}$ ) to  $584 \pm 46$  at 20 minutes ( $p < 0.01$ ) but lung platelet accumulation was insignificant.

Transient fall in blood pressure due to contaminating particles can be avoided by slow injection or  $0.2\mu\text{m}$  in-line filters. Particles stimulate a loss of circulating platelets but with insignificant pulmonary accumulation and no impairment of pulmonary function after 4 weeks of daily particle injection at considerably higher doses than patients receive.

1. Chia C, Cattell V. The role of platelets in mesangial localisation: carbon uptake in thrombocytopaenic rats. Br J Exp Path 1985; 66: 465-474.

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HAEMOSTATIC PARAMETERS IN VARIOUS ETHNIC GROUPS IN SAUDI ARABIA. A.M.A. Gader, H. Bahakim, S. Malaika, and F.A. Jabbar, College of Medicine and King Khalid University Hospital, P.O. Box 2925, Riyadh-11461, Saudi Arabia.

Geographical and racial differences in the incidence of thrombo-embolism could be related to basic dissimilarities in the haemostatic system in different ethnic groups. However reliable comparative population studies in haemostatic parameters is lacking. The large expatriate community in Saudi Arabia offers such a chance.

Subjects tested were all healthy blood donors (aged 20-50 years) and were classified on the basis of ethnic origin into three categories (1) Arabs  $n=750$ , (2) Westerns (Americans and Europeans)  $n=400$ , and (3) S.E. Asians (Filipinos)  $n=570$ . The measurements done included PT, PTT, TT, Reptilase time, Plasma fibrinogen, AT III, Plasminogen, F.VIII:C, FX,  $\alpha_2$ -Antiplasmin and Platelet aggregation in response to ADP (20.0, 2.0, 1.0, 0.5 & 0.25  $\mu\text{M}$ ), Collagen, Arachidonic acid, Adrenaline and Ristocetin (1.5, 1.2 & 1.0  $\text{mg/ml}$ ).

There were no significant ethnic differences in the measured plasmatic clotting tests. This contrasts the finding of many smaller studies. Besides no significant ethnic differences were noted in platelet aggregation response to high doses of ADP (20  $\mu\text{M}$ ) or Ristocetin (1.5  $\text{mg/ml}$ ) and to Collagen. However, 45% of the S.E. Asians displayed abnormally inhibited responses to Adrenaline when compared to Arabs (34%) and Westerns (35.2%). Asians also displayed more inhibited responses to lower doses of ADP (2.0 & 1.0  $\mu\text{M}$ ). On the other hand, S.E. Asians showed the lowest incidence of inhibited Arachidonic acid responses (9%) when compared to Arabs (24%) and Westerns (26%). Similar racial differences were noted in response to low doses of Ristocetin (1.2 & 1.0  $\text{mg/ml}$ ) where Arabs and Asians showed high incidence of abnormally reduced responses (26-28%) when compared to Westerns (15%). No evidence of enhanced aggregation could be detected in Westerns. Changes of climate and/or dietary habits could be important factors influencing the haemostatic system in such a way that reduces ethnic dissimilarities.

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WINE CONSUMMATION AND PLATELET AGGREGATION. M. Seigneur, J. Bonnet, B. Dorian, P. Hourdille, G. Gouverneur, J. Larrue, R. Crockett, M. Boisseau, P. Ribereau-Gayon, H. Bricaud. Hôpital Cardiologique de Bordeaux, 33604 PESSAC, FRANCE.

To compare the effects of ethanol and wine on factors inducing thrombosis, 16 healthy male volunteers had to drink 3 kinds of beverage according to the following regimen :

|     |         |           |         |      |         |      |
|-----|---------|-----------|---------|------|---------|------|
|     | ethanol |           | white   |      | red     |      |
|     | washout | reference | washout | wine | washout | wine |
| t : | t0      | t15       | t30     | t45  | t60     | t75  |
|     | t90     |           |         |      |         |      |

t : time in days

Ethanol reference is hydroethanolic solution at PH and ethanolic titre of wine.

White wine is the reference of all wine cofactors excepting phenolics.

Red wine is the reference all wine cofactors.

At the beginning and at the end of each period, aggregation was measured with ADP 2  $\mu\text{mole}$ , Adrenaline 0,75  $\text{mg/l}$ , Arachidonic Acid 0,5  $\text{mg/l}$ .

Results show statistically significant hyperaggregation with the 3 aggregation inductors during the ethanol period, no variation during white wine period and statistically significant hypoaggregation with adrenaline and ADP during red wine period.

In contrast of ethanol, red wine seems to induce antiaggregant properties that could explain low incidence of CAD in countries of south of Europa.

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EFFECTS OF BLOOD CELLS ON PLATELET AGGREGATION BY IMPEDANCE METHOD. L. Mannucci, R. Redaelli and E. Tremolli. Institute of Pharmacol. Sci., E. Grossi Paoletti Centre, and Dept of Hematology, Niguarda Hospital, Milan, Italy.

To evaluate the effects of blood cells on the response of platelets to aggregating agents using whole blood impedance aggregometer, studies were carried out on whole blood (WB) of normal subjects and of patients with: polycythemia vera (PV), iatrogenic anemia (IA), primary thrombocytosis (PT), idiopathic thrombotic purpura (ITP), myeloid chronic leukemia (MCL), iatrogenic leukopenia (IL). The *in vitro* effects of red blood cells (RBC) and of white blood cells (WBC) on platelet rich plasma (PRP) aggregation were also evaluated. WB, PRP, WBC and RBC were prepared by conventional methods. Aggregation was performed using the impedance aggregometer (mod. 540, Chrono Log Corp). In normal subjects the concentration of collagen giving 50% aggregation ( $\text{AC}_{50}$ ) found in PRP did not differ from that of WB, indicating that hematocrit values within the normal range did not appreciably affect platelet aggregation. The results obtained in WB of patients are summarized in the table:

|                | Aggregation (%)        |                                |
|----------------|------------------------|--------------------------------|
|                | ADP (1 $\mu\text{M}$ ) | Collagen (1 $\mu\text{g/ml}$ ) |
| Controls (n=8) | 7.6 $\pm$ 2.4          | 13.4 $\pm$ 1.4                 |
| PV (n=4)       | 9.3 $\pm$ 3.6          | 7.6 $\pm$ 2.8 *                |
| IA (n=4)       | 7.2 $\pm$ 3.3          | 11.4 $\pm$ 3.0                 |
| PT (n=4)       | 15.7 $\pm$ 3.4 *       | 15.1 $\pm$ 0.2                 |
| ITP (n=4)      | 0                      | 3.1 $\pm$ 1.7 **               |
| LMC (n=4)      | 0                      | 5.4 $\pm$ 1.1 *                |
| IL (n=4)       | 0.6 $\pm$ 0.6 **       | 3.4 $\pm$ 1.3 **               |

*In vitro* data showed that aggregation in PRP and in WB of normal subjects was related to the number of platelets present in the sample. RBC added to PRP significantly reduced aggregation only when the RBC number was greater than  $4 \cdot 10^{12}$  cells. No effect of WBC on collagen induced aggregation of PRP was observed, whereas significant inhibition was detected after ADP. It is concluded that the aggregation evaluated in WB with impedance method is dependent on the platelet number. Also, *in vitro* data and studies in WB of patients indicate that aggregation is significantly affected by the presence of cells other than platelets only in conditions of changes of the ratio between platelets and leukocytes and/or red cells.