## 1079

PATIENTS WITH ARTIFICIAL BUT NOT BIOLOGICAL HEART VALVE PROSTHESIS PRESENT A HYPERCOAGULABILITY RELATED TO THE INTENSITY OF ANTICOAGULATION.

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Long term anticoagulant therapy is mandatory for patients with artificial heart valve prosthesis and is suggested for some patients with biological heart valve prosthesis. Oral anticoagulants reduce but not abolish thromboembolic complication in these patients. They act lowering the level of vitamin K-dependent coagulation factors and that in turn should result in a depression of "in vivo" thrombin formation. Fibrinopeptide A (FpA) is a good marker of thrombin formation and therefore we ascertained in several occasions the thrombin formation in 43 patients with artificial and 18 with biological heart valve prosthesis, all the patients being on oral anticoagulant treatment at least from 1 year. FpA was significantly higher in patients with artificial (determinations n=138) with respect to biological (n=73) heart valve prosthesis (p 0.01). The FpA level in biological valves was close to that obtained in 22 not anticoagulated healthy subjects. When we divided FpA values in artificial heart valves according to the intensity of anticoagulation, we obtained a decreasing FpA mean levels with the increase of the degree of anticoagulation. In particular FpA values with an INR 4.5 were close to values obtained in healthy subjects. These data support the concept that patients with artificial heart valves are at higher risk of thromboembolism and therefore the intensity of anticoagulation should be different with respect to biological valves and probably a little higher than that recommended at the Leuven Consensus Conference.

## 1080

A PROSPECTIVE RANDOMISED CONTROLLED STUDY OF MINI-DOSE WARFARIN PROPHYLAXIS OF DEEP VEIN THROMBOSIS IN MAJOR SURGERY.

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A prospective randomised study has been undertaken to assess the clinical effectiveness of oral anticoagulation using mini-dose warfarin (1 mg daily for 2-4 weeks before major gynaecological surgery) compared with conventional oral anticoagulant prophylaxis and an untreated randomised control group. The conventional oral anticoagulant prophylaxis was based on a therapeutic range of 1.5 - 2.0 INR at the time of operation and 2.0 - 3.0 INR post-operatively. Overall the mini-dose warfarin group showed no pre-operative prolongation of the prothrombin time with the Manchester Reagent although a minority of patients showed a 1-2 second prolongation of the prothrombin time before operation. Post operatively the mini-dose warfarin group showed an exaggerated prolongation of the prothrombin time which normally occurs after operation and was observed in the untreated controls. Factor VII assays paralleled these findings. Mini-dose warfarin, while not prolonging the prothrombin time before operation, resulted in delayed platelet aggregation with the Chandler's tube technique in almost all patients.

The incidence of deep vein thrombosis has been reduced in both mini-dose and conventional dose oral anticoagulant series compared with the untreated group. It appears that the minimal changes in the prothrombin time, factor VII and platelet aggregation tests, observed in the mini-dose warfarin group, may offer sufficient protection against post-operative thrombosis in a moderate risk group undergoing abdominal or pelvic surgery.

## 1081

CALIBRATED PLASMA PROCEDURE AND INR FOR PT STANDARDIZATION. DATA FROM THE FRENCH ETALONORME QUALITY CONTROL SURVEYS.

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One of the aim of the survey conducted in last december 1986 was to assess the efficacy of 2 procedures of standardization :

1) the INR system, derived from thromboplastin calibration and adopted in 1983 by the WHO,

2) the Reference Calibrated Plasmas (RCP) procedure, evaluated on large scale, through French interlaboratory trials (1977-85), exhibiting net improvement of the dispersion of overall data.

Labs were asked to perform with their local thromboplastin and method, the PT of a human lyophilized plasma 86 H/I, originated from long term antivitamines-K (AVK) treated patients. Results were expressed *in time ; *in % activity, according to the traditional procedure based on saline dilutions of normal plasma ; *in INR using the ISI of the local reagent calibrated by the manufacturer. Calibrated plasmas procedure allow the determination of corrected activity ; *in % activity and INR, according to the linear calibration curve obtained from the PT of 2 reference calibrated plasmas with determinated activities in INR and % activity. These RCP were provided with and tested under the same conditions as plasma 86 H/I6 (2 systems of RCP : AVK and artificially depleted).

Statistical analysis shows that the "RCP" procedure leads to the best improvement of the interlaboratory variation for the overall data, and the best uniformization of mean results, whatever the way of expression (%, INR), the thromboplastin brand, and the method of PT testing. Results play also in favour of a system of AVK reference plasmas, giving a better grouping than the artificial calibrated plasmas. The INR system nevertheless provides a common scale of data reporting, but might hold profit from an efficient procedure of standardization, such as the calibrated AVK plasmas procedure.

| Procedure Expression | Usual % Act. | Calibrated plasmas % Act. | INR | INR syst. | |
|---|---|---|---|---|---|
| AVK Ref. Plasmas | 14.1 | 8.9 | 12.5 | 18.5 | 1457 labs |
| Artif. Ref. Plasmas | 14.8 | 12.3 | 15.2 | 20 | 1000 labs |

Coefficient of variation (CV) expressed in %. Overall data PT of 86 H/I. French Etalonorme Survey.

## 1082

USE OF INR FOR THE EXPRESSION OF PT IN PATIENTS UNDER ORAL ANTICOAGULANTS : COMPARISON OF RESULTS OBTAINED WITH FIVE THROMBOPLASTINS AND THREE DEVICES.

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The aim of our study is to know if INR (International Normalized Ratio) is really the best way to express PT (Prothrombin Time) in patients under oral anticoagulants (AVK). In this way, PT of 85 patients treated by AVK and 30 normal controls were determined with 5 different reagents and three devices : manual technic, KC10 (AHS Dade), Coag A Pet 200 (Gal Diagnostics, Organon). The reagents were : Thromborel S (Behring) extracted from human placenta, Thrombotest (Nyegaard) from ox brain, and 3 rabbit thromboplastins : Neoplastine (Diagnostica Stago), Thromboplastine calcique (Bio-Merieux), Simplastin + (Gal Diagnostics). The results are expressed in seconds, percentage according to the dilution curve and INR with ISI given by the manufacturers.

Analysis of results shows :

- Influence of the technic : Whatever the technic is, mean results obtained with the same reagent, expressed in % are very close ; expressed in INR mean results are dispersed with all the reagents, ex :

| Stago | % | INR |
|---|---|---|
| Manuel | 33.4 | 3.4 |
| KC10 | 33.8 | 2.1 |
| CAP | 35.6 | 2.6 |

- Influence of the reagent : Results performed with the same technic whatever the reagent is expressed in INR are very close, whereas in % the dispersion is large.

| KC10 | Thrombotest | Behring | Stago | Merieux | GD |
|---|---|---|---|---|---|
| % | 14.1 | 26.1 | 33.8 | 37 | 44.25 |
| INR | 2.9 | 3 | 3.1 | 2.9 | 2.9 |

Analysis of variance and Student test show highly significant differences between all reagents for expression in %, whereas expressed in INR (KC10) the difference is not statistically significant.

INR leads an improvement in the dispersion of results but it seems necessary to have at least two ISI for each reagent, one determined by manual technic or device like KC10, the other one determined on photo-optical device.