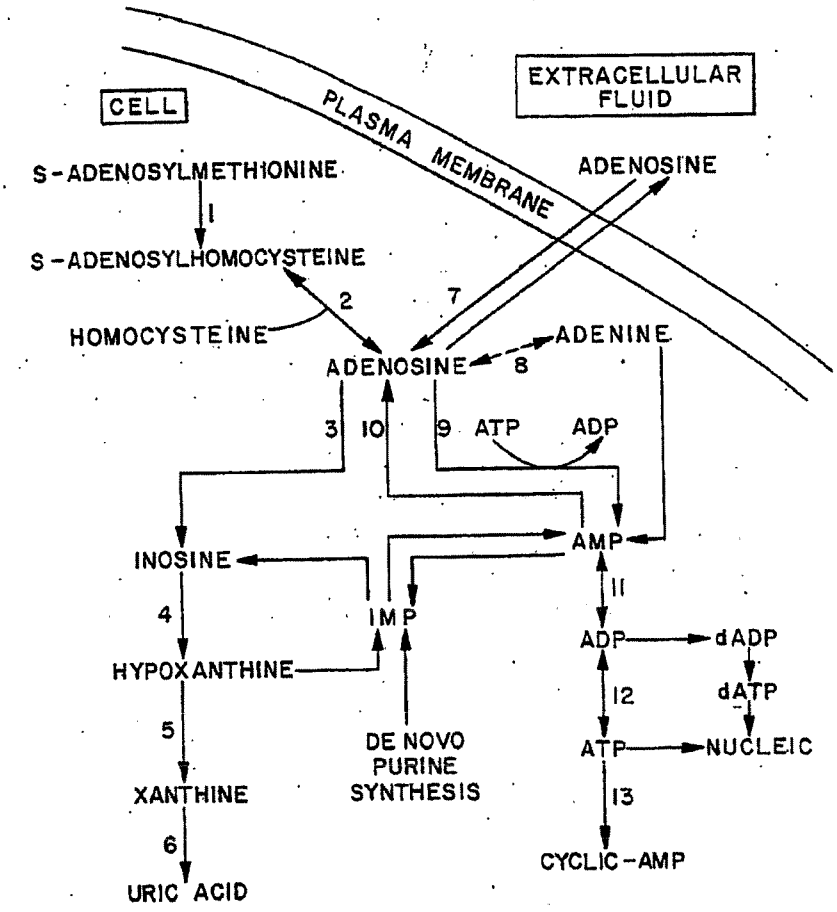

CELL
PLASMA MEMBRANE
EXTRACELLULAR FLUID
S-ADENOSYLMETHIONINE
ADENOSINE
1
S-ADENOSYLHOMOCYSTEINE
2
7
HOMOCYSTEINE
ADENINE
ADENOSINE
8
3
10
9
ATP
ADP
AMP
INOSINE
11
4
IMP
ADP
dADP
HYPOXANTHINE
12
dATP
5
DE NOVO PURINE SYNTHESIS
ATP
NUCLEIC
XANTHINE
13
6
CYCLIC-AMP
URIC ACID

FIG. 1

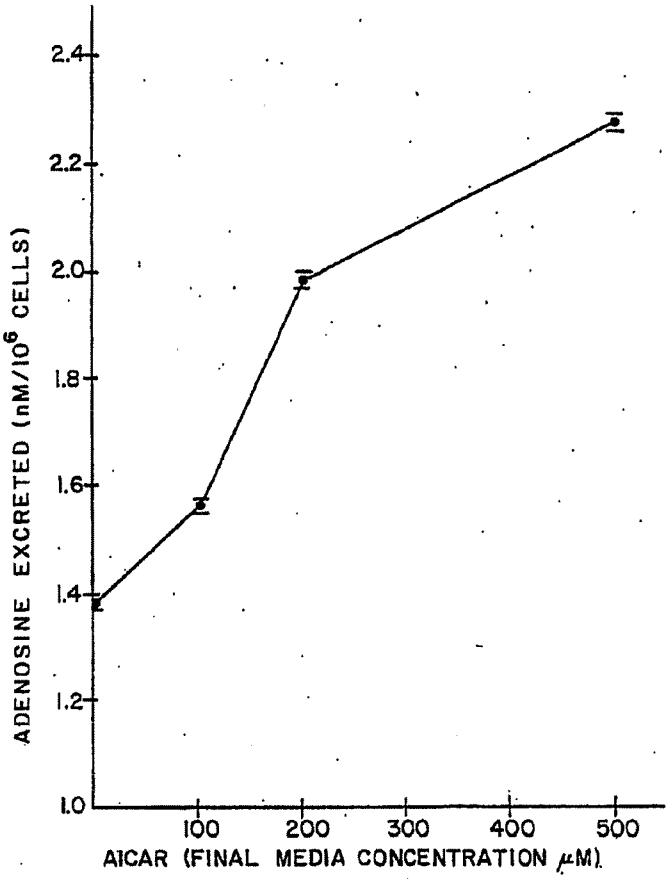

ADENOSINE EXCRETED (nM/10^6 CELLS)
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
100
200
300
400
500
AICAR (FINAL MEDIA CONCENTRATION μM)

FIG. 2

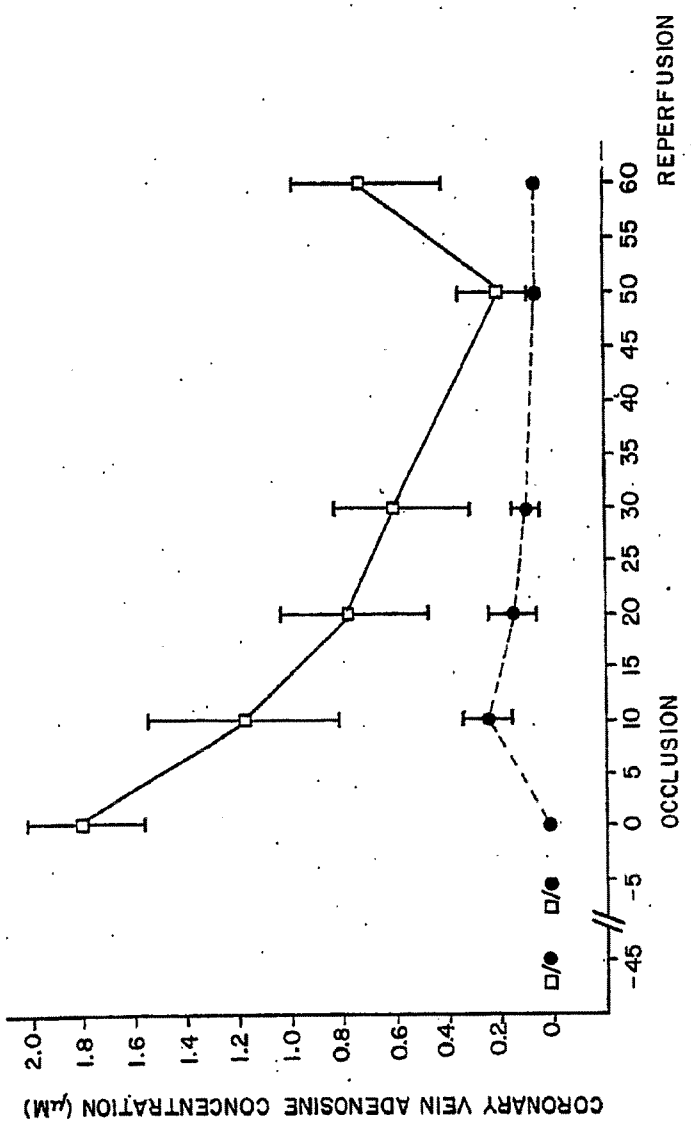

CORONARY VEIN ADENOSINE CONCENTRATION (μM)
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
□/●
□/●
-45
-5
0
5
10
15
20
25
30
35
40
45
50
55
60
OCCLUSION
REPERFUSION
TIME (MINUTES)

FIG. 3

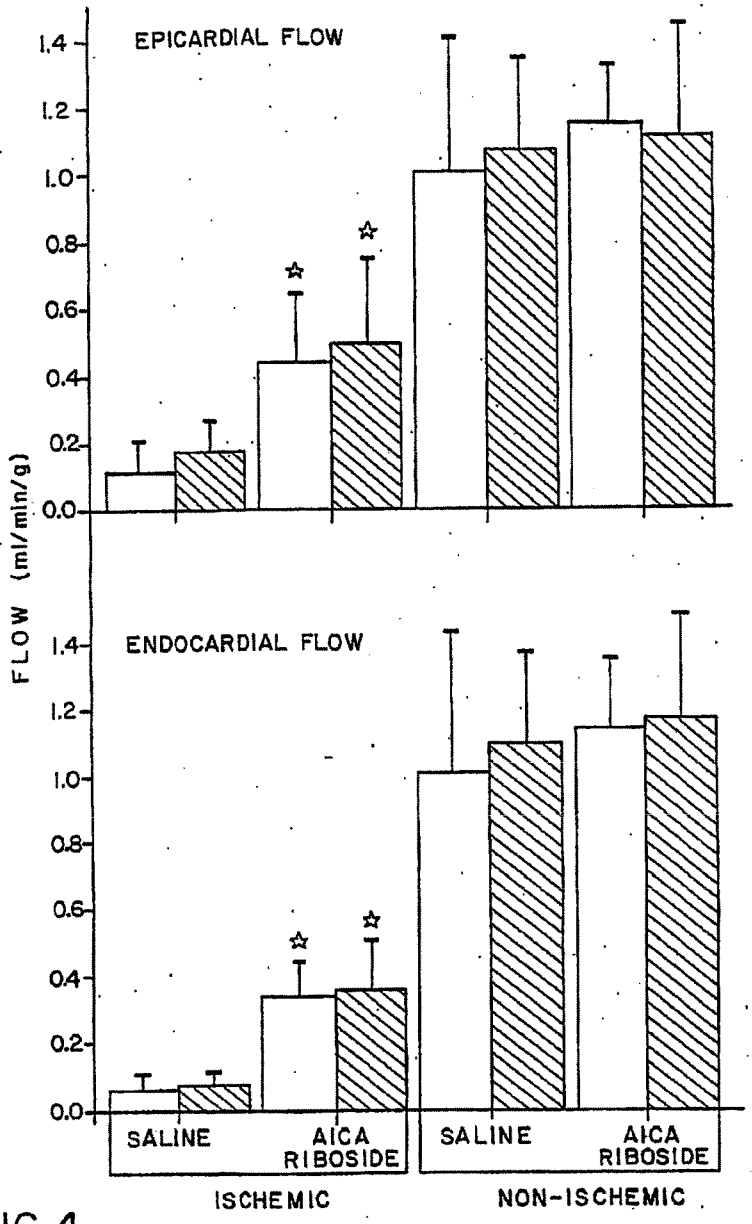

EPICARDIAL FLOW
ENDOCARDIAL FLOW
FLOW (ml/min/g)
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
SALINE
AICA RIBOSIDE
SALINE
AICA RIBOSIDE
ISCHEMIC
NON-ISCHEMIC

FIG.4

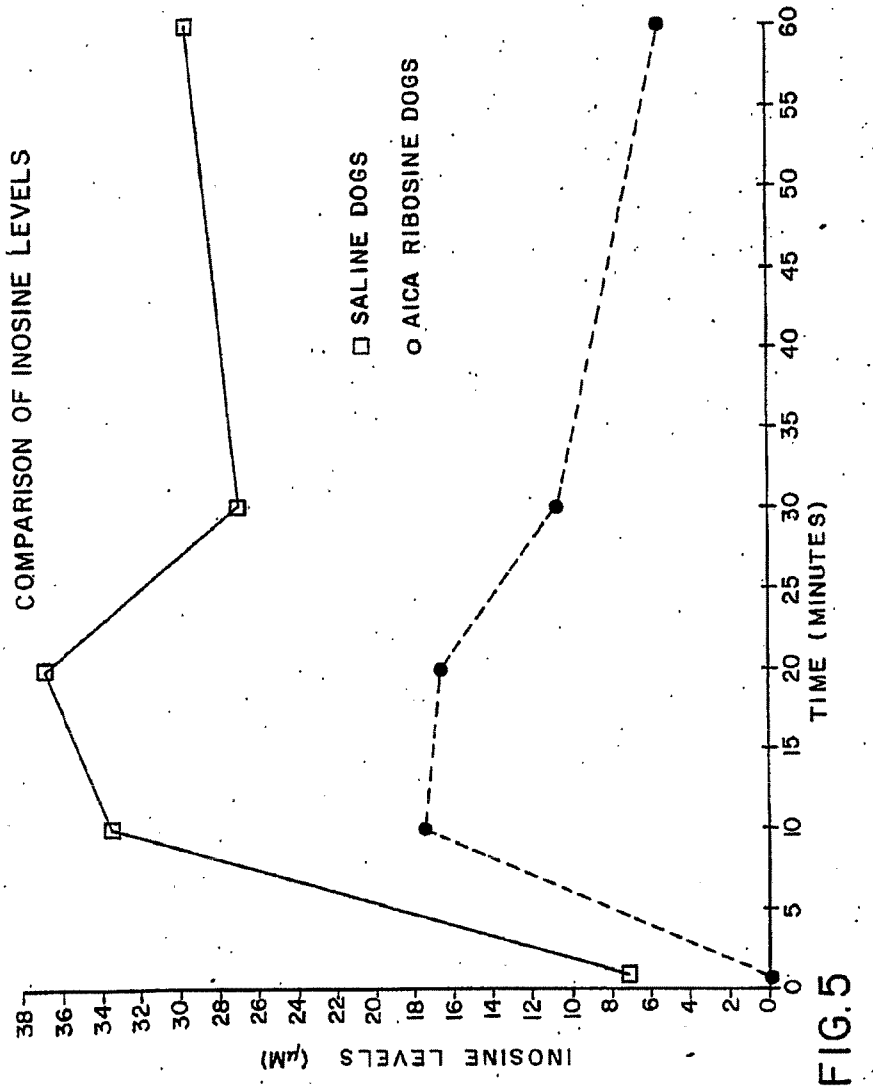

COMPARISON OF INOSINE LEVELS
□ SALINE DOGS
o AICA RIBOSINE DOGS
INOSINE LEVELS (μM)
TIME (MINUTES)
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
0
5
10
15
20
25
30
35
40
45
50
55
60

FIG. 5

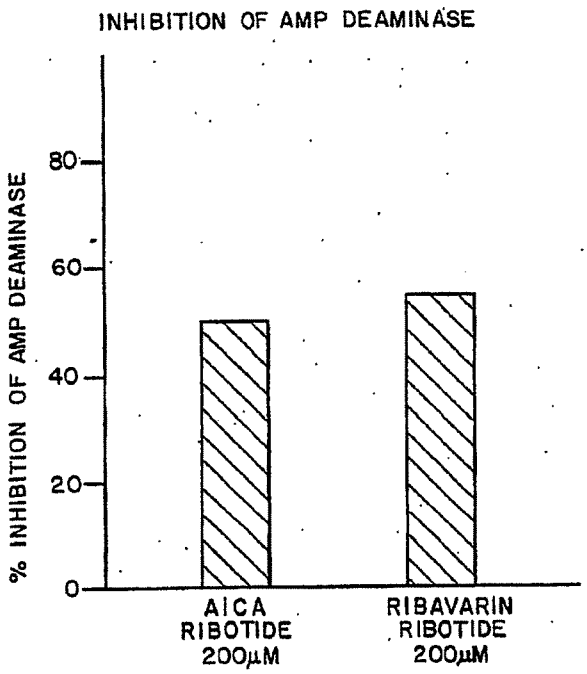

INHIBITION OF AMP DEAMINASE
% INHIBITION OF AMP DEAMINASE
80
60
40
20
0
AICA RIBOTIDE 200μM
RIBAVARIN RIBOTIDE 200μM

FIG. 6

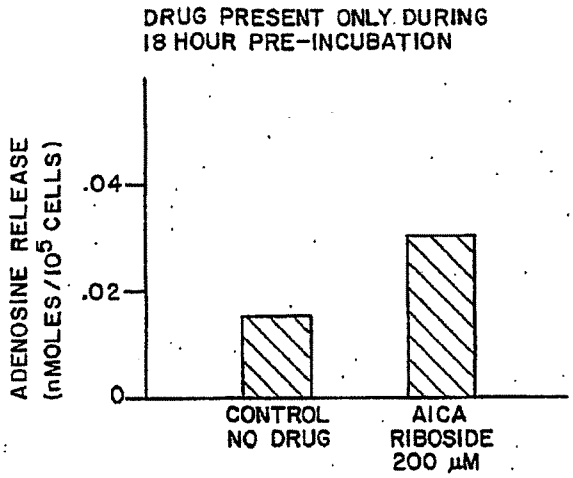

DRUG PRESENT ONLY DURING
18 HOUR PRE-INCUBATION
ADENOSINE RELEASE
(nMOLES/10^5 CELLS)
.04
.02
0
CONTROL
NO DRUG
AICA
RIBOSIDE
200 μM

FIG. 7

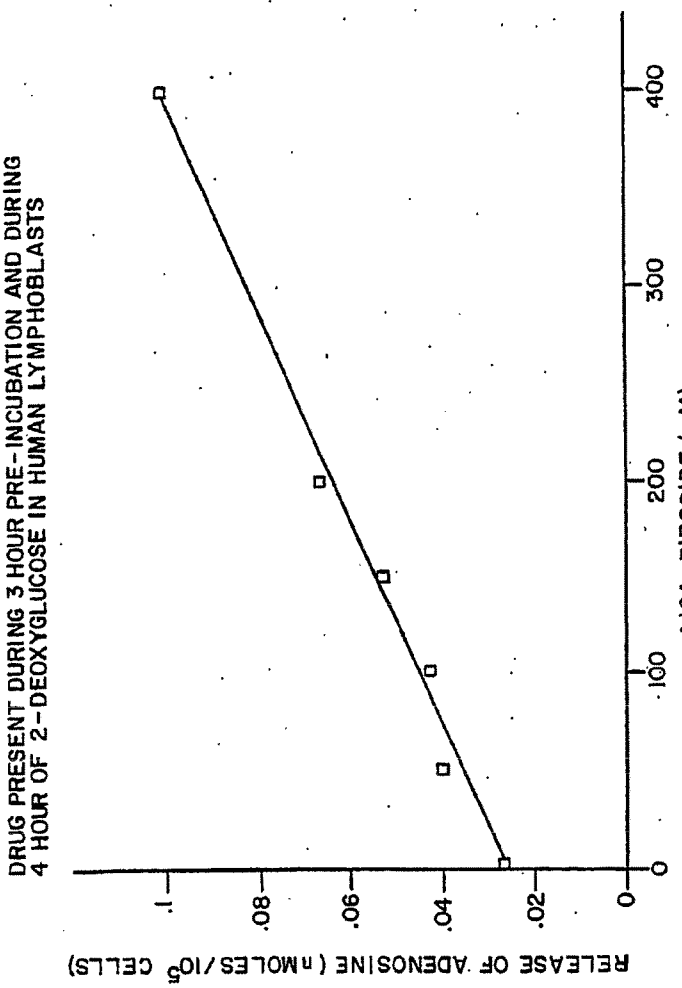

DRUG PRESENT DURING 3 HOUR PRE-INCUBATION AND DURING
4 HOUR OF 2-DEOXYGLUCOSE IN HUMAN LYMPHOBLASTS
RELEASE OF ADENOSINE (nMOLES/10⁵ CELLS)
.1
.08
.06
.04
.02
0
0
100
200
300
400
AICA RIBOSIDE (μM)

FIG. 8

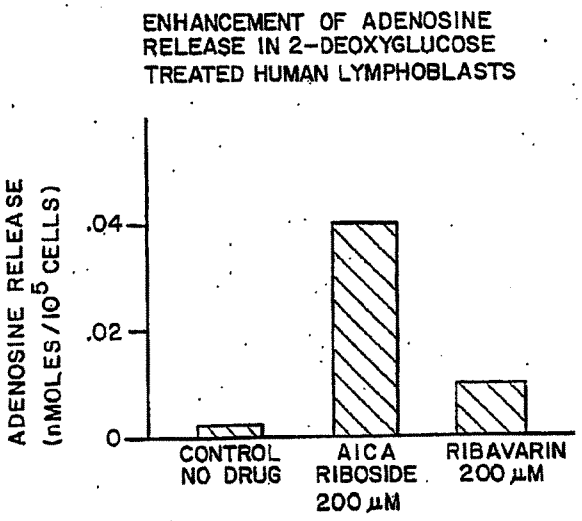

ENHANCEMENT OF ADENOSINE
RELEASE IN 2-DEOXYGLUCOSE
TREATED HUMAN LYMPHOBLASTS
ADENOSINE RELEASE
(nMOLES/10^5 CELLS)
.04
.02
0
CONTROL
NO DRUG
AICA
RIBOSIDE
200 µM
RIBAVARIN
200 µM

FIG. 9

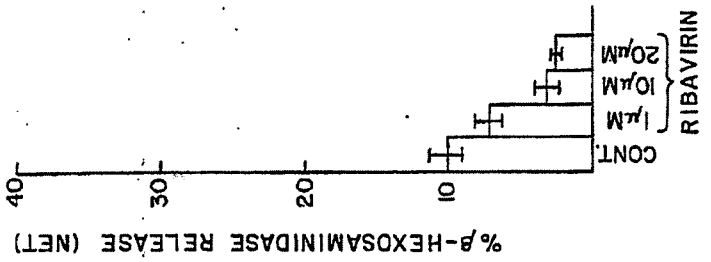

% β-HEXOSAMINIDASE RELEASE (NET)
40
30
20
10
CONT.
1μM
10μM
20μM
RIBAVIRIN

FIG. 11

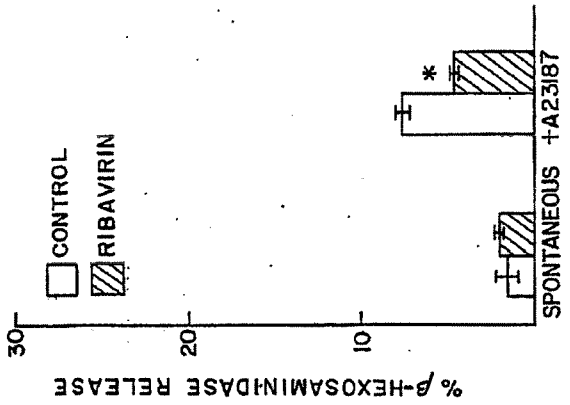

% β-HEXOSAMINIDASE RELEASE
30
20
10
CONTROL
RIBAVIRIN
*
SPONTANEOUS
+A23187

FIG. 10

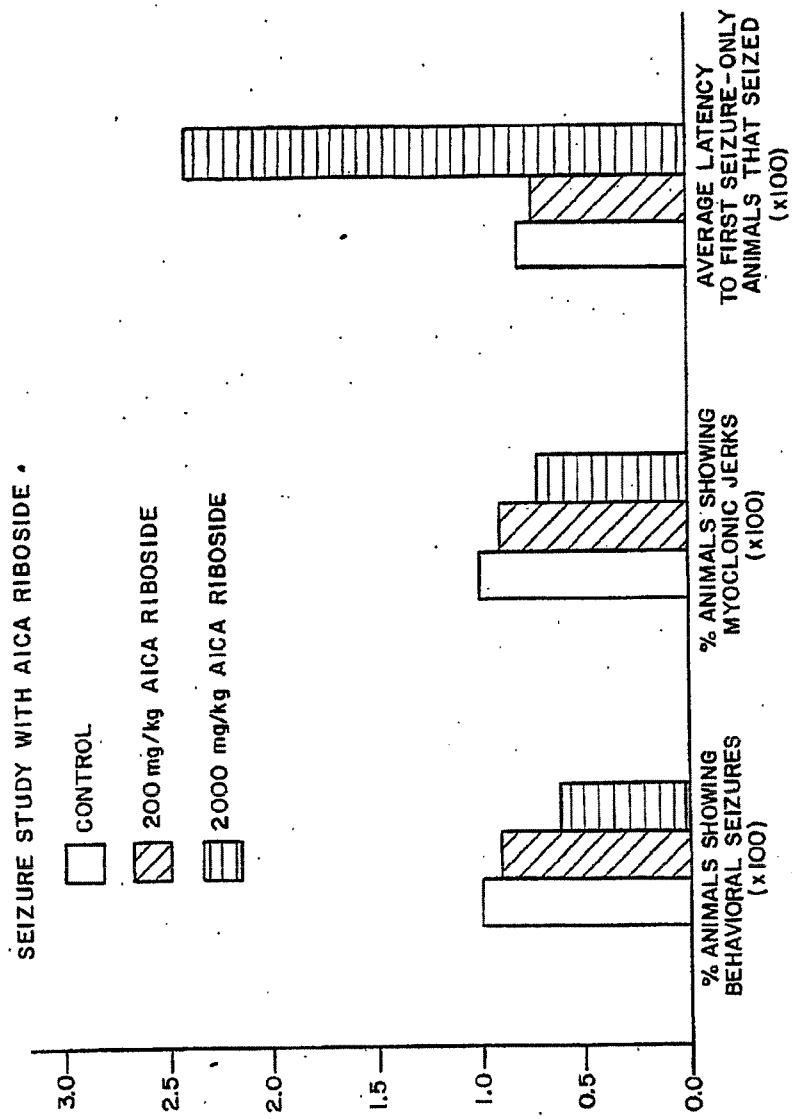

SEIZURE STUDY WITH AICA RIBOSIDE
CONTROL
200 mg/kg AICA RIBOSIDE
2000 mg/kg AICA RIBOSIDE
3.0
2.5
2.0
1.5
1.0
0.5
0.0
% ANIMALS SHOWING BEHAVIORAL SEIZURES (x100)
% ANIMALS SHOWING MYOCLONIC JERKS (x100)
AVERAGE LATENCY TO FIRST SEIZURE-ONLY ANIMALS THAT SEIZED (x100)

FIG. 12

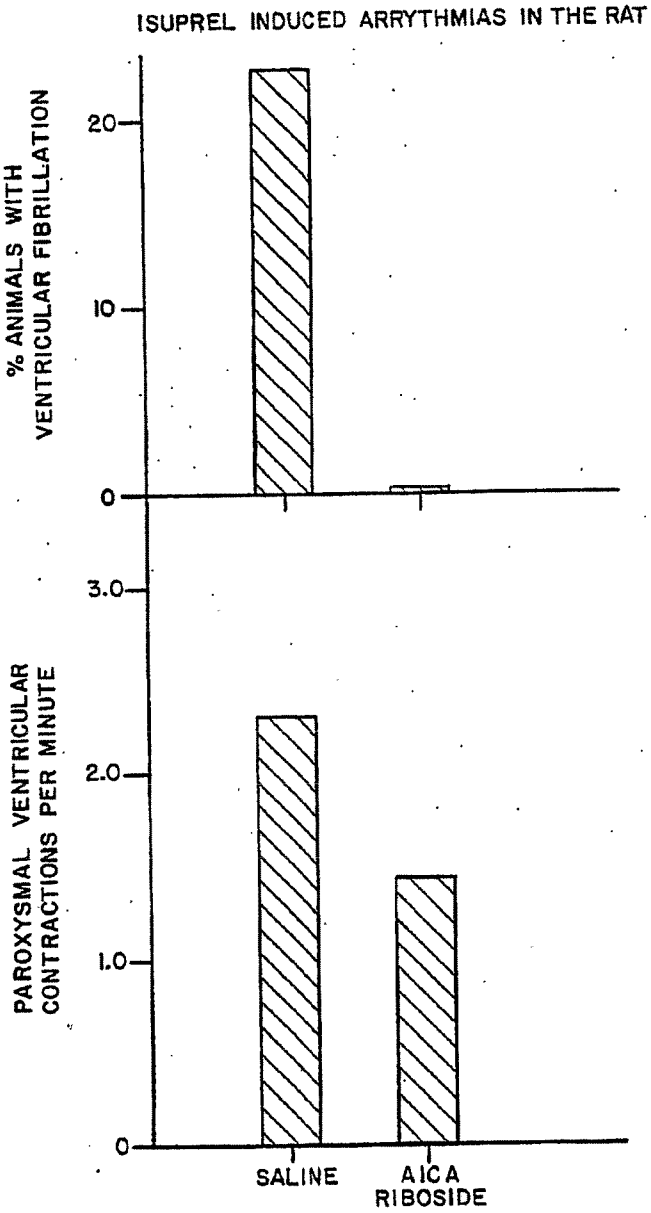

ISUPREL INDUCED ARRYTHMIAS IN THE RAT
% ANIMALS WITH VENTRICULAR FIBRILLATION
20
10
0
PAROXYSMAL VENTRICULAR CONTRACTIONS PER MINUTE
3.0
2.0
1.0
0
SALINE
AICA RIBOSIDE

FIG. 13

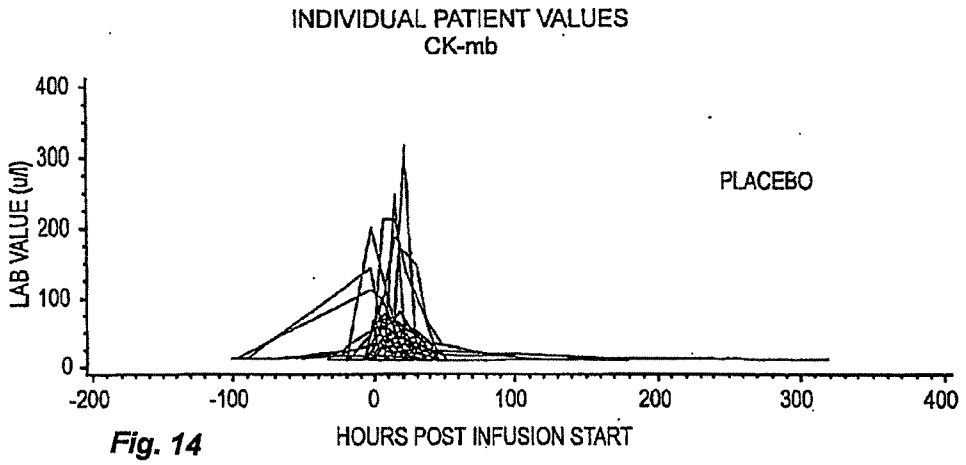


Fig. 14

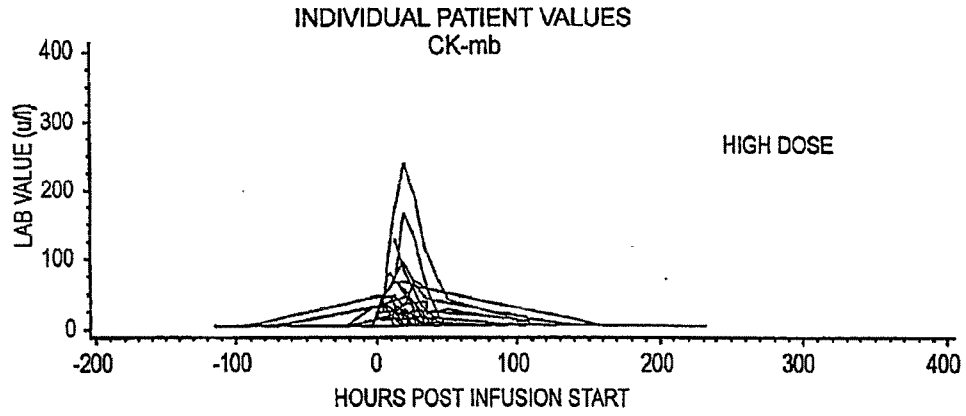


Fig. 15

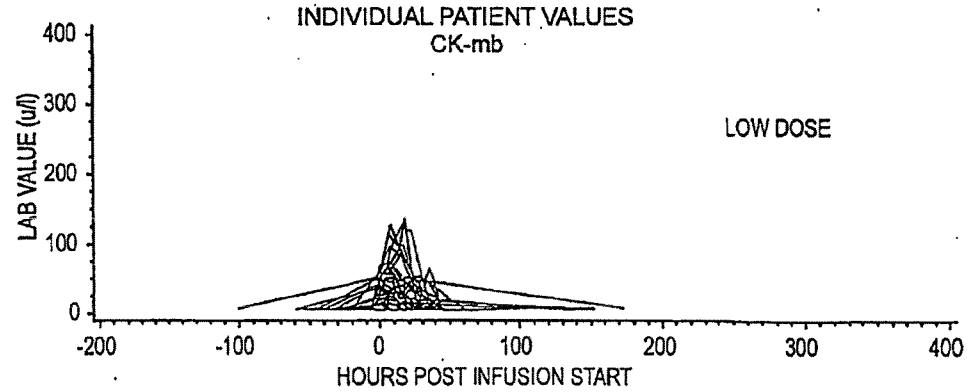


Fig. 16

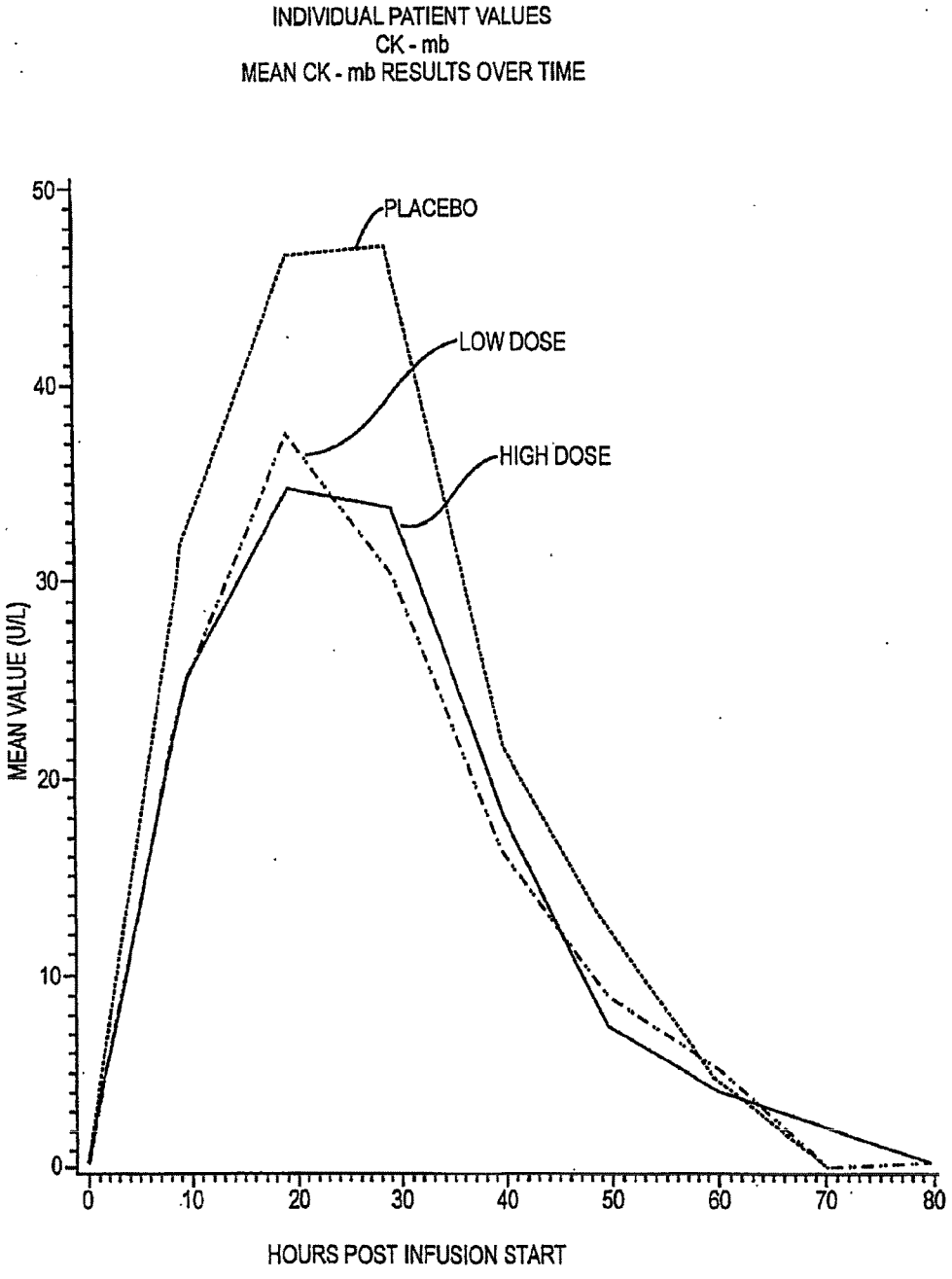

INDIVIDUAL PATIENT VALUES
CK - mb
MEAN CK - mb RESULTS OVER TIME
PLACEBO
LOW DOSE
HIGH DOSE
MEAN VALUE (U/L)
HOURS POST INFUSION START
0
10
20
30
40
50
60
70
80

Fig. 17

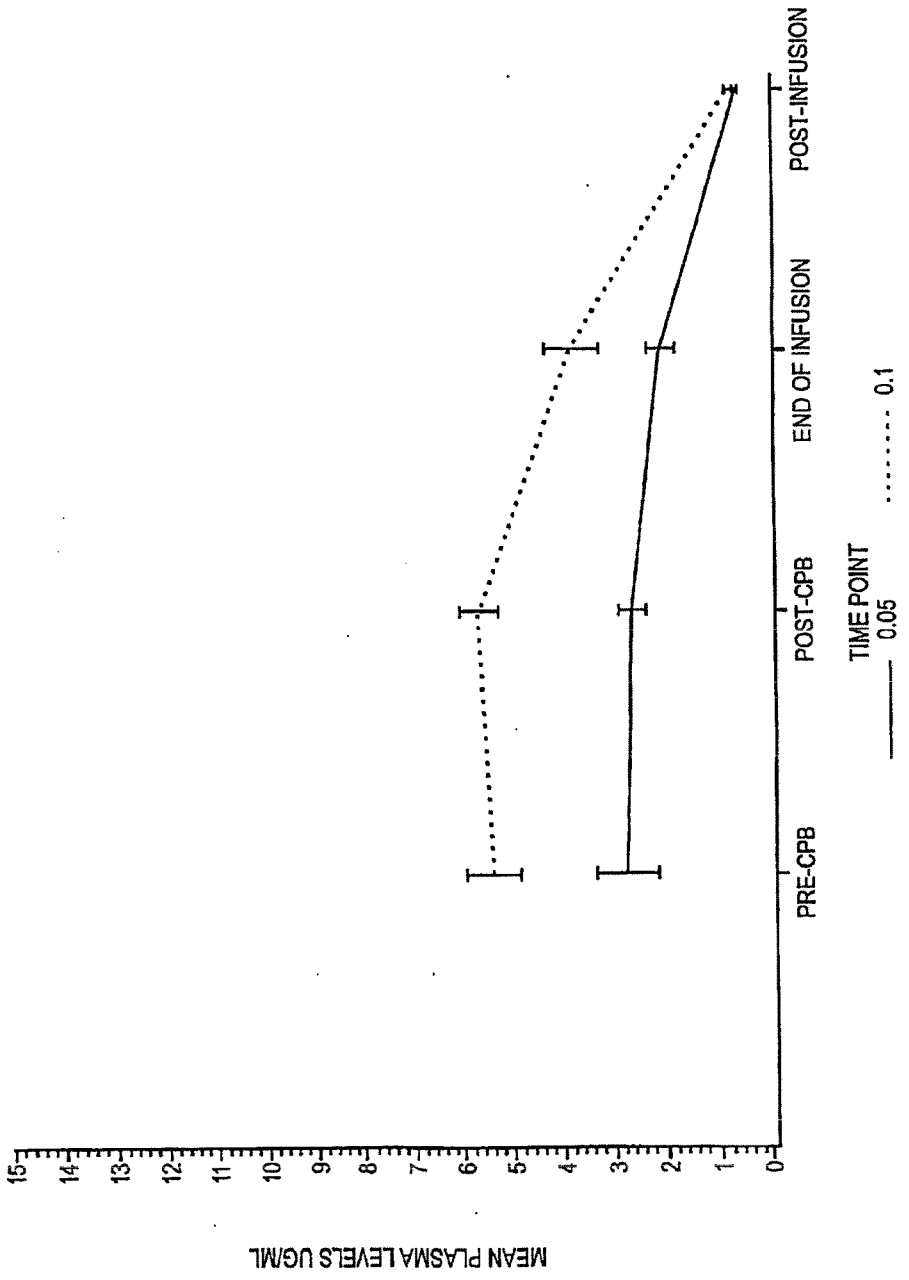

MEAN PLASMA LEVELS UG/ML
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
PRE-CPB
POST-CPB
END OF INFUSION
POST-INFUSION
TIME POINT
0.05
0.1

Fig. 18

Fig. 19

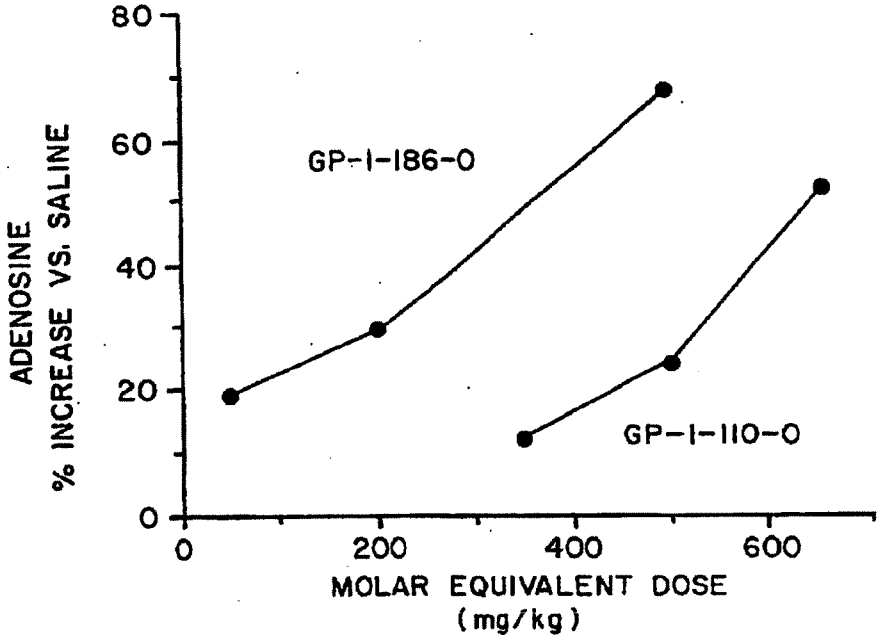


Fig. 20A

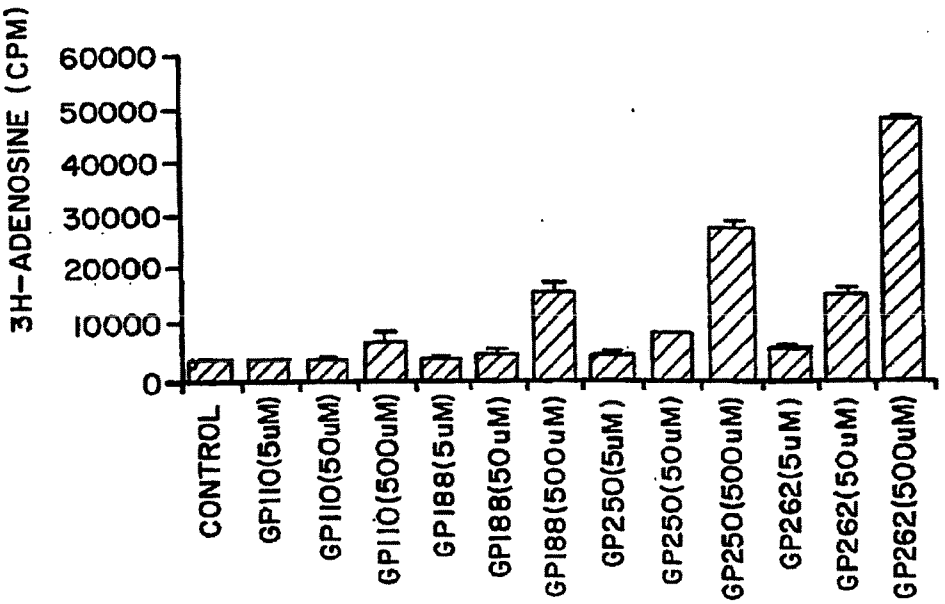


Fig. 20B

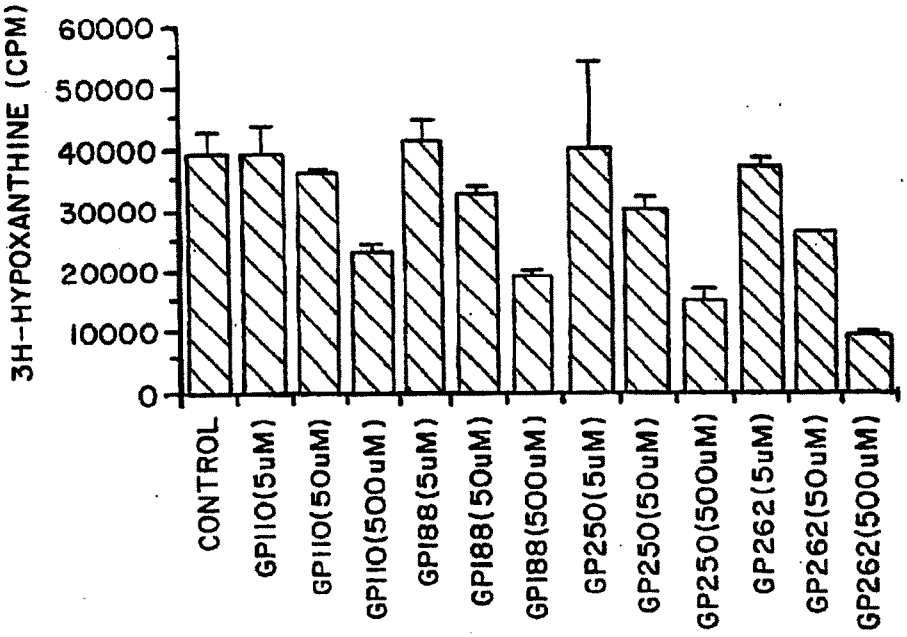


Fig. 20C

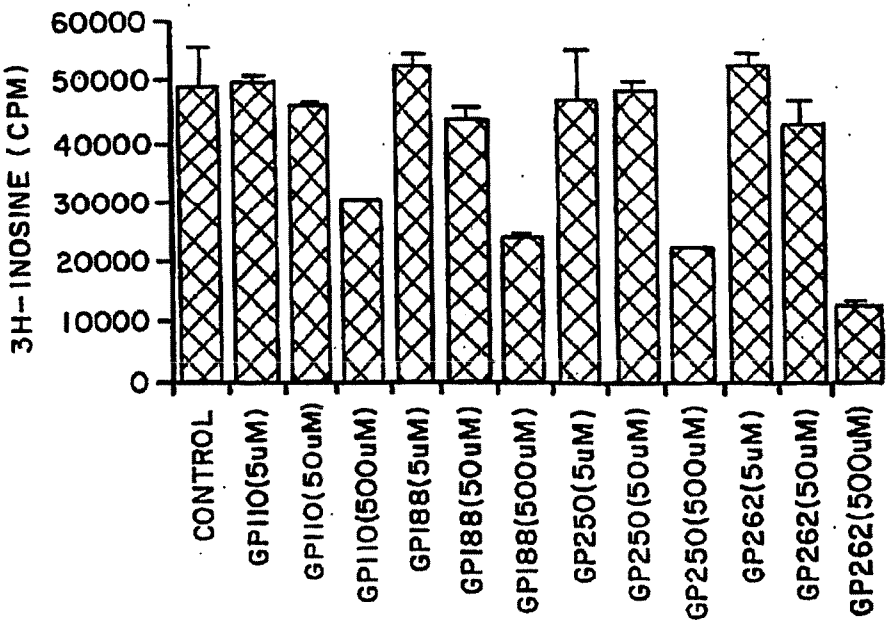


Fig. 21

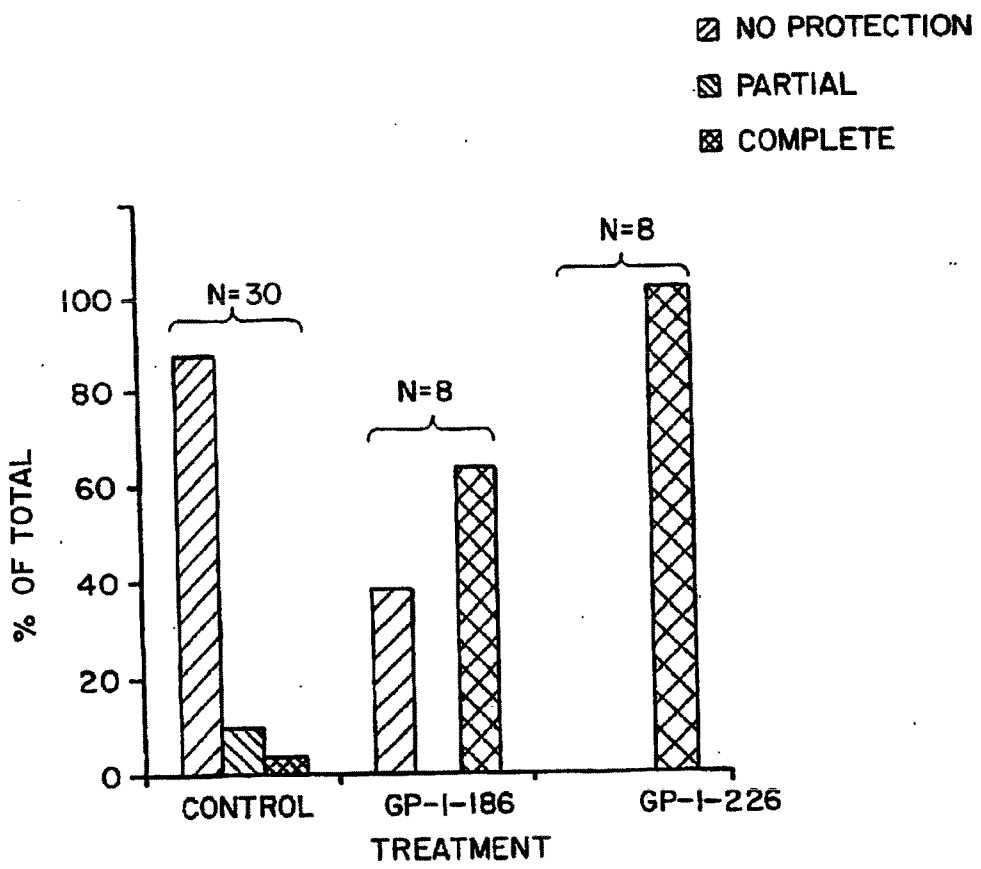

NO PROTECTION
PARTIAL
COMPLETE
N=30
N=8
N=8
100
80
60
40
20
0
% OF TOTAL
CONTROL
GP-I-186
GP-I-226
TREATMENT

Fig. 22

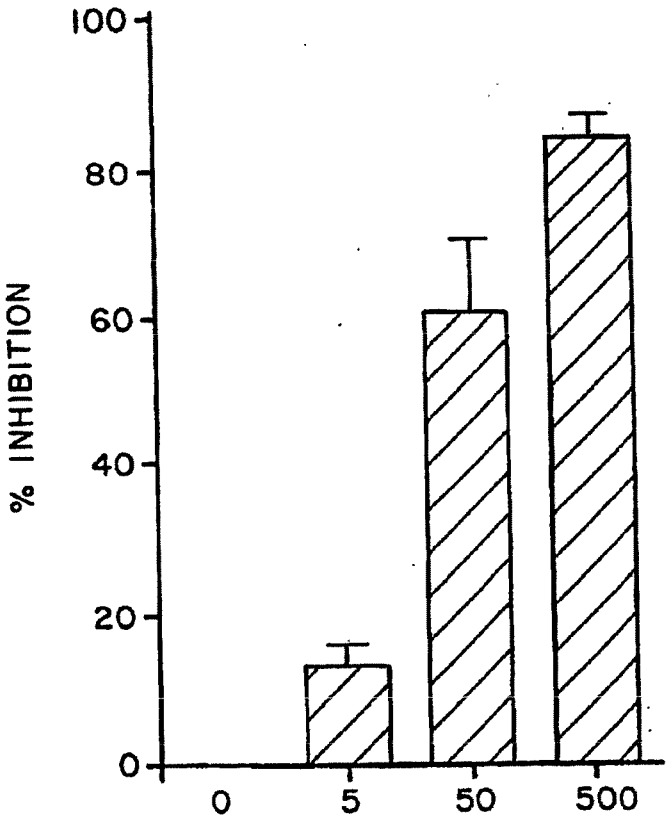


Fig. 23

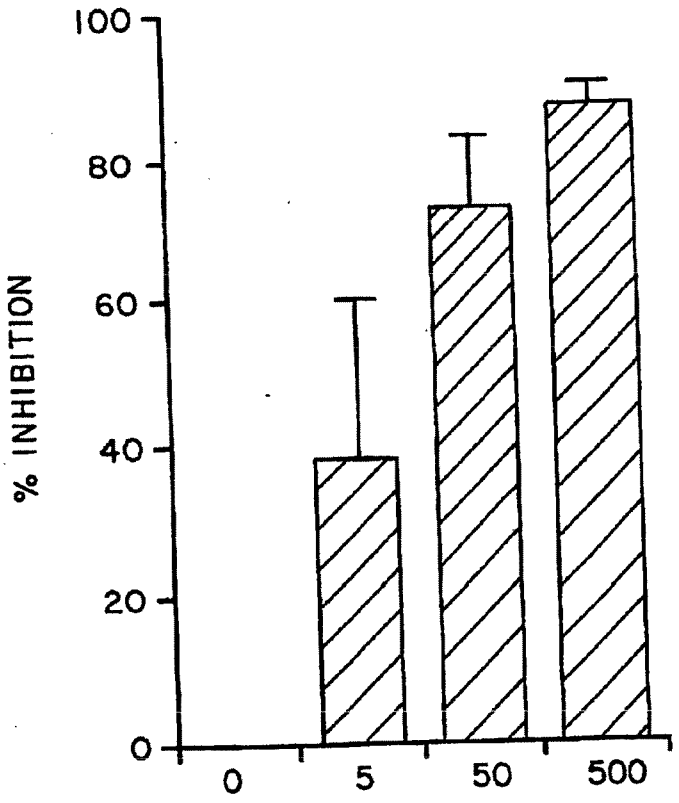
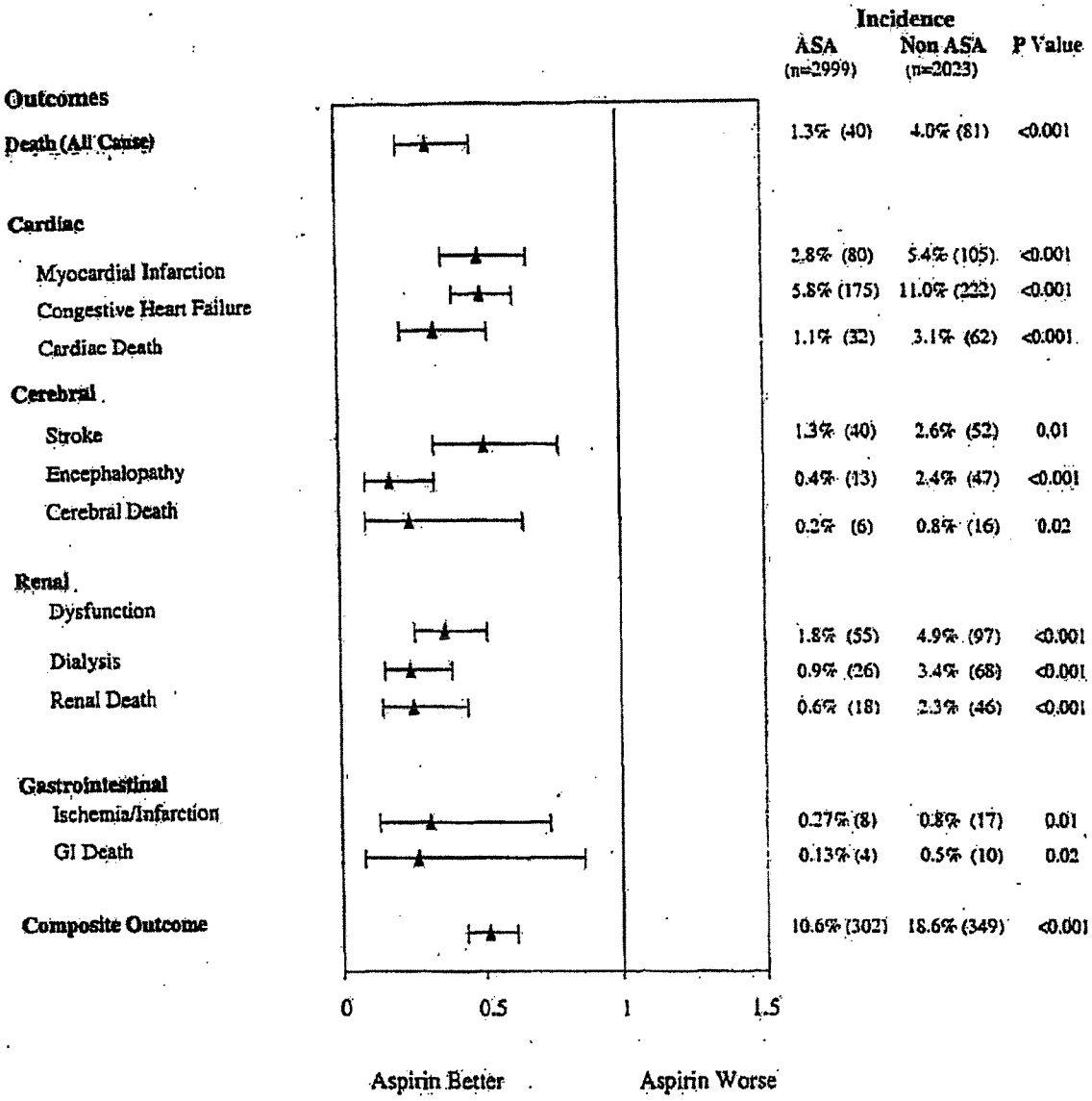
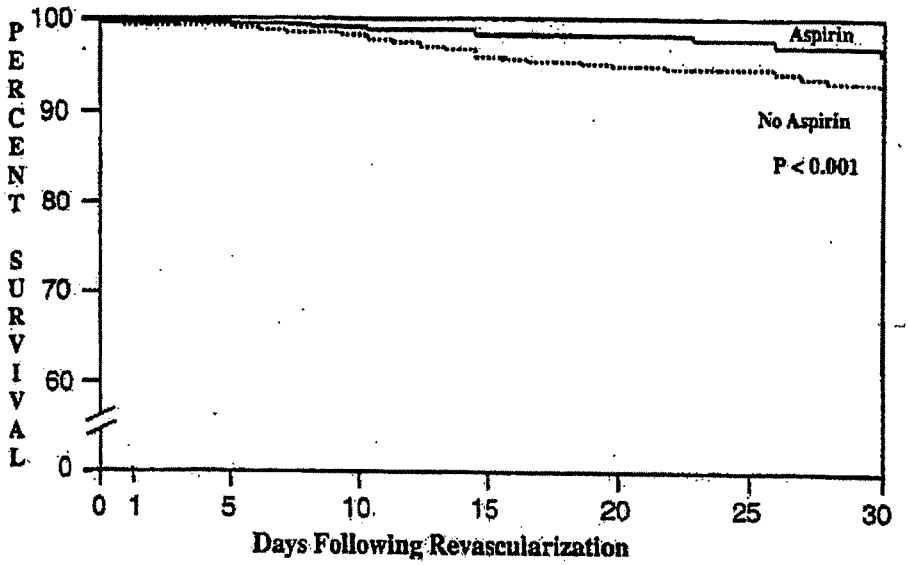


Fig. 24


Incidence
ASA (n=2999)
Non ASA (n=2023)
P Value
Outcomes
Death (All Cause) 1.3% (40) 4.0% (81) <0.001
Cardiac
Myocardial Infarction 2.8% (80) 5.4% (105) <0.001
Congestive Heart Failure 5.8% (175) 11.0% (222) <0.001
Cardiac Death 1.1% (32) 3.1% (62) <0.001
Cerebral
Stroke 1.3% (40) 2.6% (52) 0.01
Encephalopathy 0.4% (13) 2.4% (47) <0.001
Cerebral Death 0.2% (6) 0.8% (16) 0.02
Renal
Dysfunction 1.8% (55) 4.9% (97) <0.001
Dialysis 0.9% (26) 3.4% (68) <0.001
Renal Death 0.6% (18) 2.3% (46) <0.001
Gastrointestinal
Ischemia/Infarction 0.27% (8) 0.8% (17) 0.01
GI Death 0.13% (4) 0.5% (10) 0.02
Composite Outcome 10.6% (302) 18.6% (349) <0.001
0
0.5
1
1.5
Aspirin Better
Aspirin Worse



Aspirin	0	13	21	28	28	29	31
No Aspirin	0	18	41	58	63	64	68

Cumulative Deaths by Day

Fig. 25

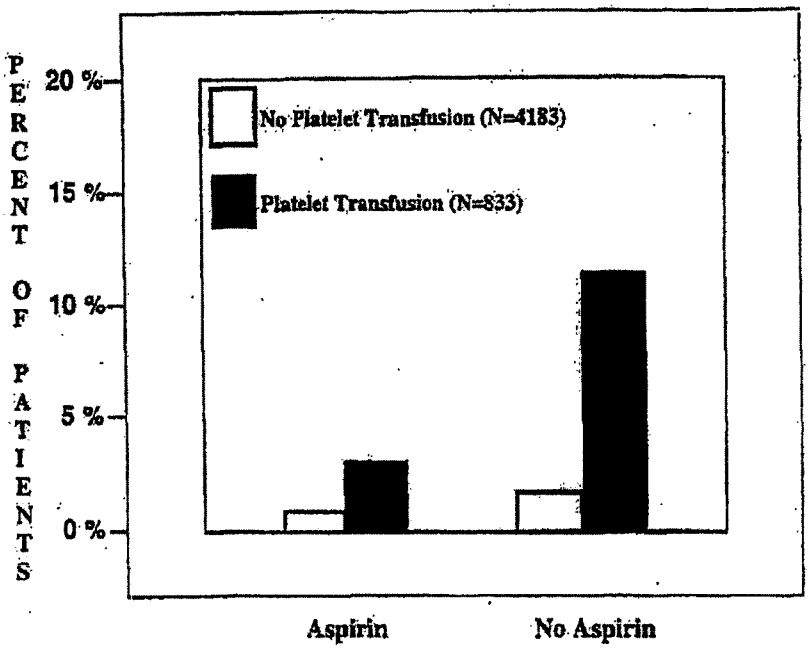

PERCENT OF PATIENTS
20 %
15 %
10 %
5 %
0 %
No Platelet Transfusion (N=4183)
Platelet Transfusion (N=833)
Aspirin
No Aspirin

FIG. 26

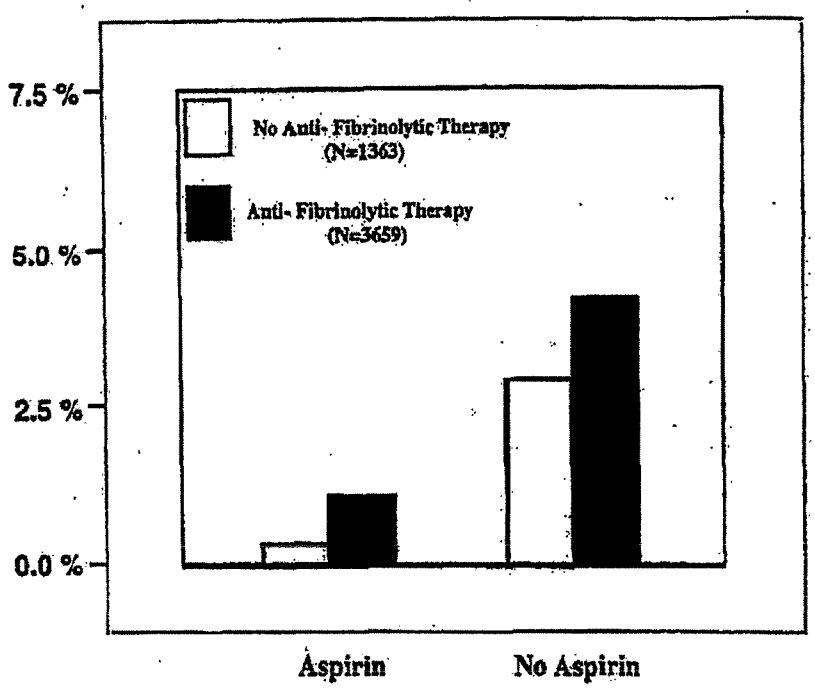

7.5 %
5.0 %
2.5 %
0.0 %
No Anti- Fibrinolytic Therapy
(N=1363)
Anti- Fibrinolytic Therapy
(N=3659)
Aspirin
No Aspirin

Fig. 27