

FIG.1

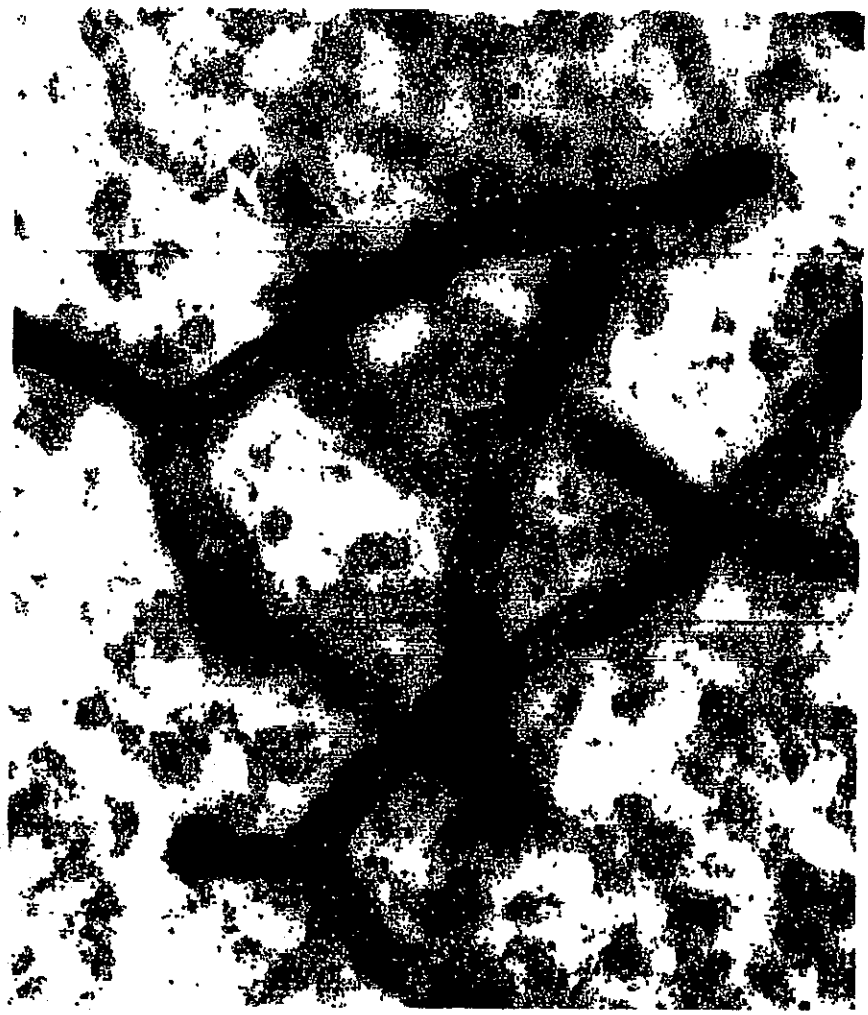


FIG.2



FIG.3



FIG.4

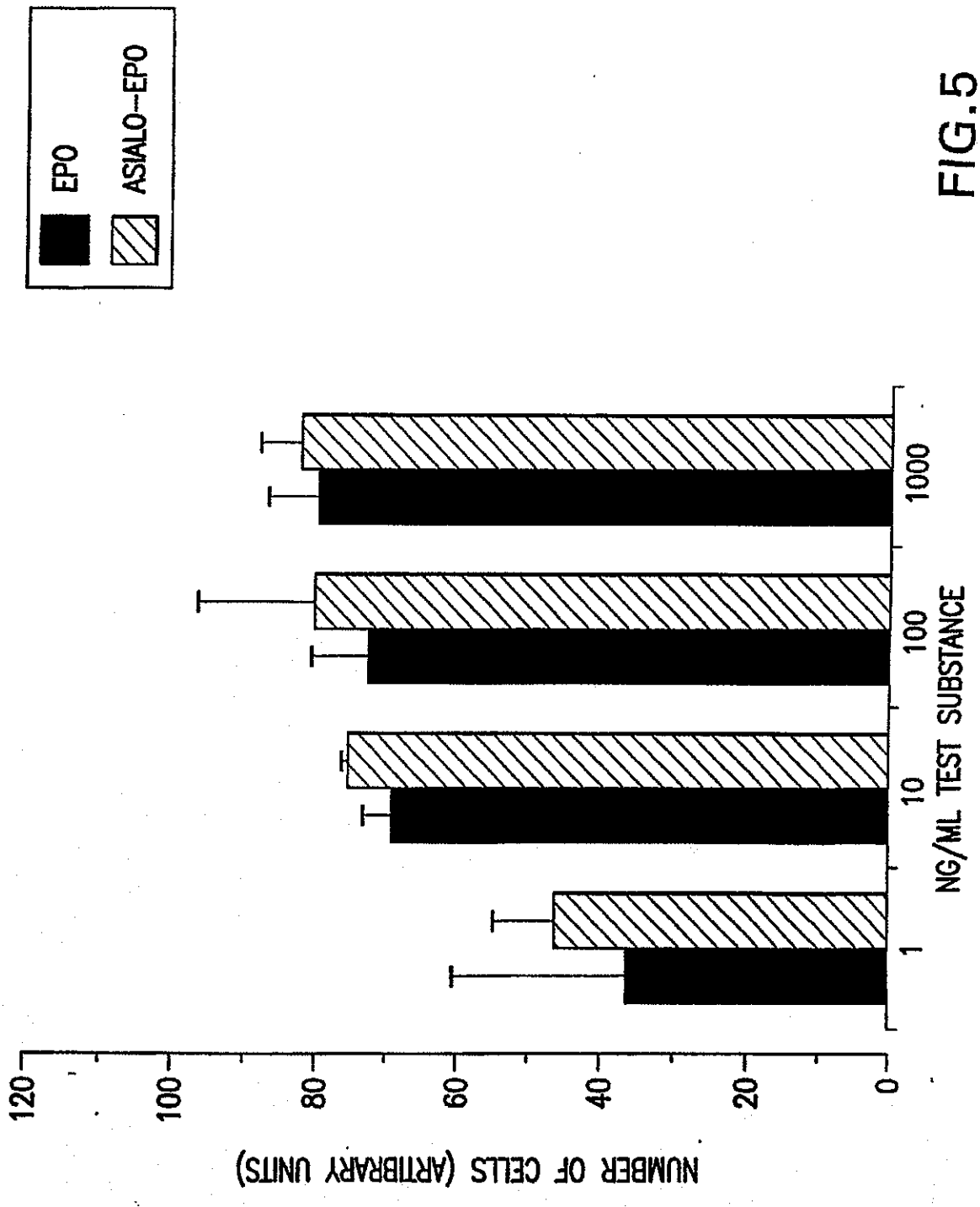

EPO
ASIALO-EPO
NUMBER OF CELLS (ARTIBRARY UNITS)
120
100
80
60
40
20
0
1
10
100
1000
NG/ML TEST SUBSTANCE

FIG.5

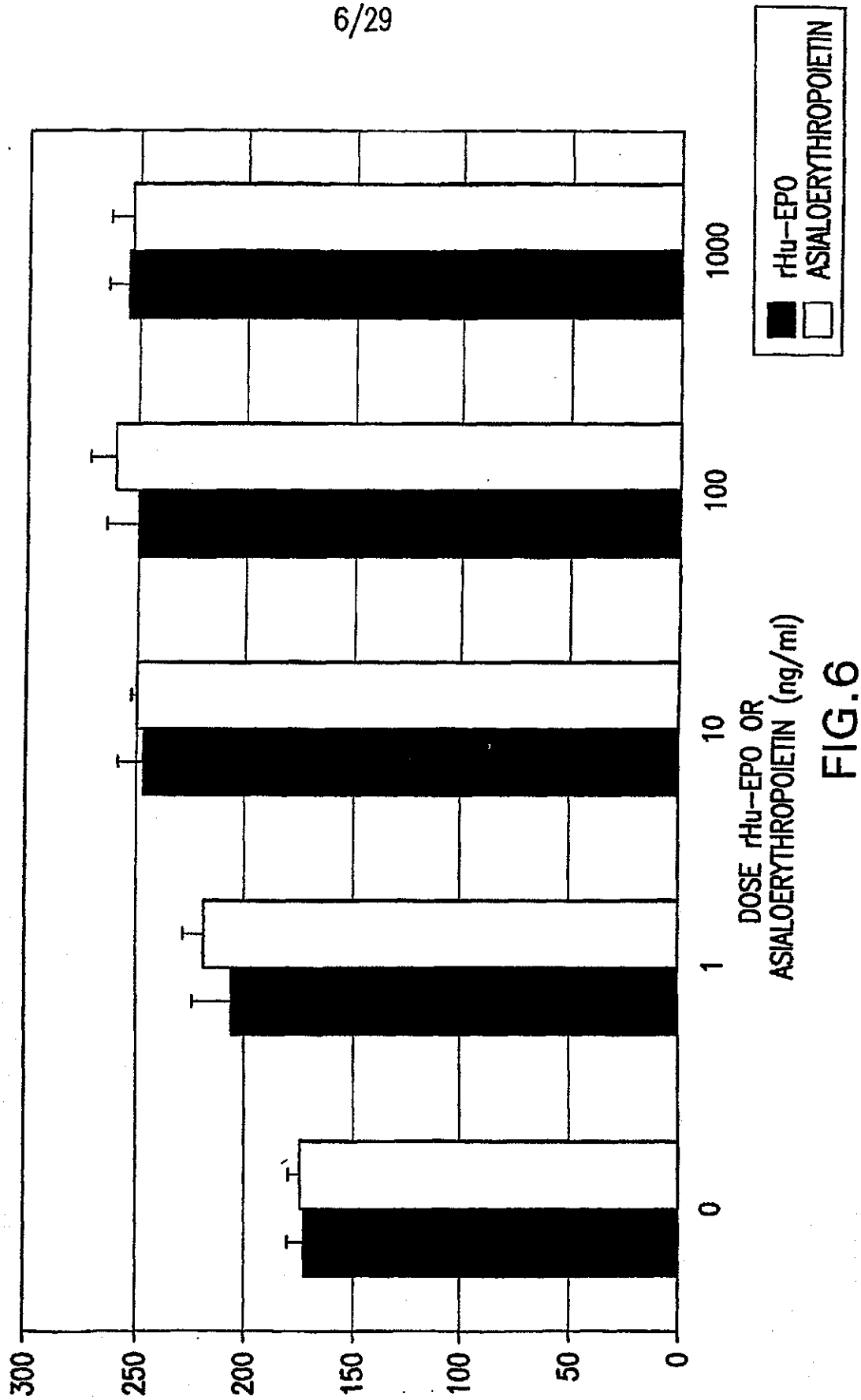
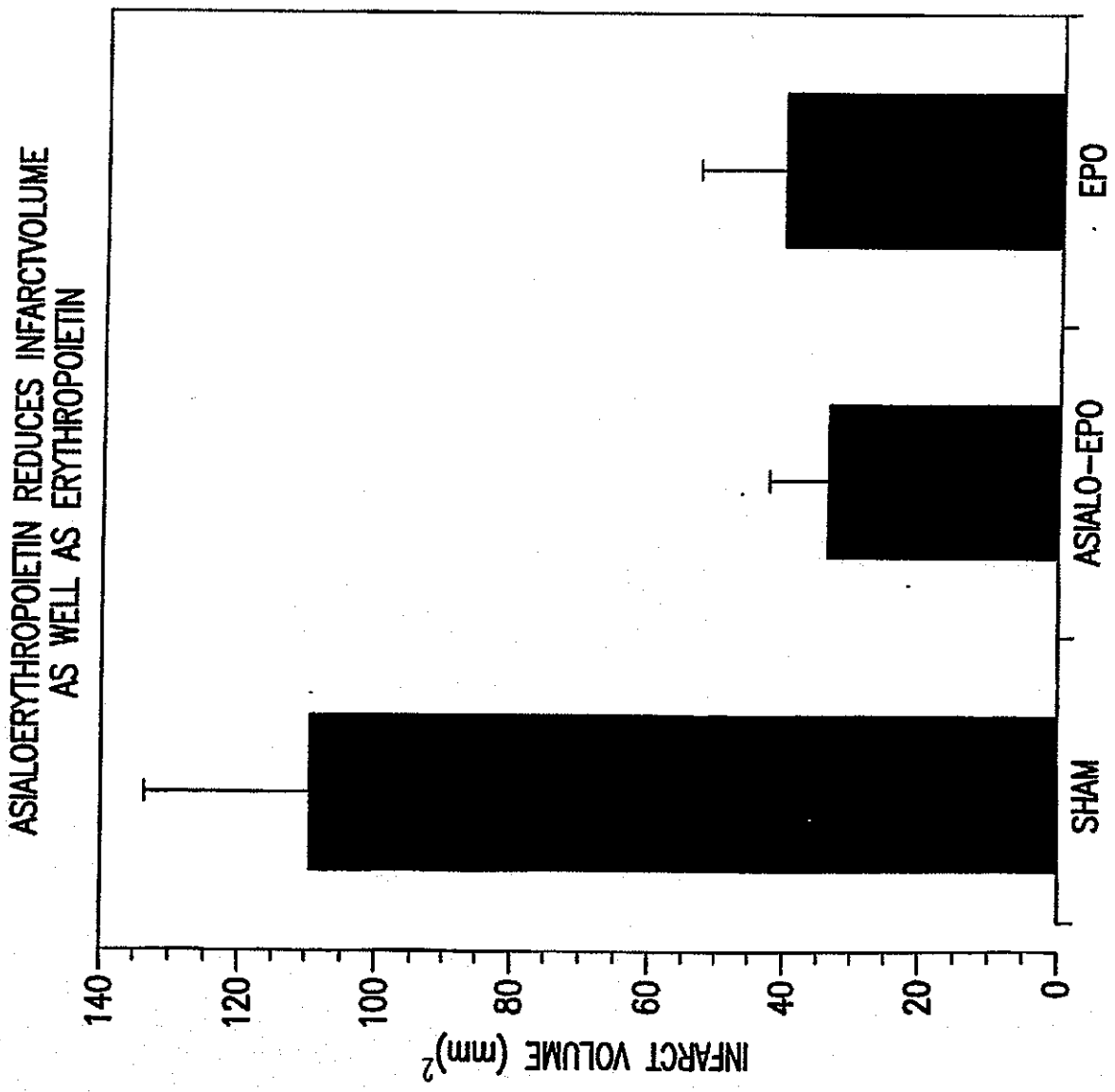
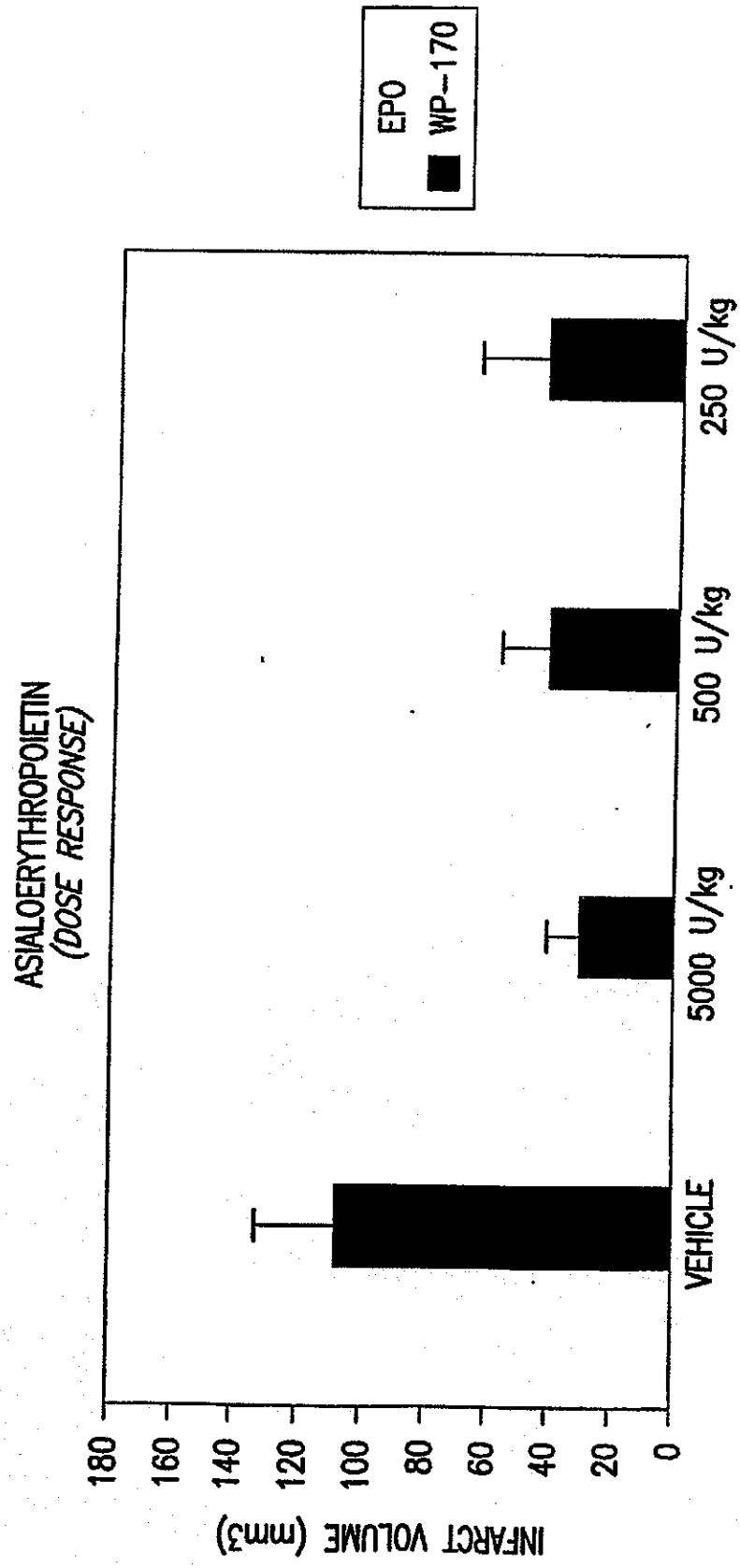

rHu-EPO
ASIALOERYTHROPOIETIN
300
250
200
150
100
50
0
0
1
10
100
1000
DOSE rHu-EPO OR
ASIALOERYTHROPOIETIN (ng/ml)

FIG.6

FIG. 7


ASIALOERYTHROPOIETIN REDUCES INFARCTVOLUME AS WELL AS ERYTHROPOIETIN
INFARCT VOLUME (mm)2
0
20
40
60
80
100
120
140
SHAM
ASIALO-EPO
EPO



n FOR EACH GROUP IS GREATER THAN OR EQUAL TO 4

FIG.8

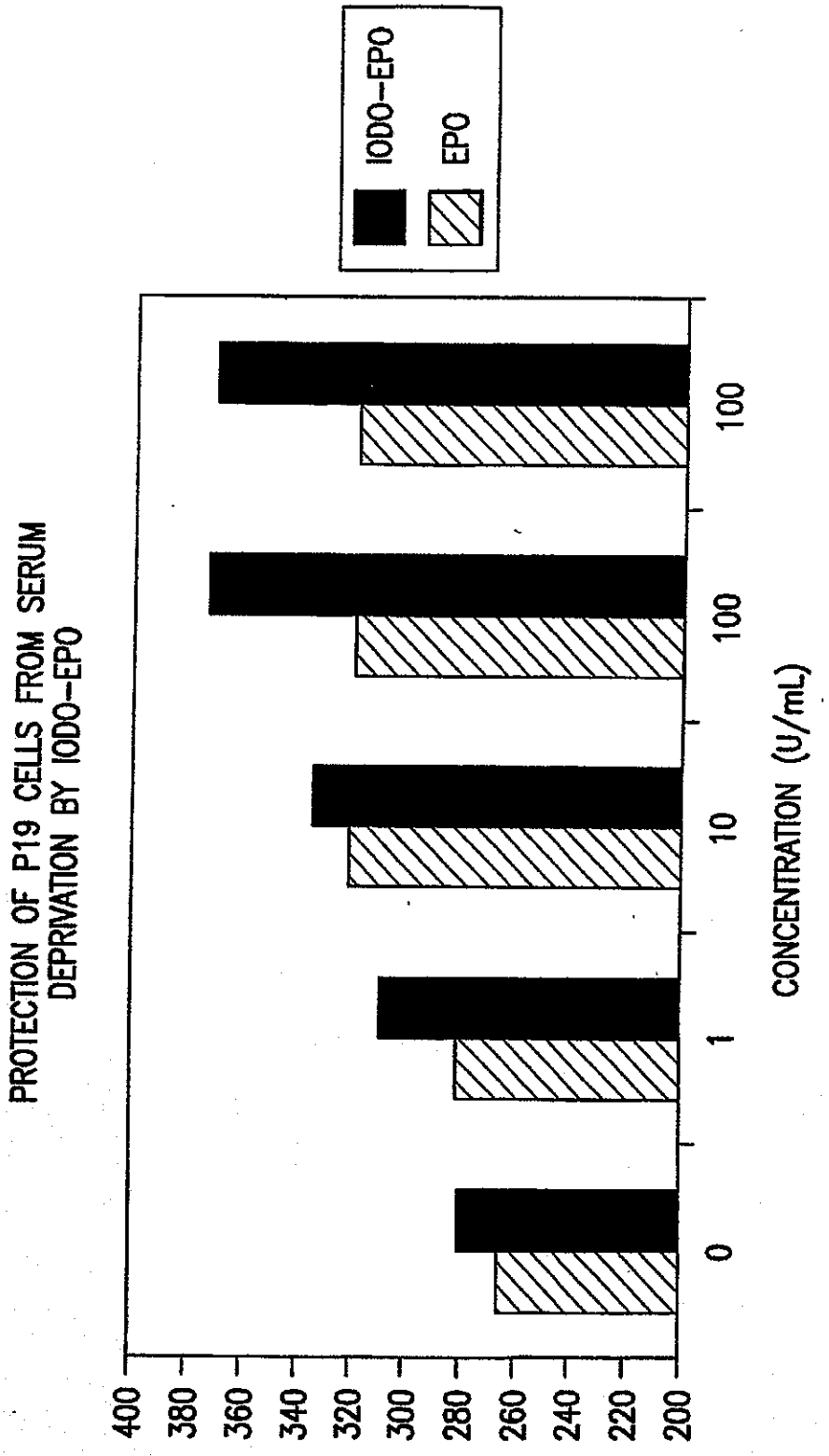

IODO-EPO
EPO
PROTECTION OF P19 CELLS FROM SERUM DEPRIVATION BY IODO-EPO
400
380
360
340
320
300
280
260
240
220
200
0
1
10
100
100
CONCENTRATION (U/mL)

FIG.9

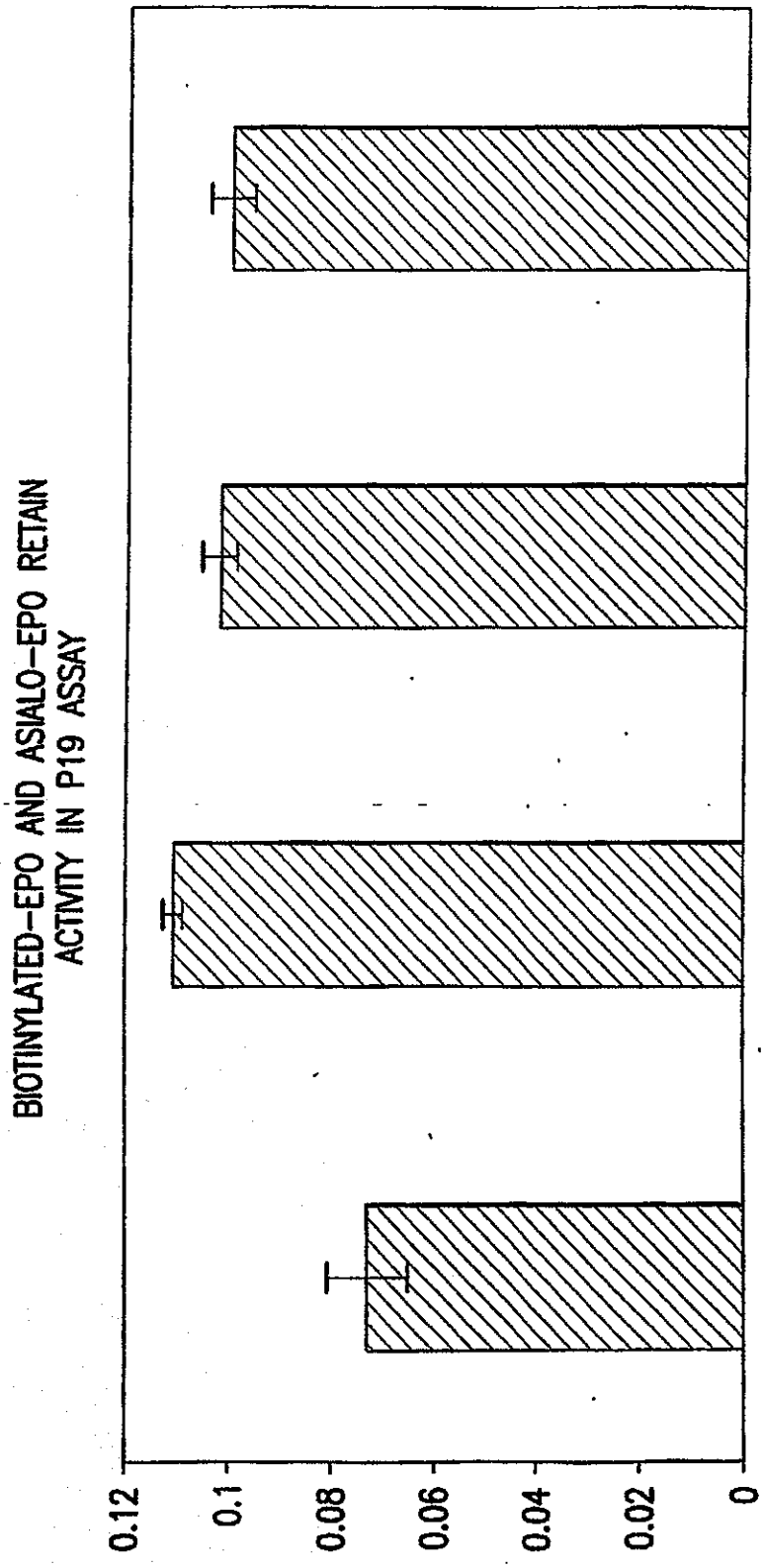

BIOTINYLATED-EPO AND ASIALO-EPO RETAIN ACTIVITY IN P19 ASSAY
0.12
0.1
0.08
0.06
0.04
0.02
0

FIG.10

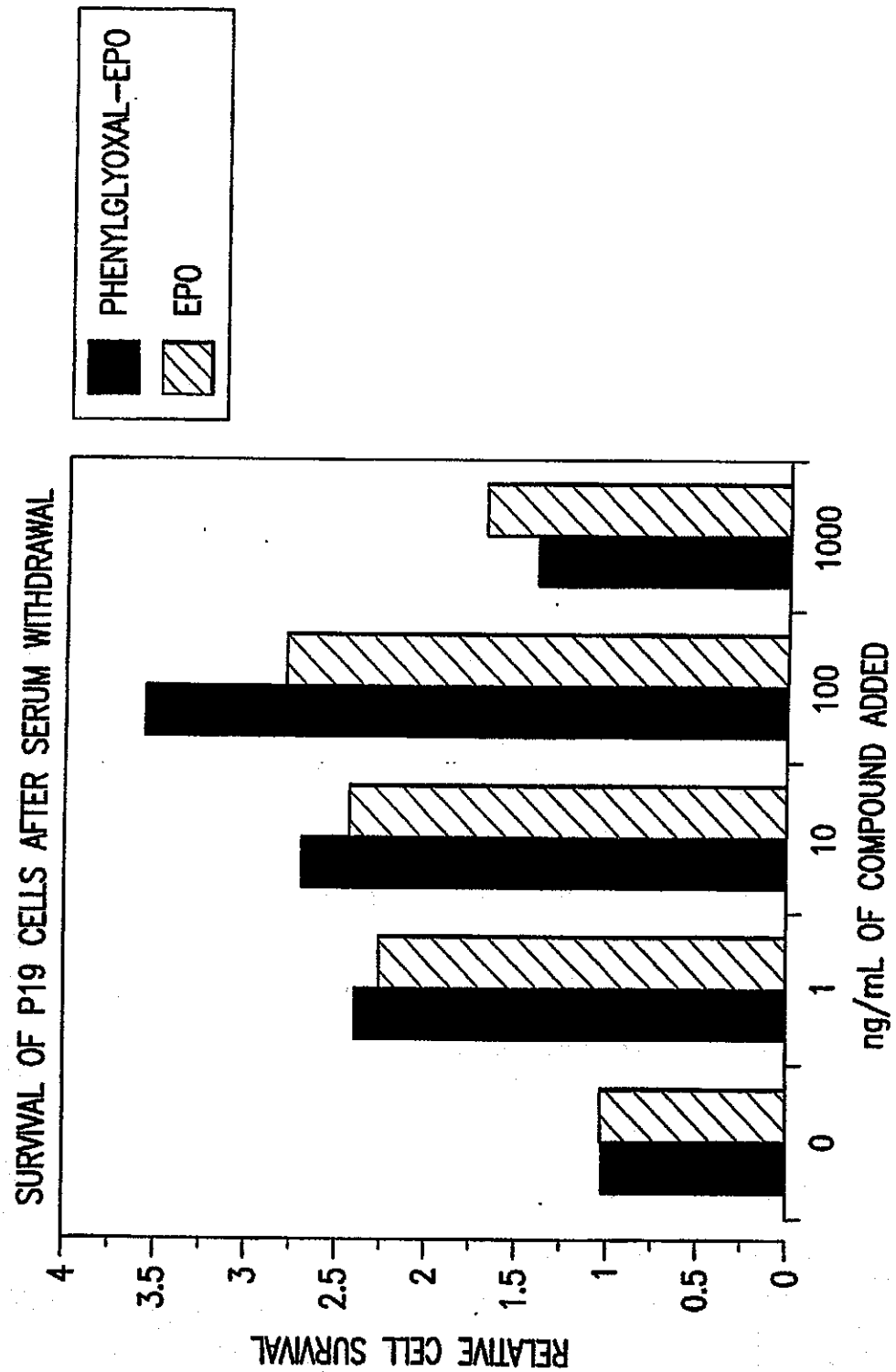

PHENYLGLYOXAL-EPO
EPO
SURVIVAL OF P19 CELLS AFTER SERUM WITHDRAWAL
RELATIVE CELL SURVIVAL
0
0.5
1
1.5
2
2.5
3
3.5
4
0
1
10
100
1000
ng/mL OF COMPOUND ADDED

FIG.11

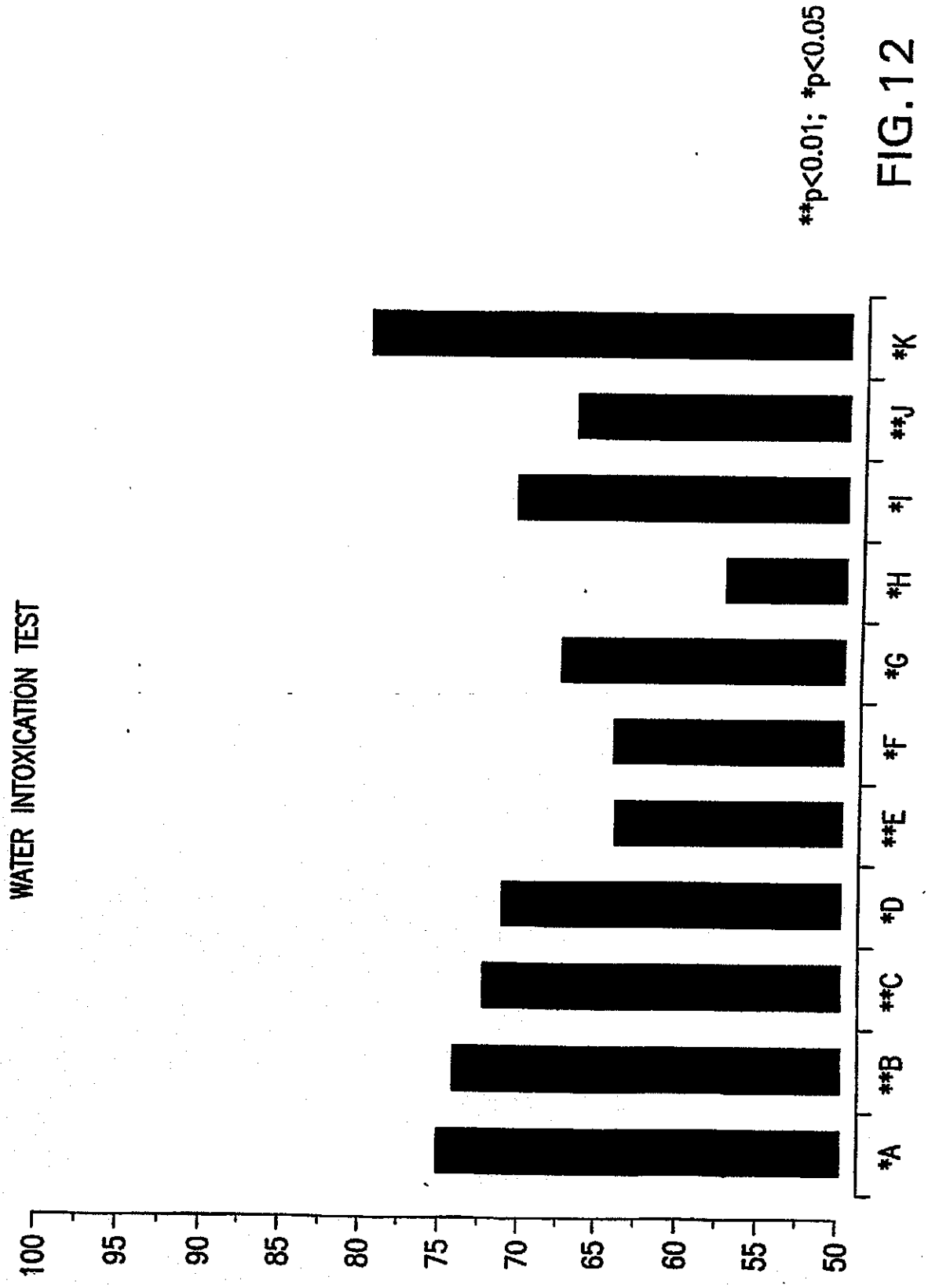

WATER INTOXICATION TEST
100
95
90
85
80
75
70
65
60
55
50
*A
**B
**C
*D
**E
*F
*G
*H
*I
**J
*K
**p<0.01; *p<0.05

FIG. 12

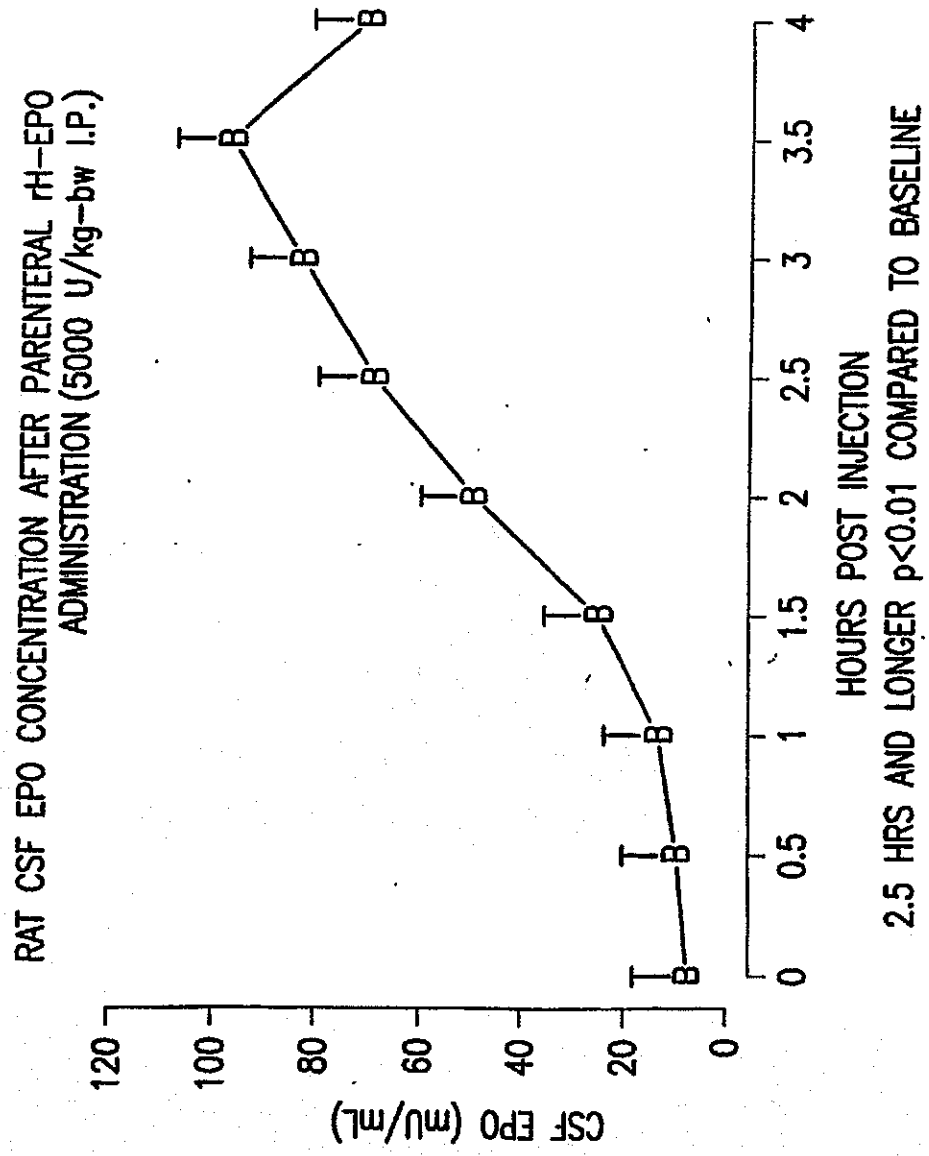

RAT CSF EPO CONCENTRATION AFTER PARENTERAL rH-EPO ADMINISTRATION (5000 U/kg-bw I.P.)
CSF EPO (mU/mL)
0
20
40
60
80
100
120
HOURS POST INJECTION
0
0.5
1
1.5
2
2.5
3
3.5
4
2.5 HRS AND LONGER p<0.01 COMPARED TO BASELINE

FIG.13

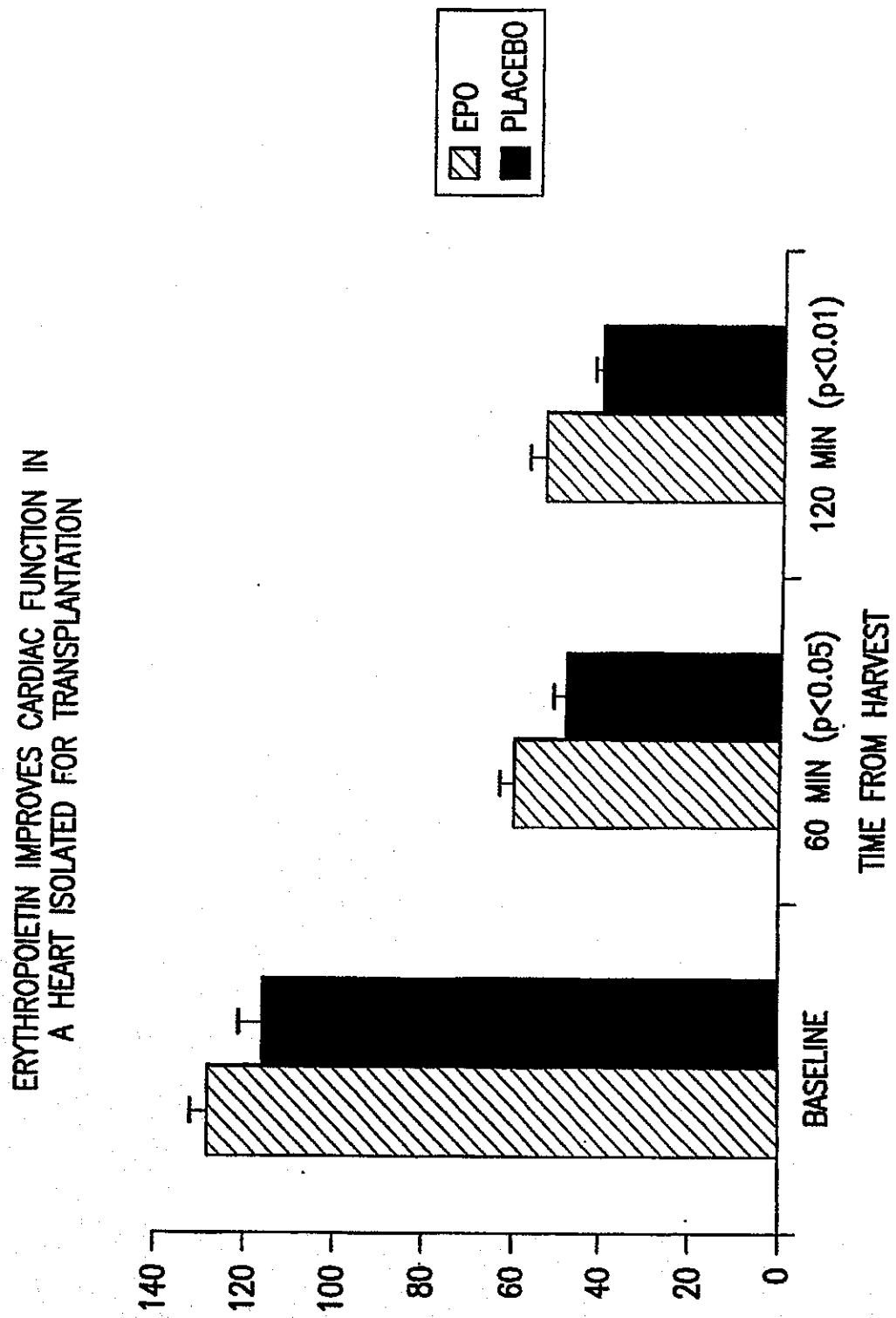
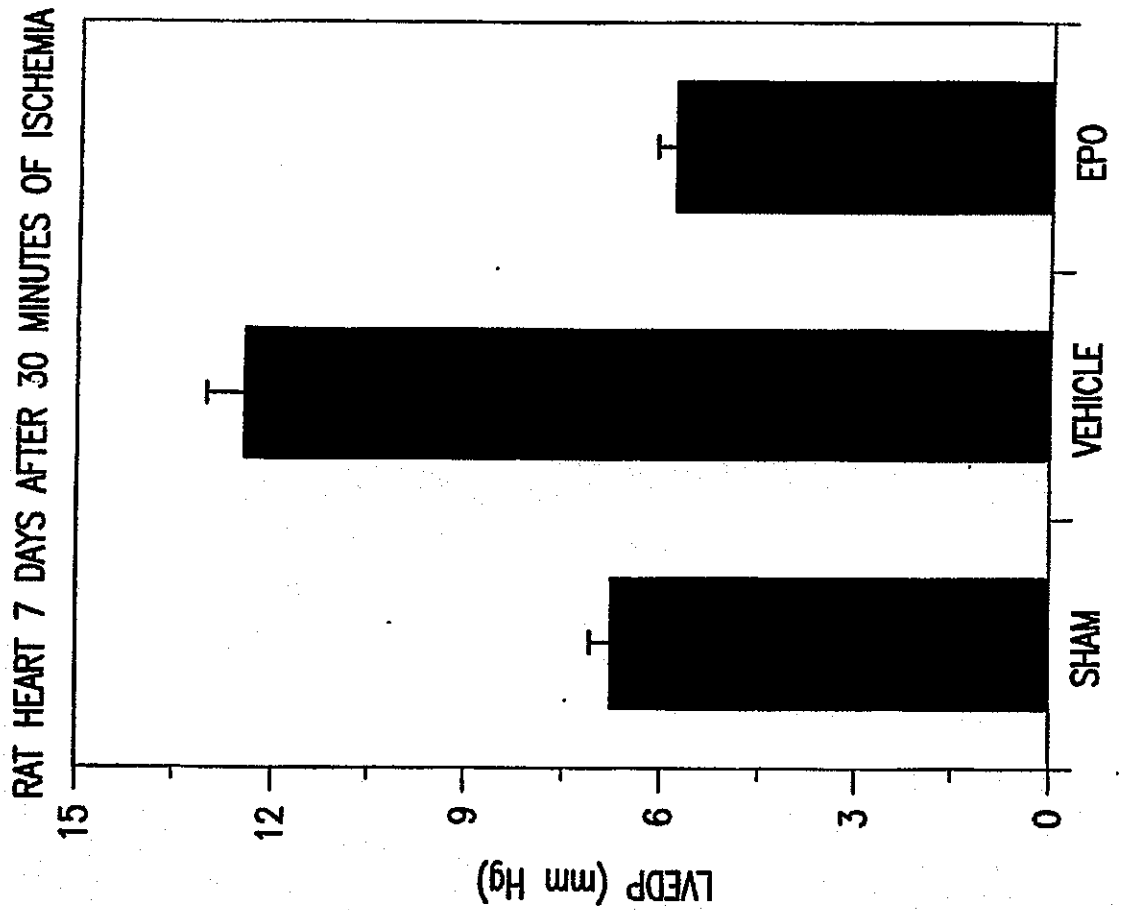

ERYTHROPOIETIN IMPROVES CARDIAC FUNCTION IN A HEART ISOLATED FOR TRANSPLANTATION
EPO
PLACEBO
140
120
100
80
60
40
20
0
BASELINE
60 MIN (p<0.05)
120 MIN (p<0.01)
TIME FROM HARVEST

FIG. 14

FIG.15


RAT HEART 7 DAYS AFTER 30 MINUTES OF ISCHEMIA
LVEDP (mm Hg)
15
12
9
6
3
0
SHAM
VEHICLE
EPO

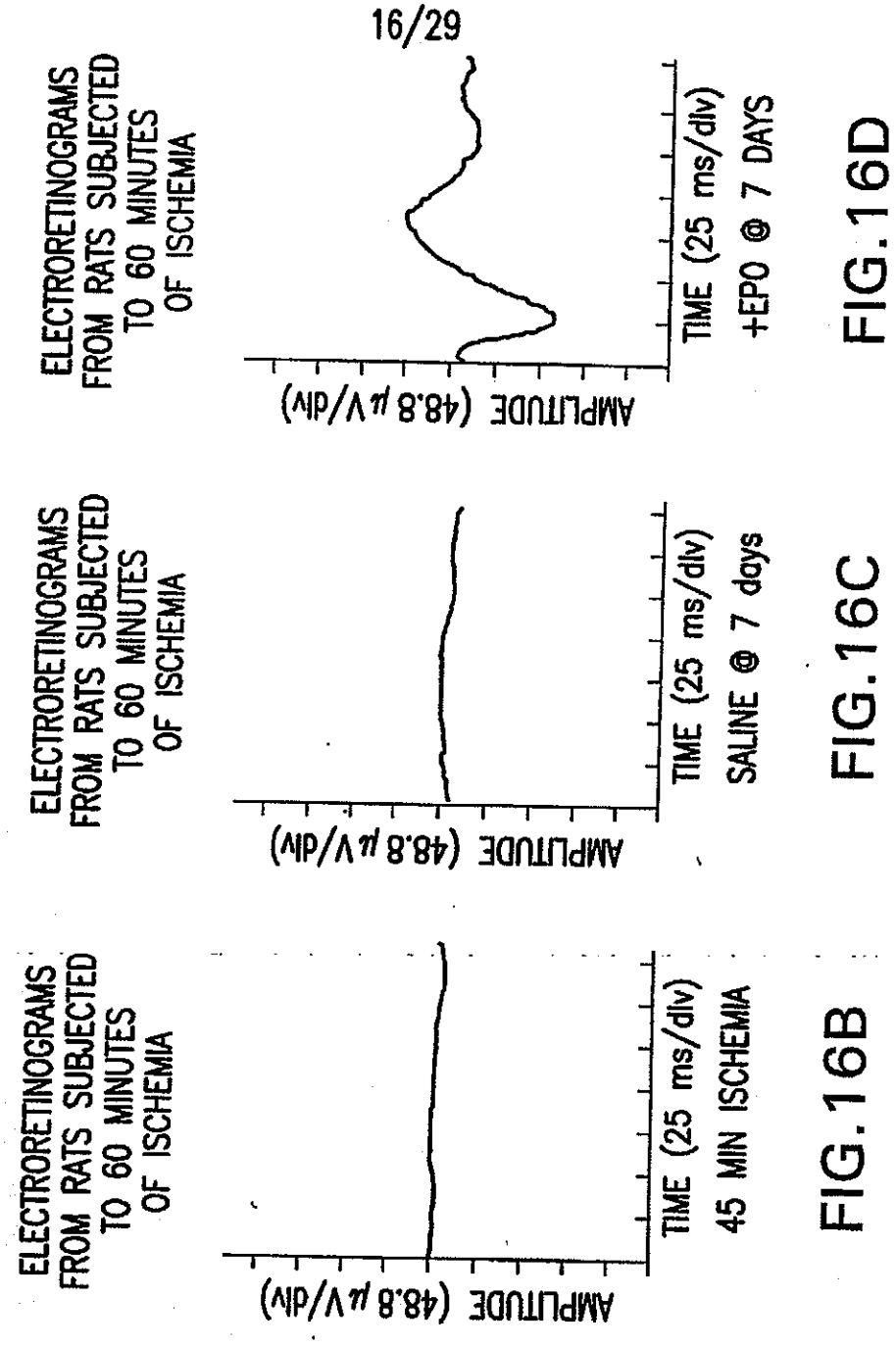


FIG.16A FIG.16B FIG.16C FIG.16D

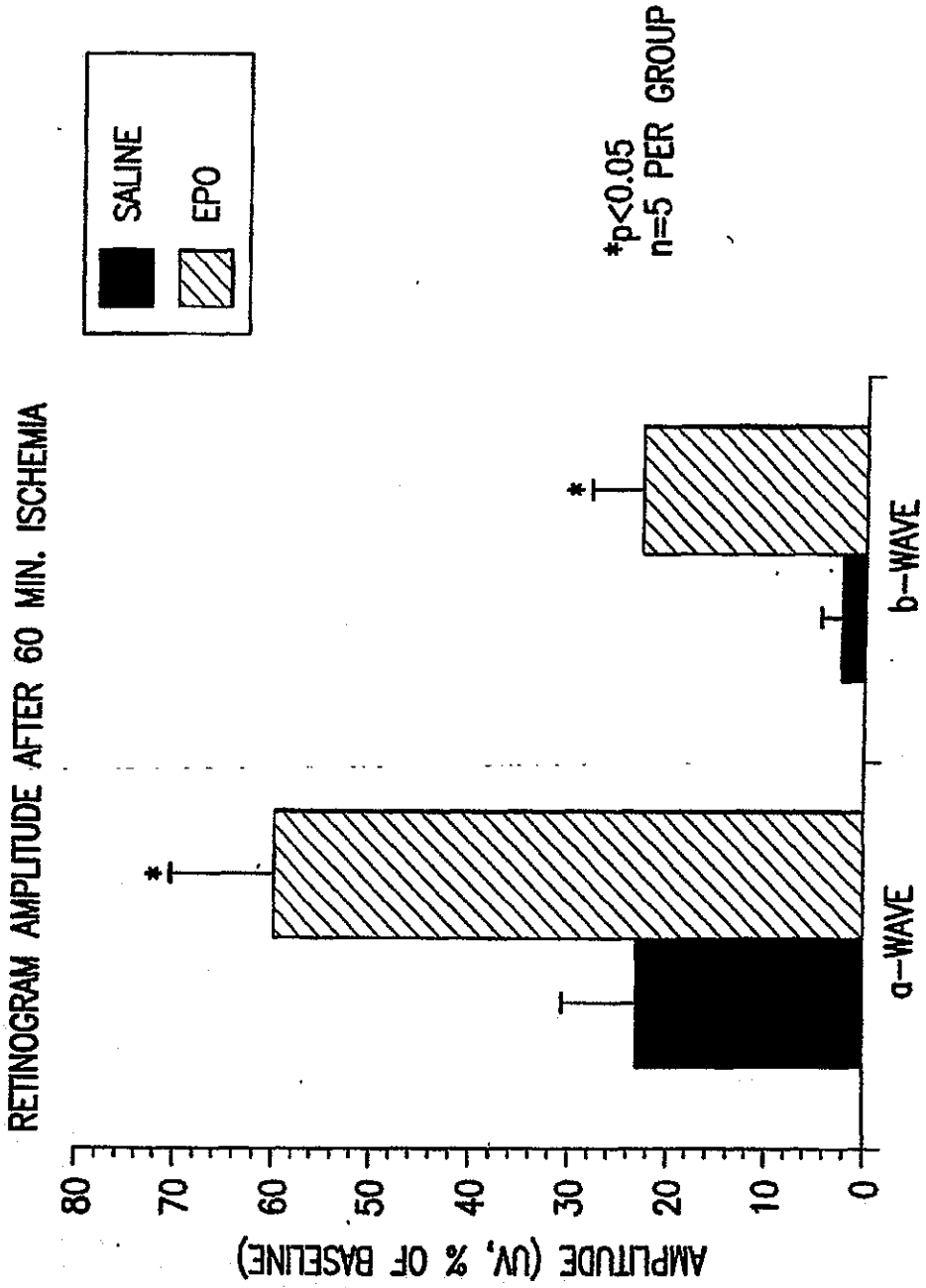

SALINE
EPO
*p<0.05
n=5 PER GROUP
RETINOGRAM AMPLITUDE AFTER 60 MIN. ISCHEMIA
AMPLITUDE (UV, % OF BASELINE)
80
70
60
50
40
30
20
10
0
a-WAVE
b-WAVE
*
*

FIG.17

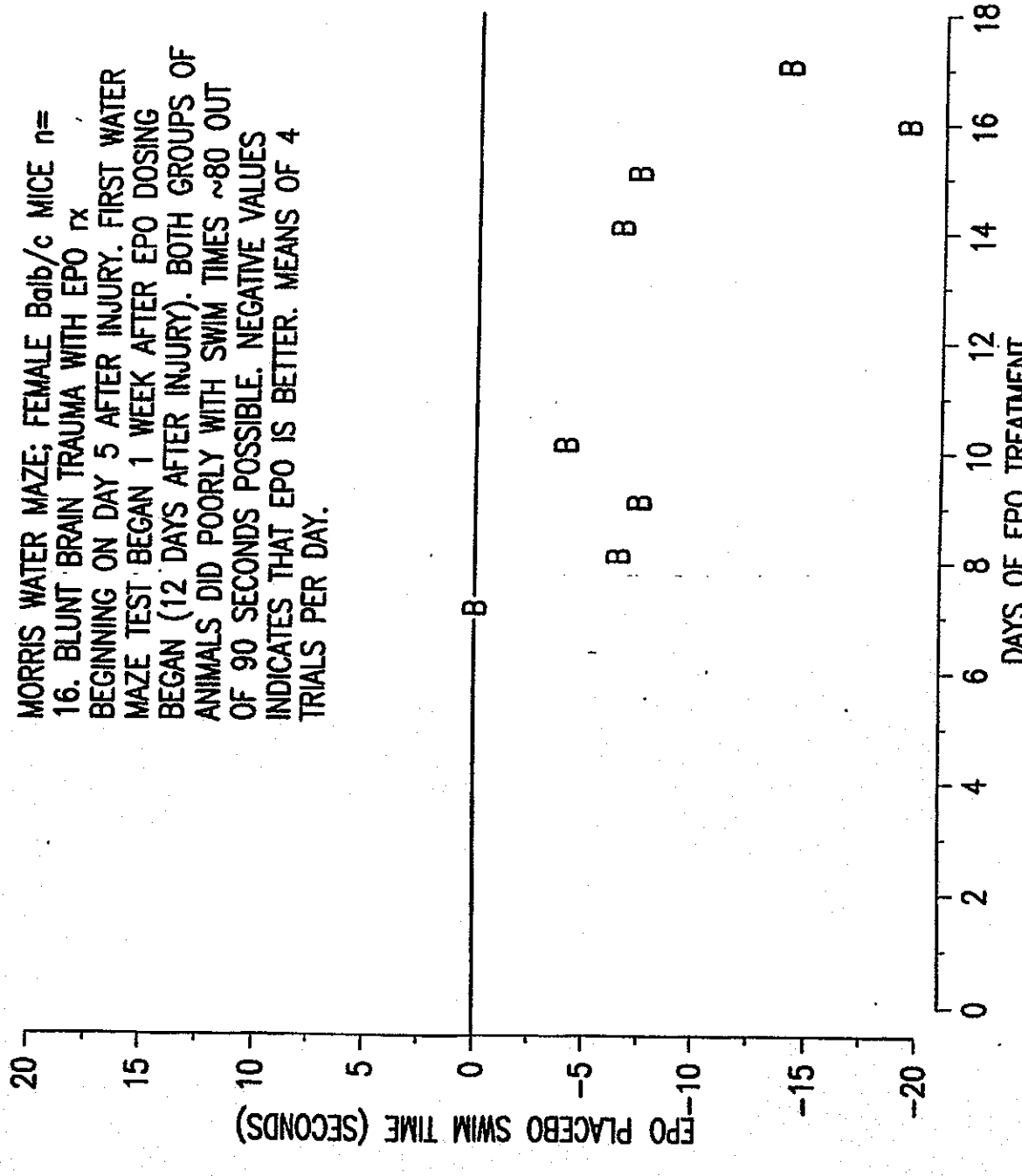

MORRIS WATER MAZE; FEMALE Balb/c MICE n=
16. BLUNT BRAIN TRAUMA WITH EPO rx
BEGINNING ON DAY 5 AFTER INJURY. FIRST WATER
MAZE TEST BEGAN 1 WEEK AFTER EPO DOSING
BEGAN (12 DAYS AFTER INJURY). BOTH GROUPS OF
ANIMALS DID POORLY WITH SWIM TIMES ~80 OUT
OF 90 SECONDS POSSIBLE. NEGATIVE VALUES
INDICATES THAT EPO IS BETTER. MEANS OF 4
TRIALS PER DAY.
EPO PLACEBO SWIM TIME (SECONDS)
20
15
10
5
0
-5
-10
-15
-20
0
2
4
6
8
10
12
14
16
18
DAYS OF EPO TREATMENT
B

FIG.18

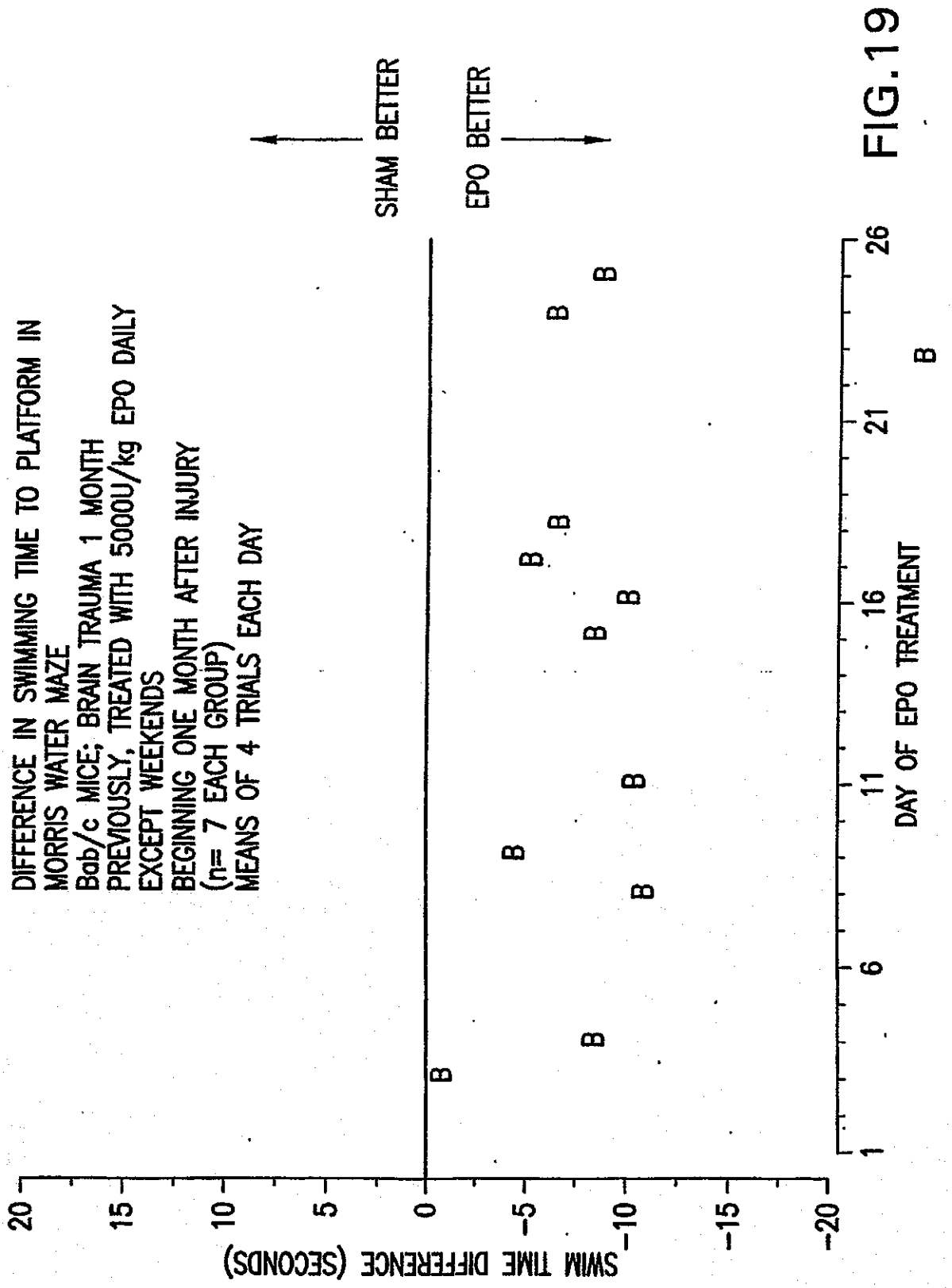

DIFFERENCE IN SWIMMING TIME TO PLATFORM IN MORRIS WATER MAZE
Bab/c MICE; BRAIN TRAUMA 1 MONTH PREVIOUSLY, TREATED WITH 5000U/kg EPO DAILY EXCEPT WEEKENDS
BEGINNING ONE MONTH AFTER INJURY
(n= 7 EACH GROUP)
MEANS OF 4 TRIALS EACH DAY
SHAM BETTER
EPO BETTER
SWIM TIME DIFFERENCE (SECONDS)
20
15
10
5
0
-5
-10
-15
-20
1
6
11
16
21
26
DAY OF EPO TREATMENT

FIG.19

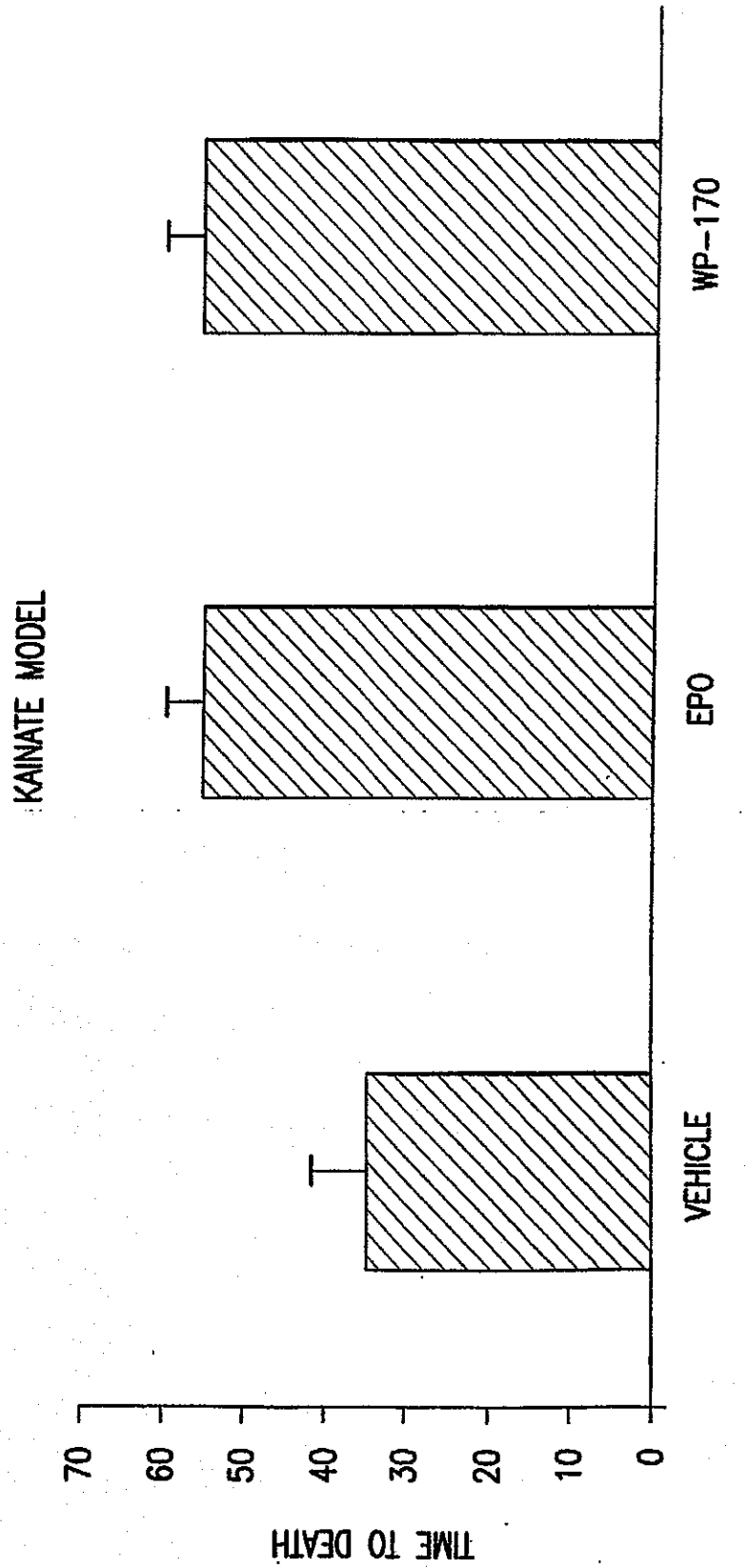

KAINATE MODEL
VEHICLE
EPO
WP-170
TIME TO DEATH
0
10
20
30
40
50
60
70

FIG.20

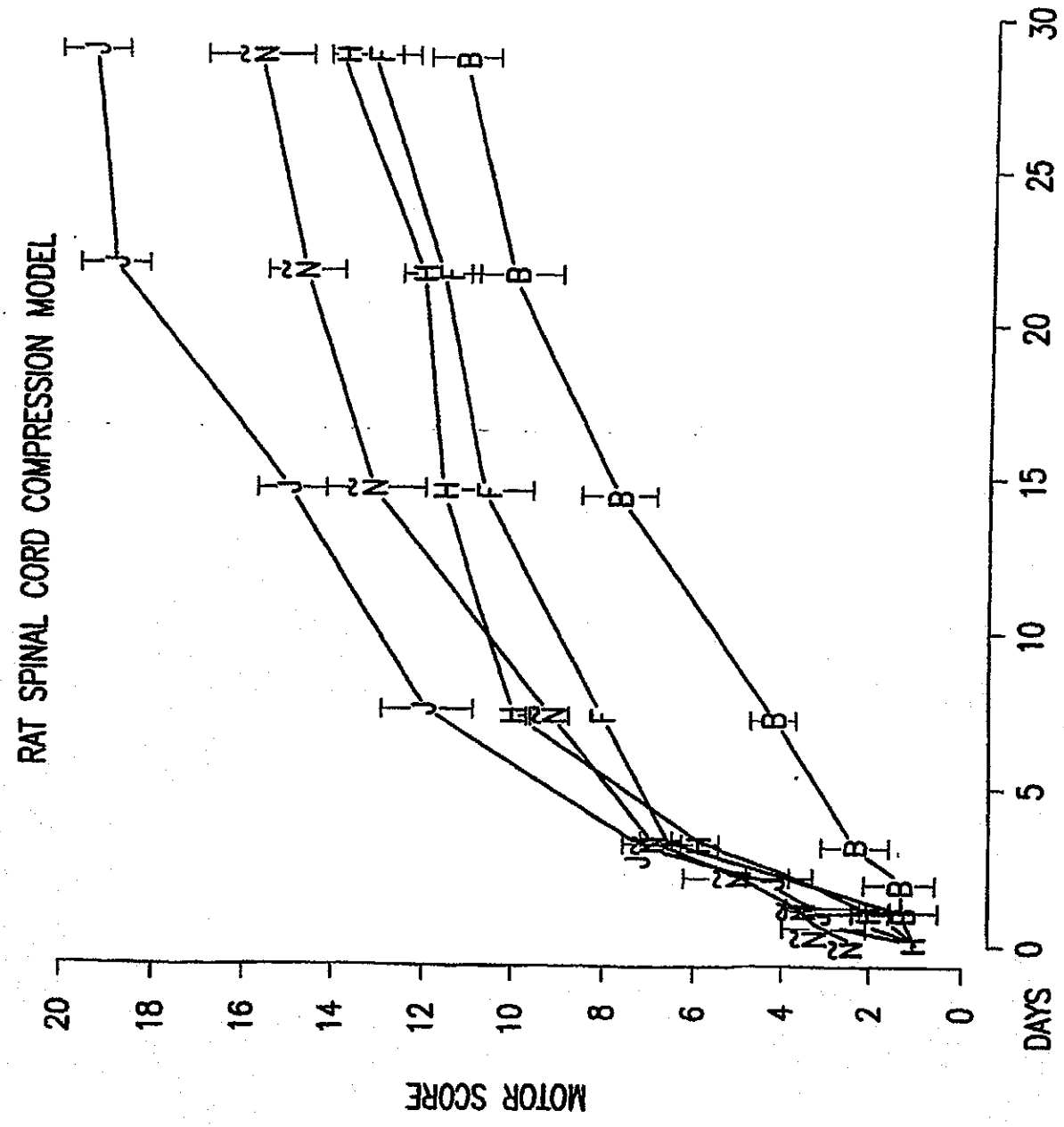
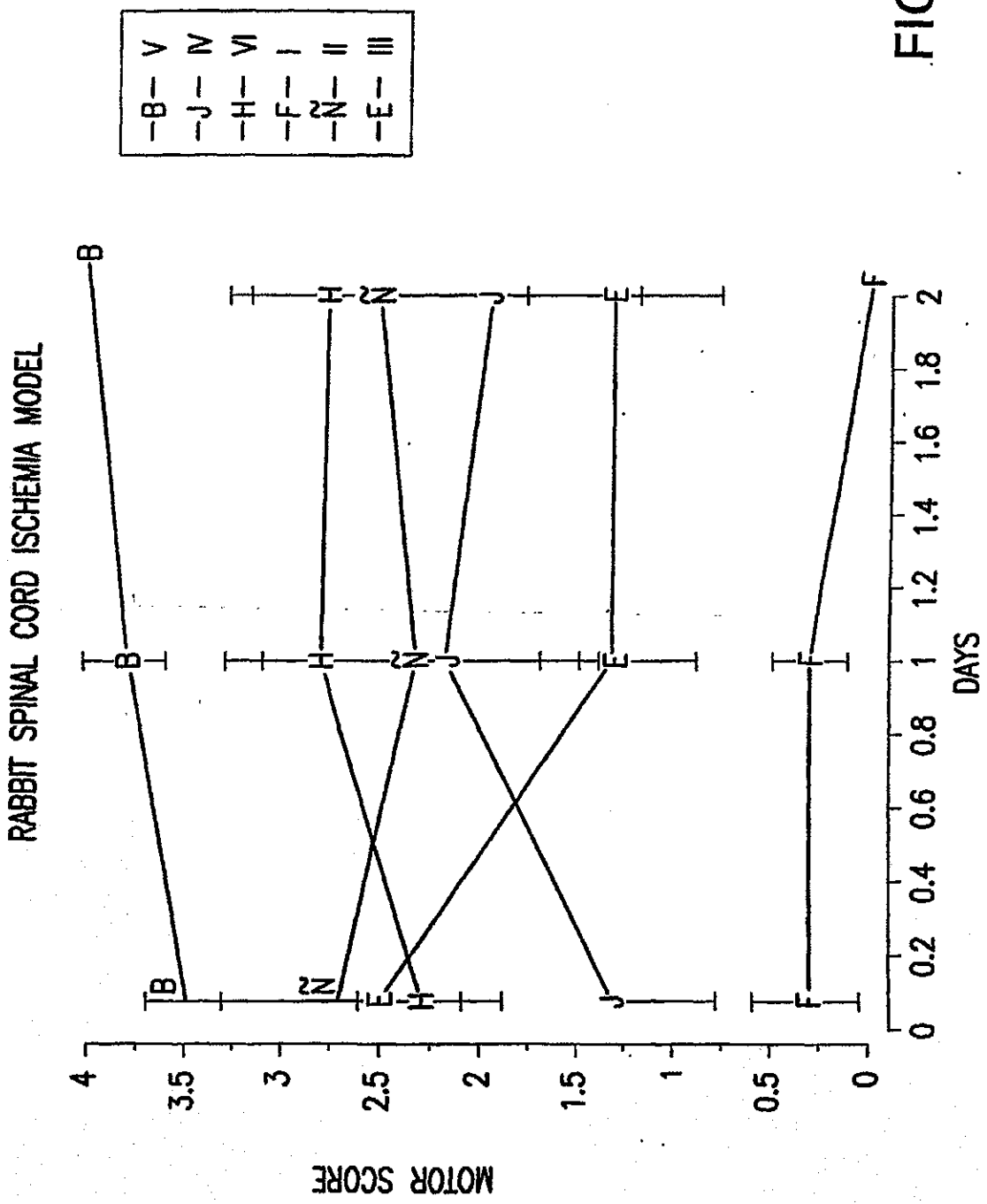

I
II
III
IV
V
B
J
H
F
N2
RAT SPINAL CORD COMPRESSION MODEL
MOTOR SCORE
DAYS
0
2
4
6
8
10
12
14
16
18
20
0
5
10
15
20
25
30

FIG.21

FIG.22


V
IV
VI
I
II
III
B
J
H
F
N2
E
RABBIT SPINAL CORD ISCHEMIA MODEL
MOTOR SCORE
DAYS
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
0.5
1.5
2.5
3.5
4

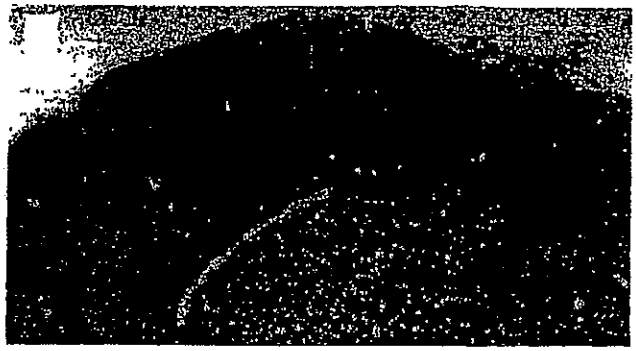


FIG.23A

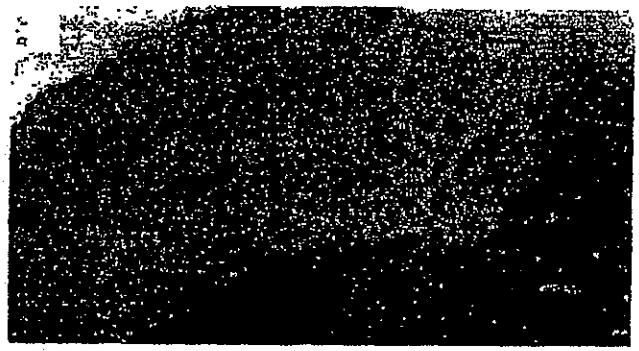


FIG.23B



FIG.23C

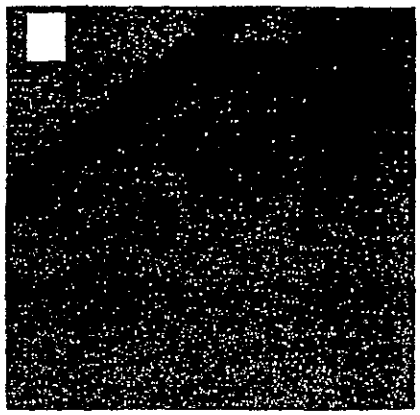


FIG.24A

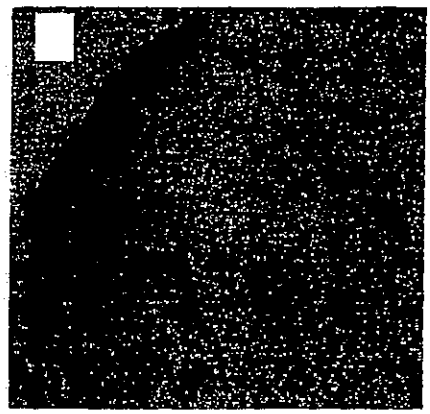


FIG.24B

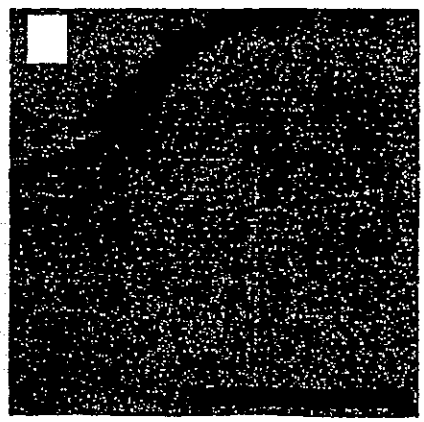


FIG 24C

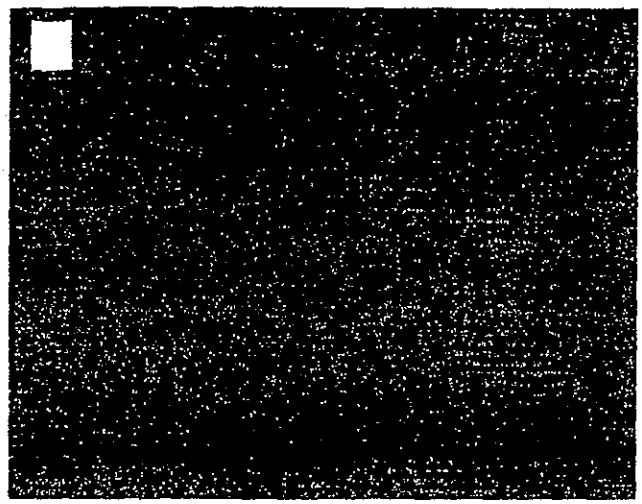


FIG.25A

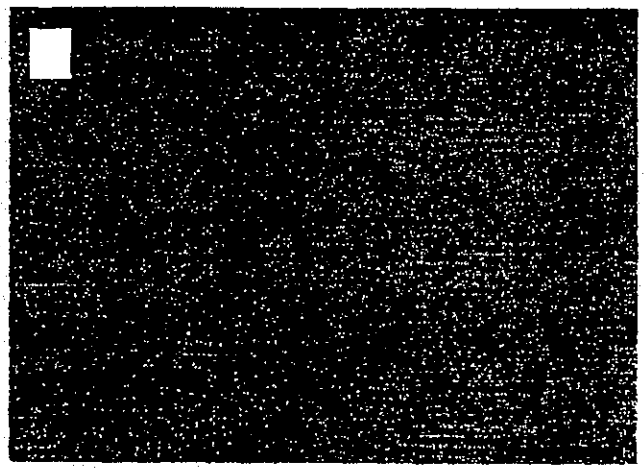


FIG.25B

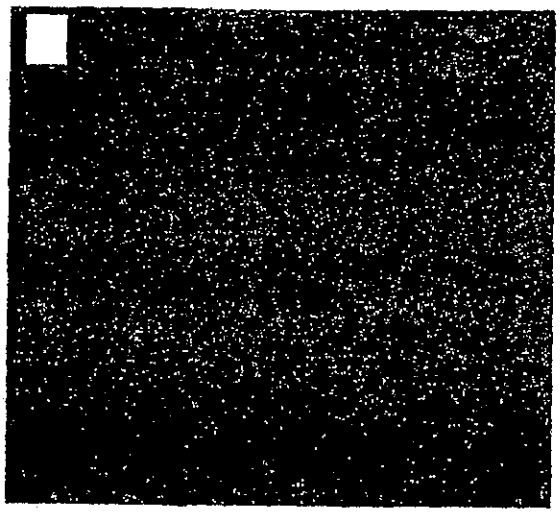


FIG.26A

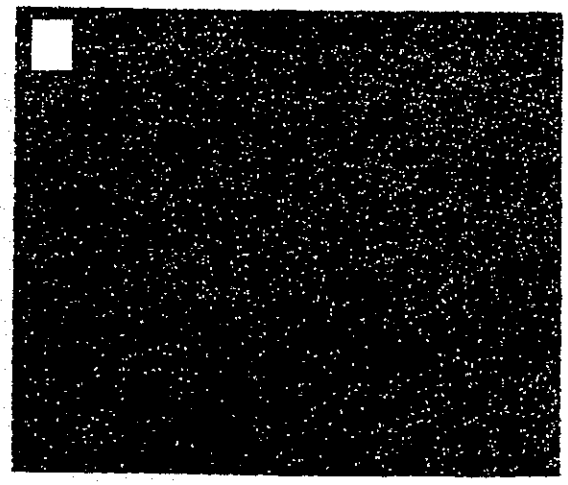


FIG.26B

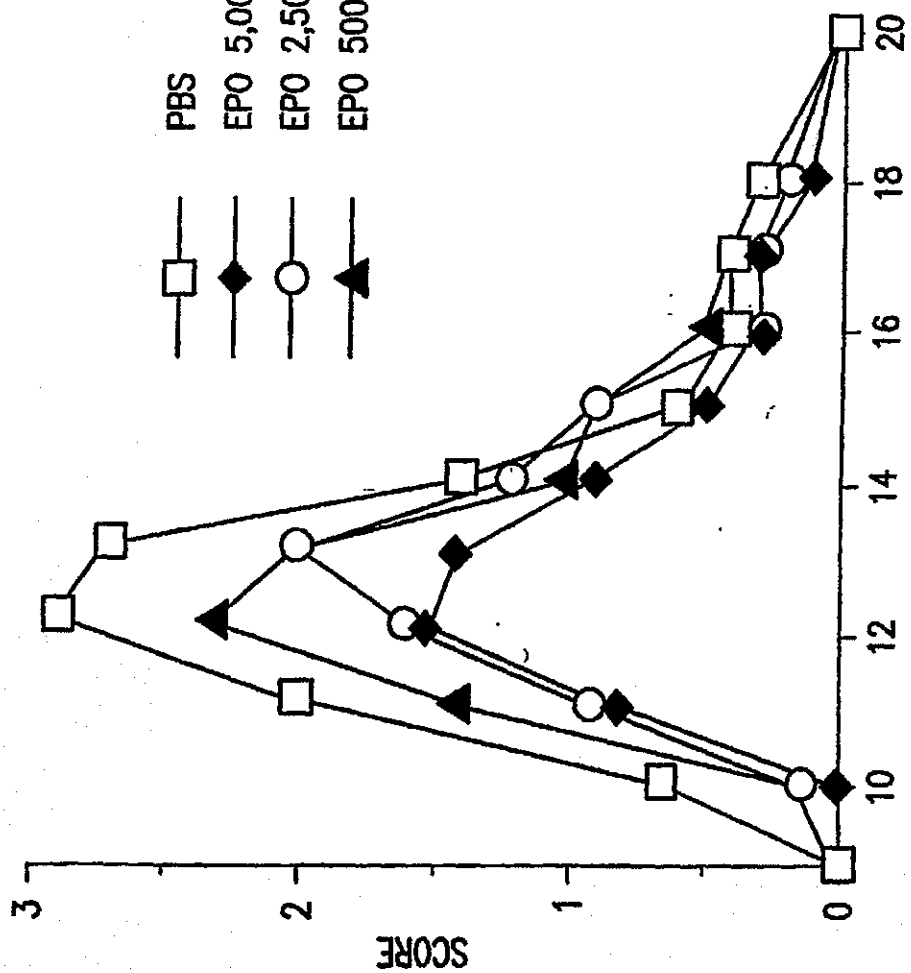

PBS
EPO 5,000 U/kg
EPO 2,500 U/kg
EPO 500 U/kg
SCORE
0
1
2
3
DAYS
10
12
14
16
18
20

FIG.27

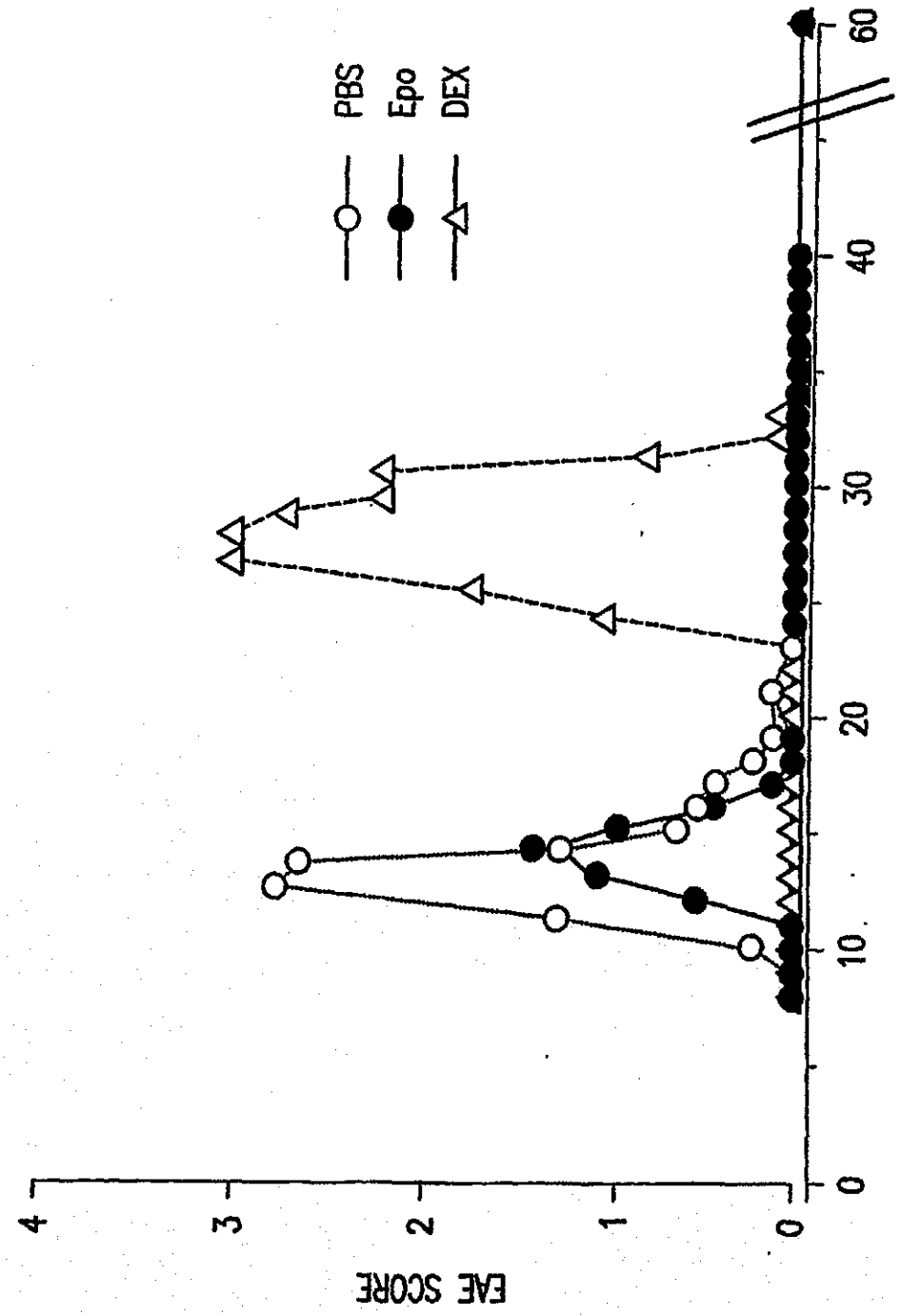

PBS
Epo
DEX
EAE SCORE
0
1
2
3
4
0
10
20
30
40
60
DAYS FROM IMMUNIZATION

FIG. 28

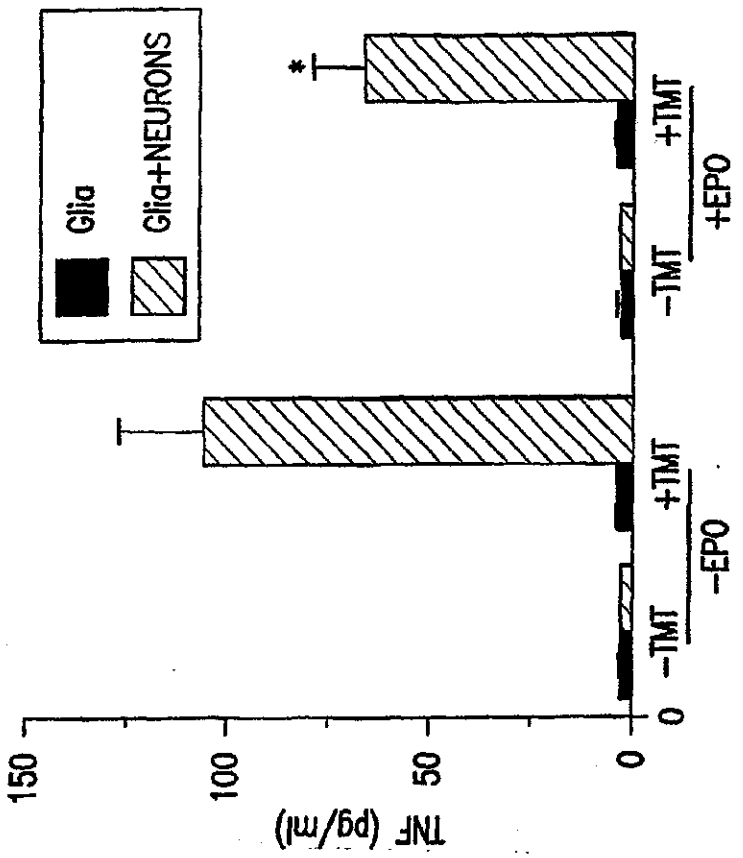


FIG.29B

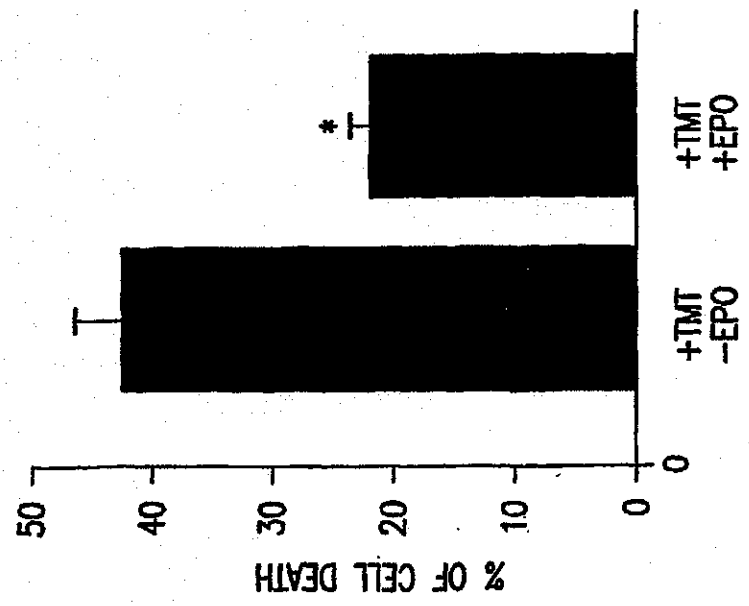


FIG.29A