RESULTS

Twenty female conditioned mongrel dogs were included in this study. Animals were randomly assigned to either control (n=10) or experimental (n=10) group. Experimental animals underwent selective diversion of pancreatic portal flow to the systemic circulation by anastomosing the splenic vein and pancreatic-duodenal vein separately to the inferior vena cava. Control animals underwent a sham operation with mobilization of the pancreas without altering venous outflow.

All animals remained normoglycemic and maintained a constant body weight throughout the study with slight tendency of weight gain in the experimental group varying from 15.6 to 17.4 Kg for the control group and 17.08 to 20.4 for the experimental group (Table 1) (P = ns).

Although both groups demonstrated similar baseline blood pressure (control=100.8, hyperinsulinemic 97.3, P=ns), at three month the hyperinsulinemic group experienced a significant rise in pressure that did not exist for the control group (114.3 Vs 80.4 mmHg $p< 0.0001$), (Table 2). This difference persisted at 6 month (89.2 for the control group Vs 117.6 mmHg for the hyperinsulinemic group $P< 0.01$), (Fig.9).

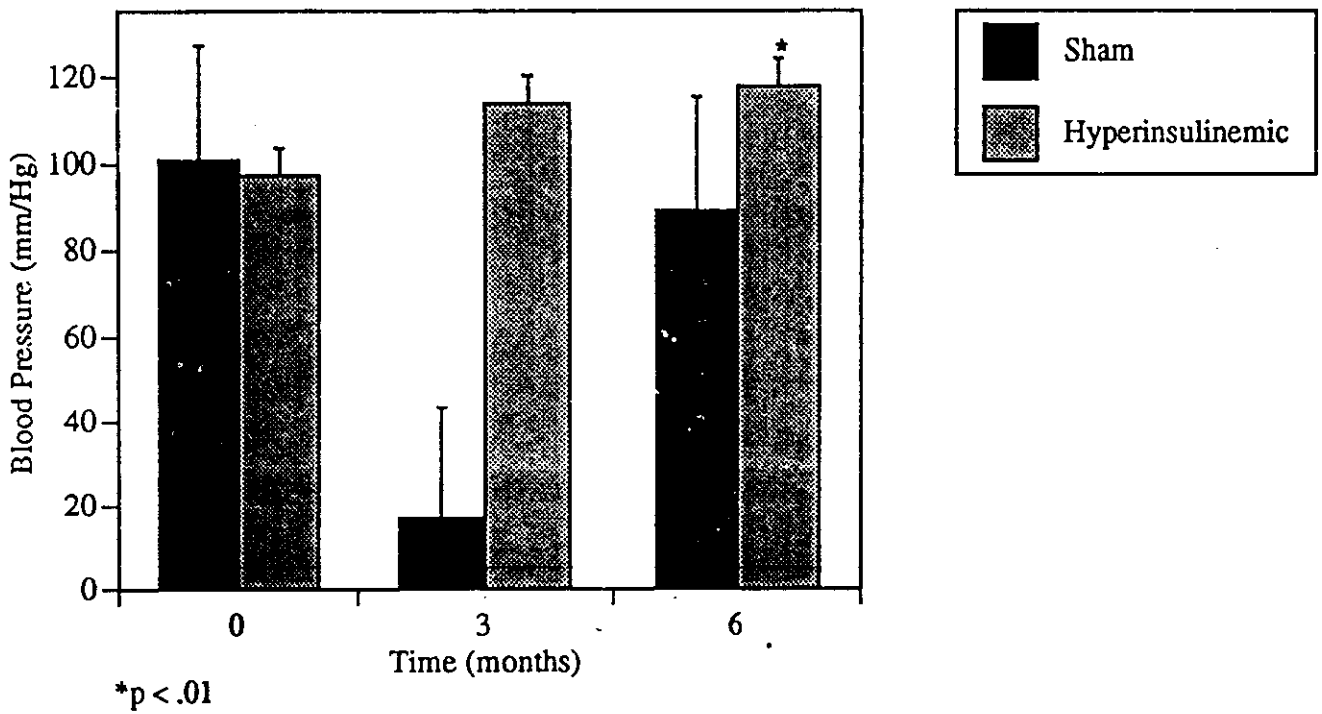
Table 1 Effect of Hyperinsulinemia on Weight

Time (months)	Control wt/kg	Hyyperinsulinemia wt/kg
Baseline	15.6	17.08
3	17.2	19.8
6	17.4	20.4

Table 2 Effect of Hyperinsulinema on Mean Arterial Blood Pressure.

Time (months)	Control (mm hg)	Hyperinsulinema (mm hg)
Baseline	100.8	97.3
3	80.4	114.3
6	89.2	117.6

Fig. 9 Effect of Hyperinsulinemia on Mean Arterial Blood Pressure



*p < .01

Fasting plasma insulin were significantly increased from base line (control = 8.4 mu/ml, hyperinsulinemic = 5.6 mu/ml, P= ns). For the hyperinsulinemic group at three and 6 month measurements (Table 3); (20.2 and 26.3 mu/ml respectively, $P < 0.05$) (Fig.10), but not for the control group (6 and 6.5 mu/ml respectively) (Fig. 10).

As this model was designed for inducing hyperinsulinemia without hyperglycemia, this has been confirmed by IVGTT and IV Tolbutamide at base line and after the end of the study (Table 4). Glucose level before surgery and after 6 month in both groups were superimposed (Fig.11) i.e. they remained normoglycemic throughout the study period. On the other hand, there was a marked difference in fasting insulin between both groups (Table 5) and this was maintained after giving glucose at time zero and Tolbutamide at 21 minute (Fig.12).

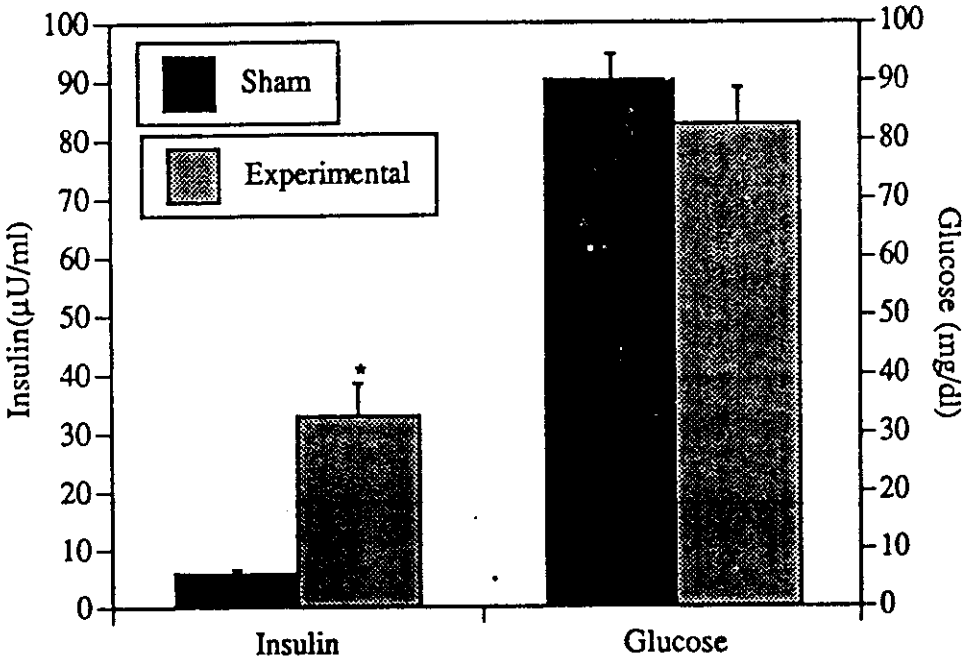
Lipid profiles demonstrated that induction of hyperinsulinemia increased total cholesterol with significant difference between the control and experimental group at three month interval (Table 6). This difference was maintained at 6 month ($P< 0.001$ between groups), (Fig.13).

In hyperinsulinemic group, HDL has markedly decreased between time zero and 6 month (Table 7). There was significant difference in HDL between the experimental group and sham operated group ($P<0.05$ between groups) (Fig. 14).

Table 3. Fasting Insulin Level

Time Months	Control (n=10)	Hyperinsulinemic (n=10)
Baseline	8.4	6.1
1	6.0	16.9
2	7.7	19.5
3	6.0	20.2
4	7.5	22.2
5	7.2	25.6
6	6.5	26.3

Fig. 10 The Effect of Hyperinsulinemia on Fasting Insulin and Glucose at 6 Months



* $p < .05$

Table 4 : IVGTT and IV Tolbutamide Glucose

Time Minutes	Control Baseline	Control 6months	Hyperinsulinemic 6months
-15	91.3	84.8	86.8
-10	90.4	87.6	88.0
-05	91.0	86.3	87.1
-01	84.5	86.1	86.5
02	228.6	221.8	230.3
03	215.5	221.8	230.3
04	210.6	217.5	224.3
05	201.5	210.0	210.0
06	195.2	206.2	207.3
08	190.5	198.0	199.0
10	180.2	187.8	186.7
14	169.9	170.3	174.6
16	157.0	163.0	167.7
19	144.6	148.1	158.0
22	129.9	134.2	149.3
25	126.0	123.0	139.7
30	114.4	113.5	124.5
40	92.0	103.1	99.3
50	80.0	92.7	82.4
70	73.8	88.7	72.2
100	76.4	86.8	71.9
140	76.4	86.2	71.7
180	77.4	85.5	73.7

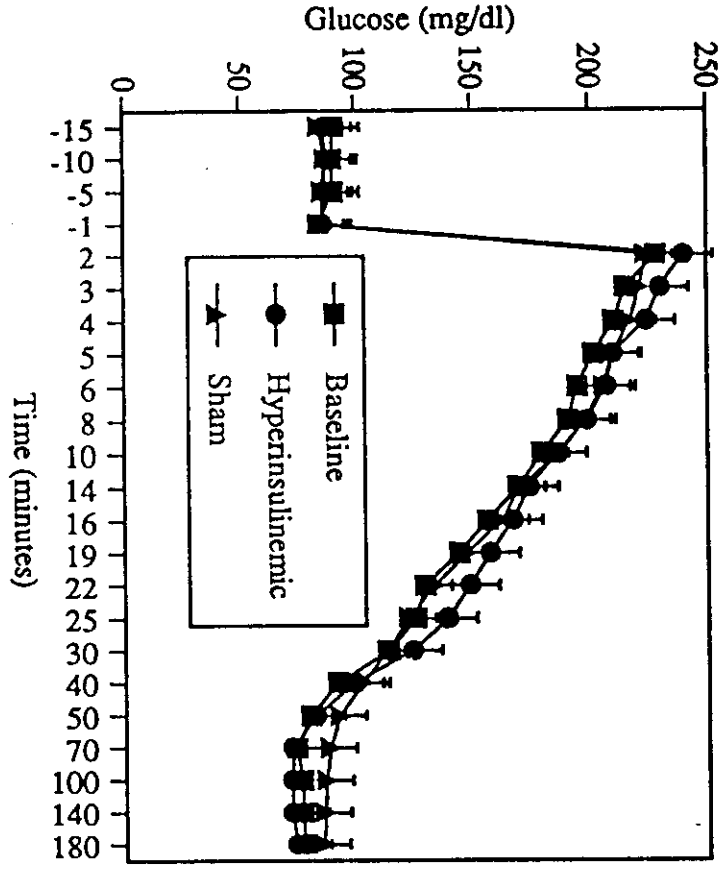
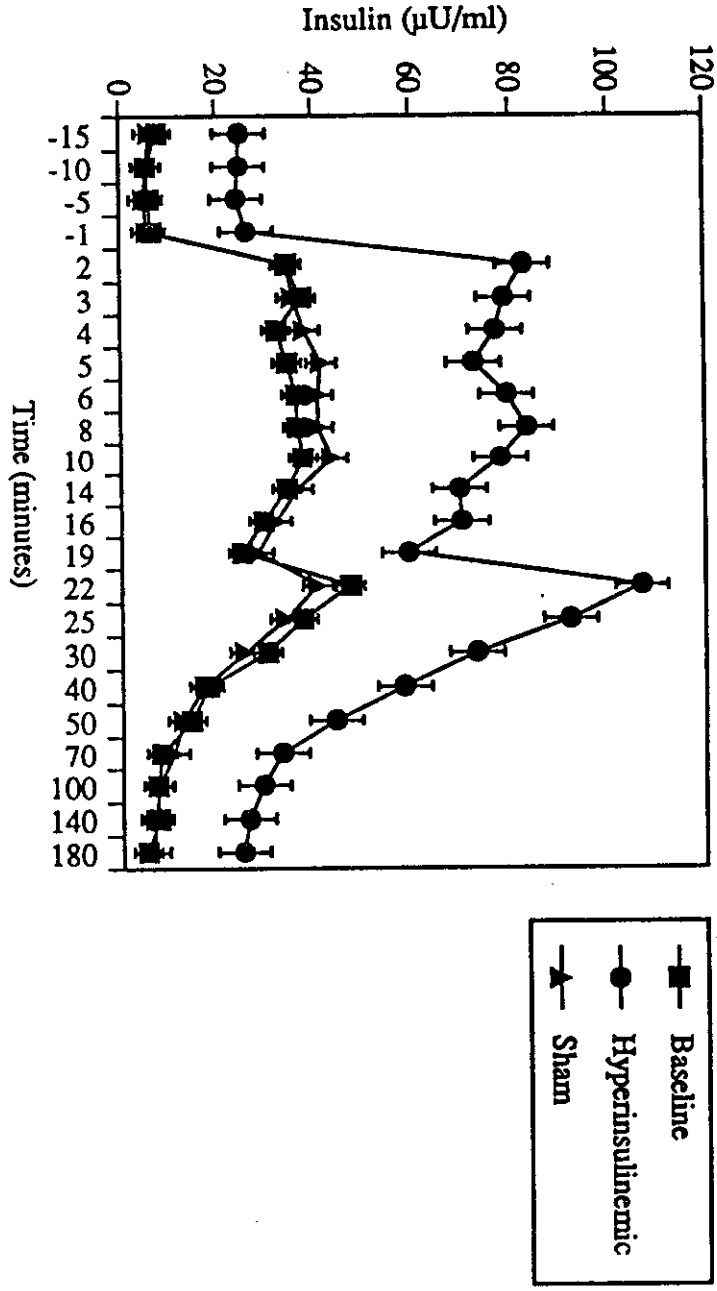


Fig. 11 Glucose Level During IVGTT- IV Tolbutamide at Baseline and 6 Months

Table 5 : IVGTT and IV Tolbutamide Isulin

Time	Baseline	6montths (mg/di)	6m (mg/di)
-15	7.9	6.3	25.1
-10	5.6	5.6	25
-5	6.2	5.1	24.4
-1	6.7	5.8	26.5
2	34.7	34.6	82.7
3	37.8	36	78.8
4	32.6	38.3	77.1
5	34.7	58.1	72.7
6	36.6	41.1	79.4
8	36	41.1	83.4
10	38	44	78
14	34.6	36.8	69.8
16	29.7	32.3	70.2
19	25.2	28.5	59.5
22	47.5	40.8	106.8
25	37.7	34.1	92.1
30	30.3	25.6	73.1
40	18	17.6	58.5
50	14.4	12.6	44.4
70	8.1	10.8	33.4
100	7.3	7.6	29.5
140	7.5	6.8	26.4
180	5.1	6.6	25.2

Fig. 12 Insulin Level During IVGTT - IV Tolbutamide at Baseline and 6 Months



. Table 6 : Table Effect of Hyperinsulinemia on total cholesterol Level

Time	control (mg/dl)	Hyperinsulinemic (mg/dl)
Baseline	155.2	176.7
3	177.1	264
6	168.2	257

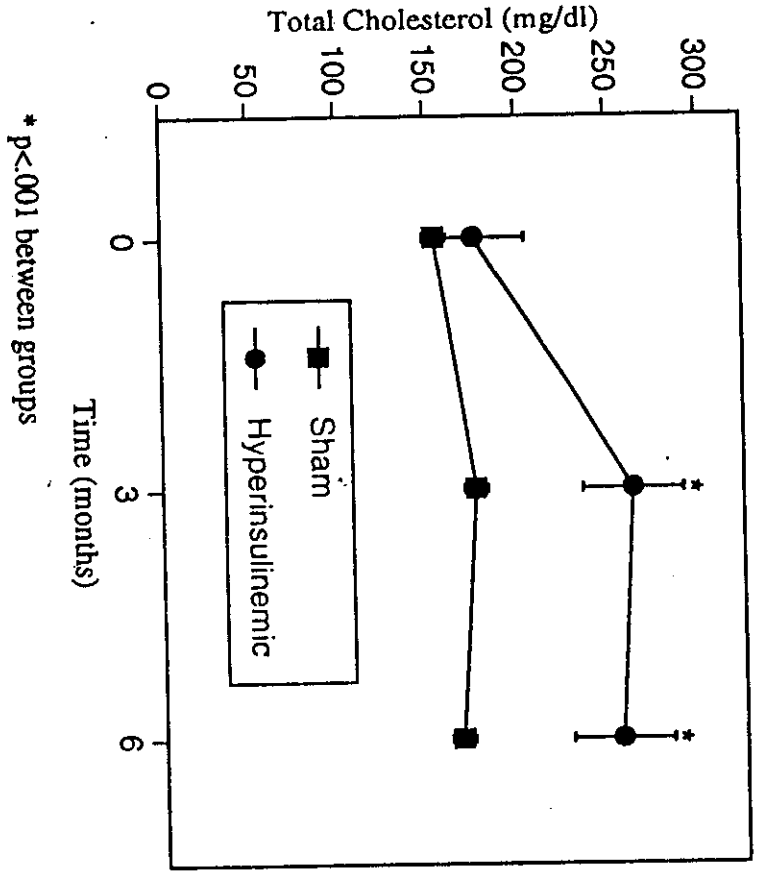


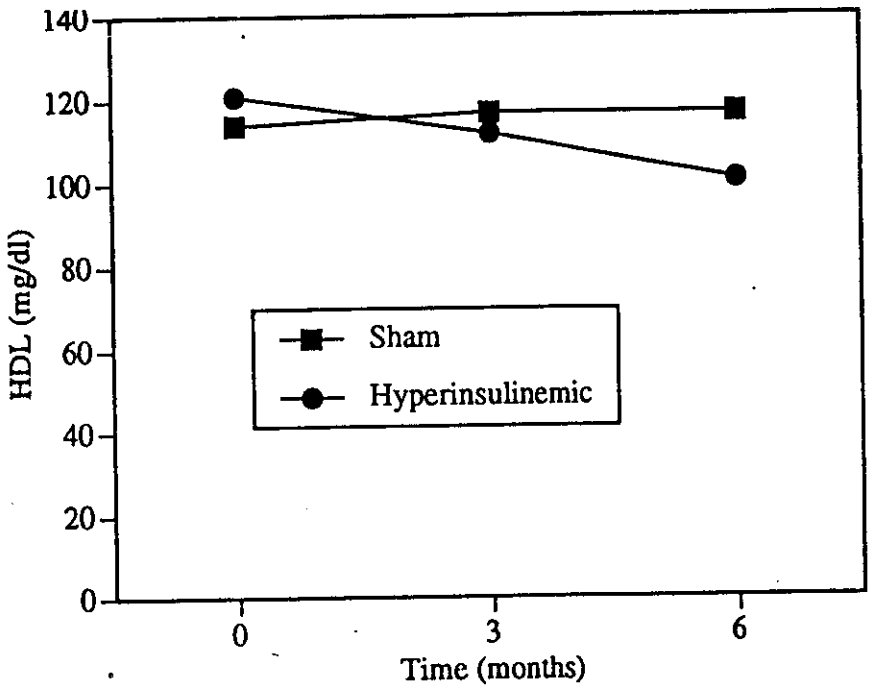
Fig. 13 Effect of Hyperinsulinemia on Total Cholesterol

* p<.001 between groups

Table 7. Effect of Hyperinsulinemia on HDL level

Time (Months)	control (mg/dl)	hyperinsulinemic (mg/dl)
Baseline	113.1	120.8
3	116.9	112.3
6	117.1	101

Fig. 14 Effect of Hyperinsulinemia on Serum HDL



* $p < .05$ between groups

LDL was significantly different between the experimental group and sham operated group (Table 8) $P < 0.001$ between groups (Fig.15).

Hyperinsulinemia increased triglyceride level (Table 9), this was highly significant between the experimental group and sham operated group $P < 0.001$ between groups, (Fig.16).

Again there was significant difference of VLDL in the experimental group and sham operated group (Table 10) ($P < 0.001$) (Fig. 17).

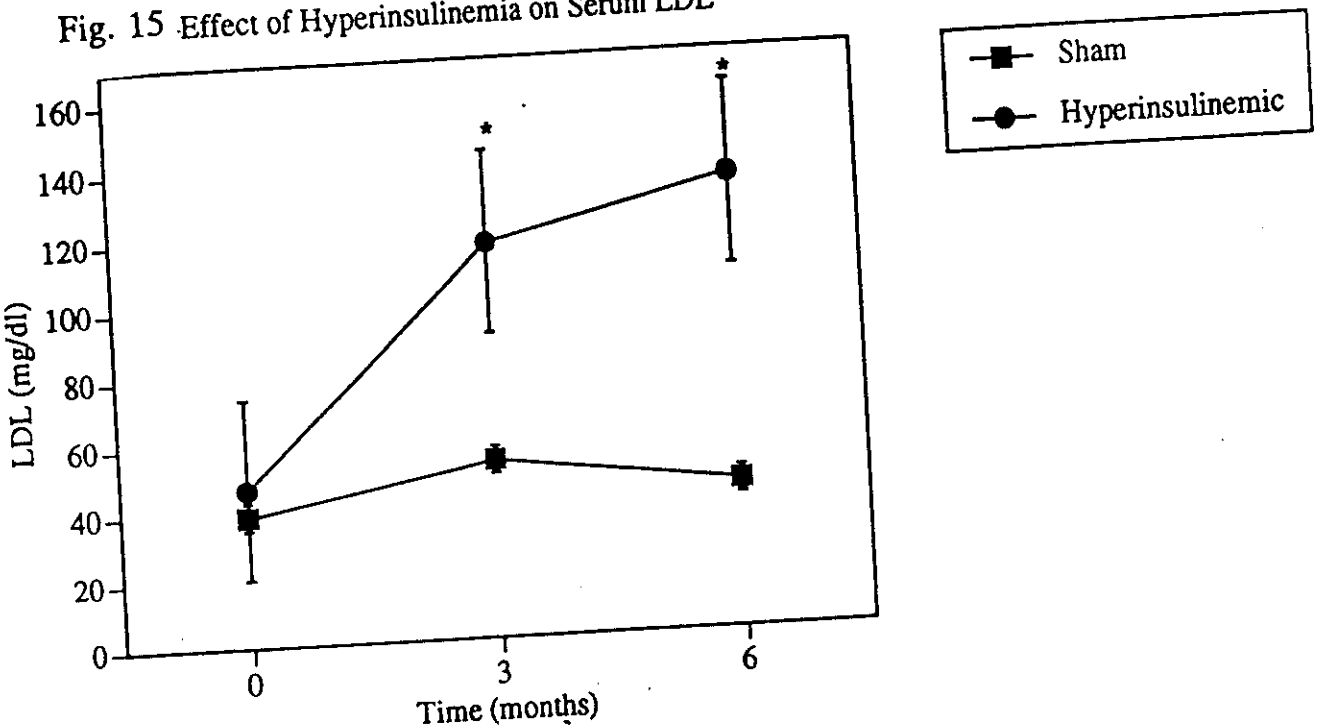
Arteriography

Completion arteriography was performed 6 months after surgery. There was significant narrowing in the iliac artery, more than 50% of the diameter, in the experimental group (Fig.18), while in the sham operated group, (Fig.19) the diameter was almost the same similar to the pre-operative arteriography.

Histology (Fig. 20)

Histological examination of vein grafts removed at necropsy, 6 month after bypass from hyperinsulinemic animals, have rvealed major structural alterations. Intimal damage has occurred, proliferation of smooth muscle cells and abrupt interruption of the elastica due to the formation of atheromatous plaque (Fig. 20). This figure shows a section of the left femoral artery in one of the hyperinsulinemic animals 6 month after bypass was harvested. One side shows an intact elastic layer lined by flat endothelium. There is abrupt interruption of the elastica due to the formation of a fibrous atheromatous plaque which can be seen on the other side of the figure.

Fig. 15 Effect of Hyperinsulinemia on Serum LDL

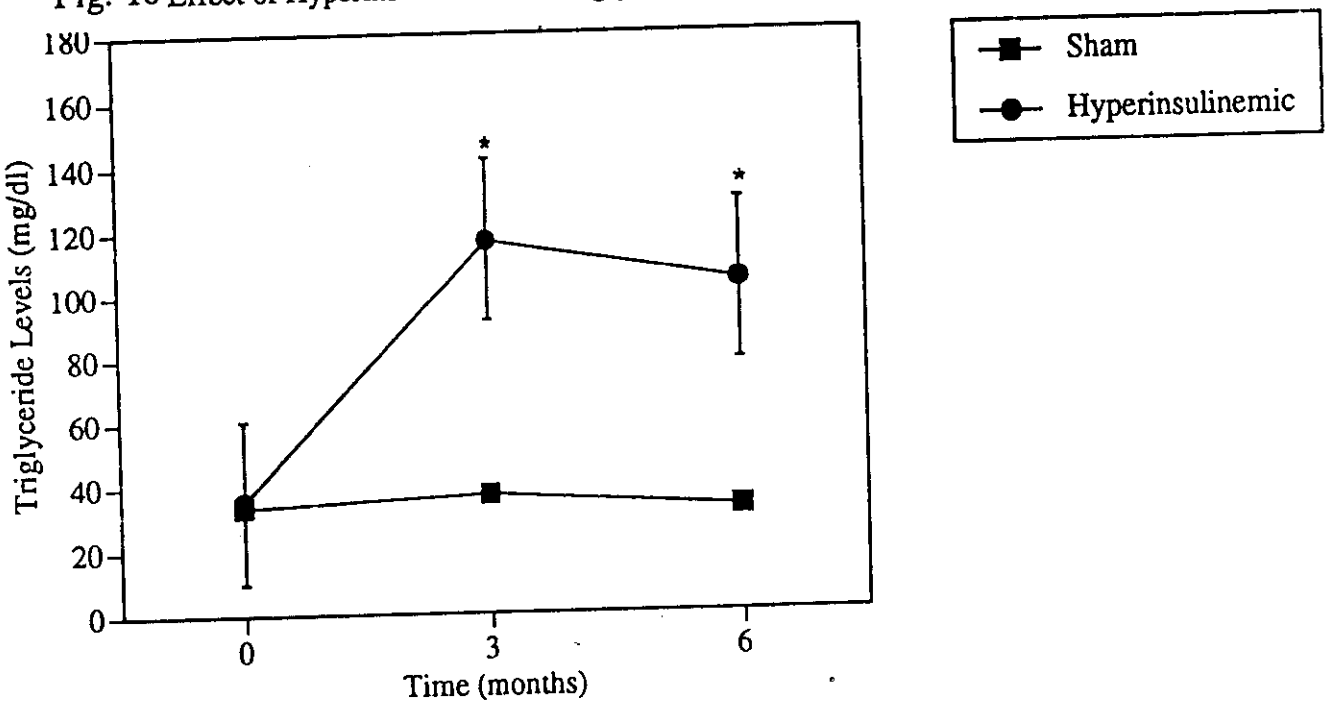


* p <.001

Table 9 : Effect of Hyperinsulinemia on Triglyceride level

Time	Control (mg/gl)	Hyperinsulinemic (mg/dl)
Baseline	33.5	35.2
3	37	116.6
6	32.7	103.8

Fig. 16 Effect of Hyperinsulinemia on Triglyceride Level



* p <.001

Table 10. Effect of Hyperinsulinemia on VLDL level

Time	Control	Hyperinsulinemic
Baseline	6.5	6.7
3	7	23.3
6	6.1	21.3

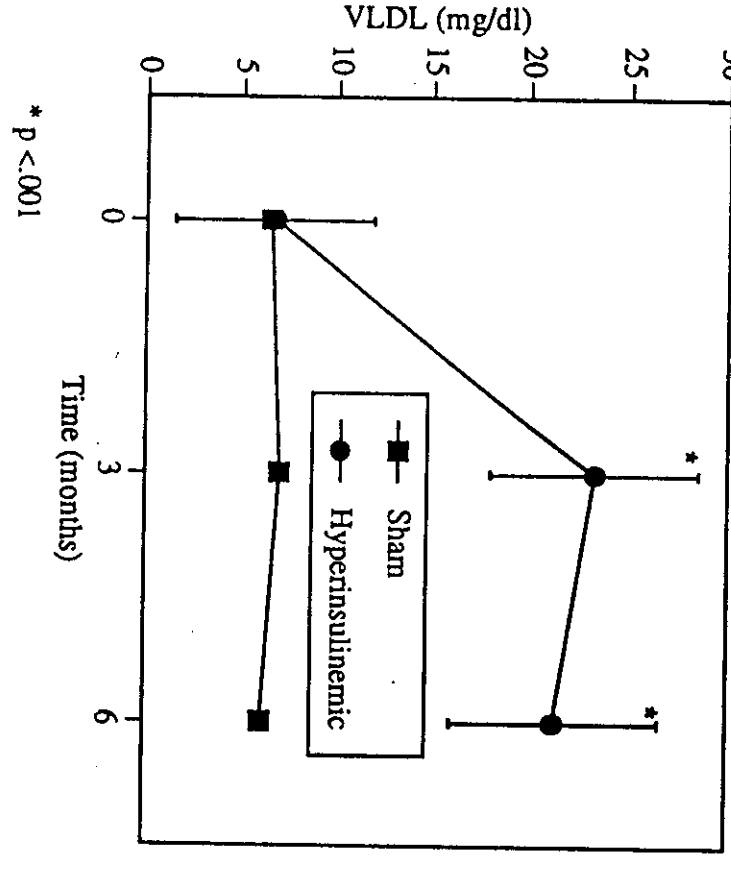


Fig. 17 Effect of Hyperinsulinemia on Serum VLDL

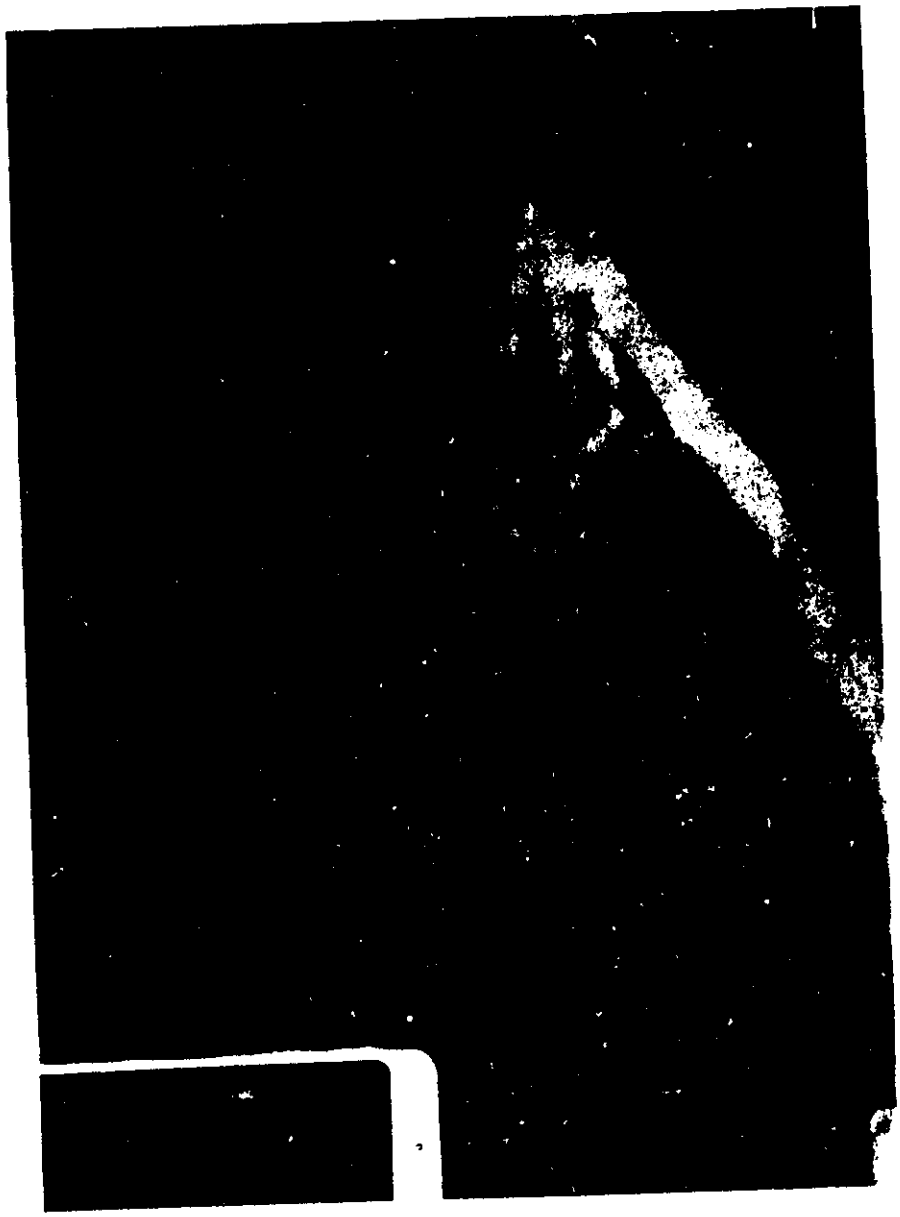


Fig.18: Completion arteriography 6 months after surgery in the experimental group showing significant narrowing of the iliac artery.

Fig.19: Completion arteriography 6 months after surgery in the sham operated group.

Fig. 20: This figure shows a section of the left femoral artery in one of the hyperinsulinemic animals 6 month after bypass was harvested. One side shows an intact elastic layer lined by flat endothelium.There is abrupt interruption of the elastica due to the formation of a fibrous atheromatous plaque which can be seen on the other side of the figure.