

## تأثير الازالة الجزئية للكبد على مكونات الدم في الكلاب

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### الملخص

أجريت جراحة الازالة التجريبية للكبد على عشرة كلاب سليمة . وقد احتملت الحيوانات العملية الجراحية بدون أى مضاعفات بعد العملية . وجمعت عينات من دم الحيوانات قبل وبعد العملية لمدة ٥٠ يوم لتحليلها .

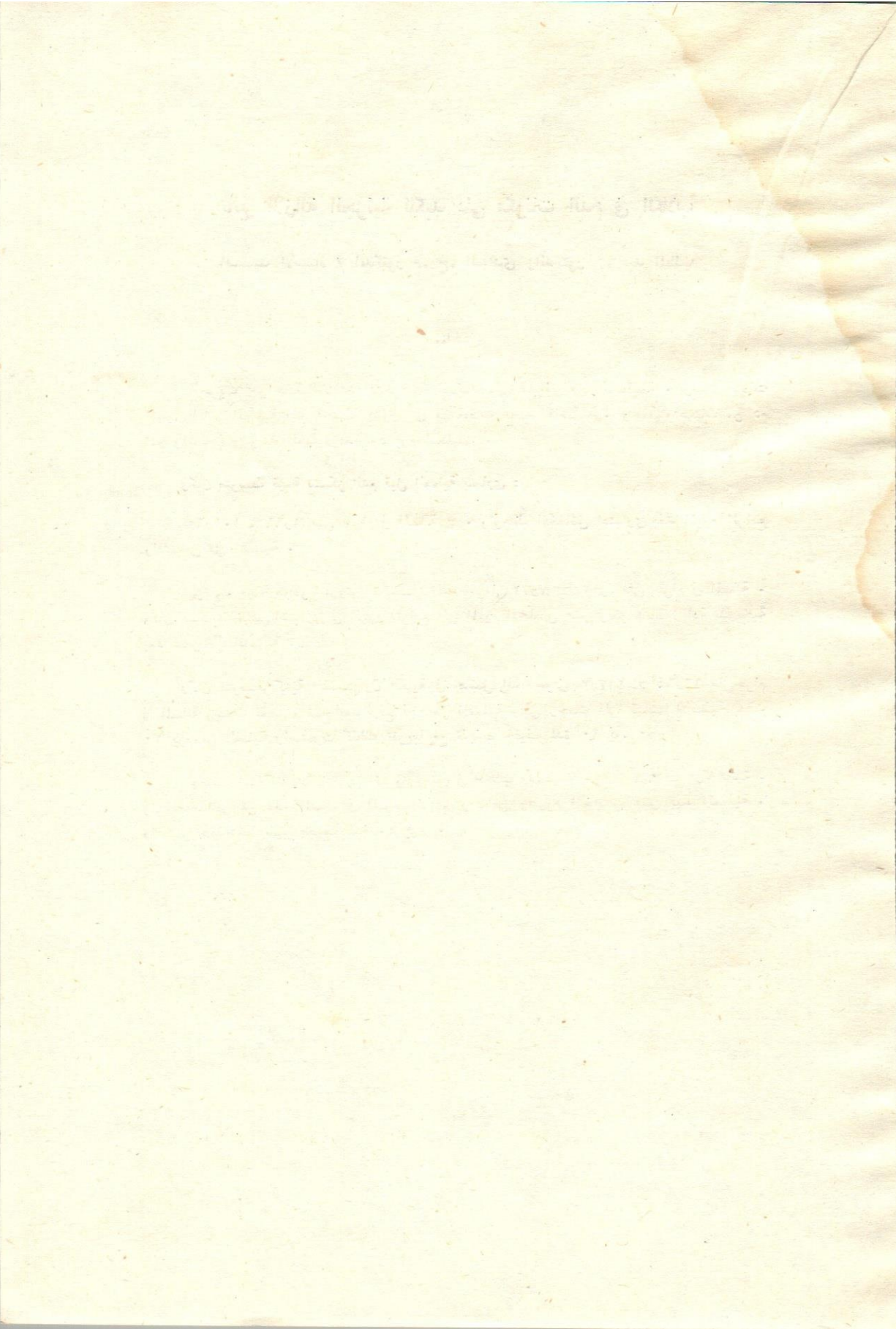
وكان متوسط قيمة سكر الدم قبل العملية يساوى :

$101.6 \pm 1.69$  مللى جرام فى المائة % . ولوحظ انخفاض اعتبارى بعد اليوم الرابع والثامن من العملية .

وكانت قيمة مجموع بروتينات مصل الدم حوالى  $7.72 \pm 0.12$  . مللى جرام فى المائة . وكان هناك انخفاض اعتبارى فى اليوم الرابع الى اليوم الخامس عشر ولكن هناك زيادة تدريجية بعد شهر من العملية .

وكان متوسط كمية الكلستيرول الكلية فى مصل الدم حوالى  $214.3 \pm 167.4$  مللى جرام فى المائة وحدث نقص واضح بعد أربع أيام من العملية ولكن رحمت الى قيمتها الاصلية بعد ٣٠ يوم من العملية واستمرت كذلك تقريبا مع تذبذب خفيف لمدة ٢٠ يوم .

وكانت المدة اللازمة لتكوين البروثرومين فى الكلاب السليمة حوالى  $9.4 \pm 0.2$  ثانية . ولوحظ تأخير عن هذا المعدل فى اليوم الرابع والثامن واليوم الخامس عشر بعد العملية . واستمر هكذا مع تغير طفيف لمدة ٢٠ يوم .



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## THE EFFECT OF PARTIAL HEPATECTOMY ON SOME BLOOD CONSTITUENTS IN DOGS

(With one table and one figure)

By

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### SUMMARY

Experimental partial hepatectomy was performed on 10 healthy dogs. Re-section of about 60 per cent of the liver was made. The animals withstood well the operation and showed no serious post-operative complications. Blood samples were collected for analysis before and after the operation for 50 days.

The mean value of fasting blood sugar before the operation was  $101.6 \pm 1.69$  mg%. A highly significant decrease was observed on the 4th and 8th days after the operation.

The pre-operative total serum proteins averaged  $7.72 \pm 0.12$  mg%. A significant decrease was observed on the 4th day after operation till the 15th day. A gradual increase was seen after one month from the operation.

Total serum cholesterol averaged  $214.3 \pm 16.64$  mg%. There was a prominent decrease four days after the operation. After 30 days of the operation it returned to its original value and remained nearly so with slight fluctuations for about 20 days.

The prothrombin time in normal dogs was  $9.4 \pm 0.2$  sec. Delay in this time was noted on the 4th, 8th and 15th days after the operation. The time returned to normal on the 30th day after the operation and remained so with slight variations for 20 days.

All the estimated blood constituents regained their physiological levels after the 50th day of the experiment.

### INTRODUCTION

Experimental partial hepatectomy in animals was carried out to investigate its post-operative complications. This went side by side with a study of the liver functions which are mostly affected by diverse metabolic activities and by the unique regenerative power of the organ (WELLS, 1962). It is

generally accepted that the liver is the site of formation of most plasma proteins as well as prothrombin (WHIPPLE, 1948, and MUNRO and AVERY, 1946).

Cholesterol is synthesized to a certain extent in all tissues, but the largest amount is formed in the liver (COLES, 1967). The liver is also the most important organ in removing and contributing glucose to the blood and is capable of synthesizing it from amino and fatty acid fragments (CORNELIUS and KANEKO, 1963). According to the available literature it seems that post-operative complications after partial hepatectomy have been thoroughly studied in canines. It is however, to study, the blood levels of sugar, total serum proteins, total serum cholesterol and prothrombin time after partial hepatectomy in dogs.

### MATERIAL AND METHODS

The study was conducted on 10 clinically healthy dogs of different ages (2-5 years) and sexes. The individual weight averaged 14 kg. The daily diet was constant in quantity and quality.

The surgical technique described by EL-AMROUSI, EL-GINDI, EL-MONZALY and MOTTELIB (1971) was adopted and about 60% of the liver was surgically removed, including the caudate, left lateral and right lateral lobes. Blood samples for analysis were collected on the 10th, 7th and 4th day before and the 4th, 8th, 15th, 30th, 40th and 50th day post-operation.

Blood sugar was determined by the method described by FOLIN and UW (1920) and total serum proteins by the method described by LEVINS ON and MacFATE (1961). Serum samples were used for the quantitative estimation of total cholesterol after the method of PEARSON, STERN and MCGAVACK (1953) as described by WATSON (1960). Reagents for this test were in the form of test kits supplied by Haurry\*. The prothrombin time in seconds was estimated according to the method described by MONTIGEL and PULVER (1952). The results were statistically analysed using student's t-test.

### RESULTS AND DISCUSSION

All the dogs withstood well the surgical intervention and manifested no post-operative complications during the course of the experiment which

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lasted for 50 days. Temperature, pulse and respiratory rates showed insignificant changes. Appetite, urination, defaecation and general behaviour of the dogs were not greatly affected.

The laparotomy wound healed by first intention and the sutures were removed 8-10 days after operation.

The mean values of the blood constituents before and after operation are shown in Table 1 and Fig. 1.

TABLE 1 : Value of blood constituents before and after partial hepatectomy in dogs

Blood Constituents	Pre-operative Average Values	Post-operative Average Values					
		4th day	8th day	15th day	30th day	40th day	50th day
Sugar (mg%) . . . . .	101.6 ±	*** 42.3 ±	*** 51.6 ±	92.8 ±	93.5 ±	95.1 ±	101.4 ±
	1.69	2.5	2.9	4.35	5.91	5.19	1.43
Total Serum proteins (gm%) . . . . .	7.72 ±	*** 6.72 ±	*** 6.76 ±	** 6.96 ±	* 7.28 ±	7.29 ±	7.73 ±
	0.12	0.17	0.14	0.17	0.14	0.17	0.02
Total Serum cholesterol (mg%) . . . . .	214.3 ±	192.7 ±	177.3 ±	188.4 ±	214.3 ±	185.0 ±	215.0 ±
	16.64	6.78	16.85	13.78	18.33	11.62	11.2
Prothrombin time (sec.)	9.4 ±	*** 12.1 ±	*** 12.4 ±	* 10.9 ±	9.4 ±	9.5 ±	9.3 ±
	0.2	0.5	0.5	0.5	0.14	0.21	0.11

± Standard error, \*\*\* p < 0.001, \*\* p < 0.01, \* P < 0.05.

#### Blood Sugar

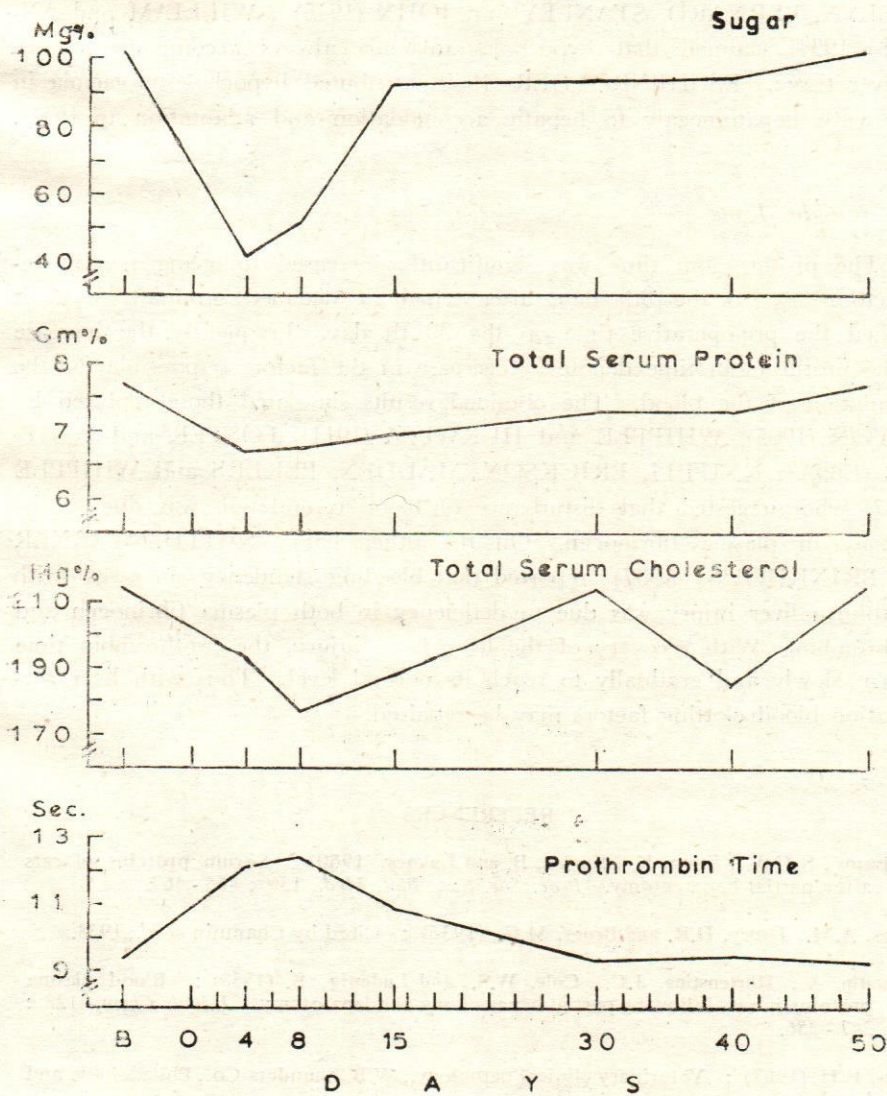
There was a highly significant fall in the concentration of blood sugar on the 4th day after the operation. On the 8th day the level started to

increase and reached an average of 92.8 mg% on the 15th day and remained approximately at that level until the end of the experiment. Thus the effect of partial hepatectomy on blood sugar level appears to be of significance for only four days, returning to normal on the 15th day. This mechanism may be due to several factors including hepatic and renal uptake and its release which is usually removed to the peripheral tissues. CORNELIUS and KANEKO (1963) reported in addition, that the blood sugar level itself may serve as a stimulus to the liver and is a factor in determining whether glycogenesis or glycogenolysis will predominate. Clinically the experimental animals showed no signs which might reflect the effect of the operation on carbohydrate metabolism. It could be added that hypoglycaemia is a late occurrence in liver diseases and rarely becomes important except in hepatic coma or precoma (WELLS, 1962).

#### *Total Serum Proteins*

Total serum proteins before operation were within the normal physiological limits as reported by CORNELIUS and KANEKO (1963) and COLES (1967). There was a highly significant decrease which remained up to the 15th day after operation, followed by a gradual rise to reach nearly the level before operation on the 30th day and the pre-operative level on the 50th day. Similar observations were reported by MUNRO and AVERY (1946) ; ALIVISATOS, STERN, SAVICH and LUKACS (1960) in dogs and rats, respectively. The authors attributed this change to mitotic activity of the liver which reached its maximum between the second and thirtieth days after operation. In this respect, MUNRO and AVERY (1946) concluded that the liver could be considered as a source of blood globulin and albumin. It was also stated that 70% of the liver substance could be removed safely HIGGINS and ANDERSON, 1931. BRUES, DRURY, and BRUES, 1936). On the other hand, CHANUTIN, HORTENSTINE, COLE, and LUDEWIG ( 1938 ) observed that the beginning of liver regeneration after partial hepatectomy in rats was started on the third post-operative day. The authors mentioned that the water content, number and size of cells, appeared to be normal about the 14th day. Recently, EL-AMROUSI *et al.* (1971) demonstrated that the activities of both S-GOT and S-GPT were regained to normal levels 15 days after experimental partial hepatectomy in dogs. However, in 2 dogs where liver abscesses were detected at autopsy a marked elevation of both enzymes was clearly evident.

FIG. 1.



B = Before operation

O = Operation

### *Total Serum Cholesterol*

Following the operation there was a fall in total serum cholesterol which reached its lowest level on the 8th day and then started to increase progressively. This hypocholesterolaemia may be due to reduction in the rate of hepatic synthesis of this steroid, and later restored by liver regeneration. EVELYN, BERNARD, STANLEY and JOHN (1945) ; WILLIAM and ANGUS (1934) claimed that hypocholesterolaemia always accompanies injury to liver tissue. ESCHENROEDER (1969) attributed hypocholesterolaemia in dogs with hepatomegaly to hepatic accommodation and adaptation to stress.

### *Prothrombin Time*

The prothrombin time was significantly increased following partial hepatectomy up to the 8th day, after which it declined gradually until it reached the pre-operative time on the 30th day. Frequently the increase in the prothrombin time denotes a decrease in the factors responsible for the coagulation of the blood. The obtained results simulated those reported by DOYON (1905), WHIPPLE and HURWITZ (1911), FOSTER and WHIPPLE (1922) ; KNUTTI, ERICKSON, MADDEN, PEKERS and WHIPPLE (1937) who suggested that disturbance of blood coagulation was due to the decrease in plasma fibrinogen. On the other hand, SMITH, WARNER and BRINKHOUS (1937) reported that bleeding tendency in cases with chloroform liver injury was due to deficiency in both plasma fibrinogen and prothrombin. With recovery of the liver from injury, the prothrombin time returns slowly and gradually to reach its normal level. Thus with liver regeneration blood clotting factors may be repaired.

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1. The first part of the paper is devoted to a general discussion of the problem.

2. In the second part, we consider the special case of a homogeneous system.

3. The third part is devoted to the study of the non-homogeneous case.

4. In the fourth part, we discuss the question of the stability of the solutions.

5. The fifth part is devoted to the study of the asymptotic behavior of the solutions.

6. In the sixth part, we consider the question of the existence of solutions.

7. The seventh part is devoted to the study of the uniqueness of the solutions.

8. In the eighth part, we discuss the question of the regularity of the solutions.

9. The ninth part is devoted to the study of the dependence of the solutions on the parameters.

10. In the tenth part, we consider the question of the continuation of the solutions.

11. The eleventh part is devoted to the study of the bifurcation theory.

12. In the twelfth part, we discuss the question of the global existence of solutions.

13. The thirteenth part is devoted to the study of the qualitative theory of differential equations.