COMPUTER MODEL OF THE RENAL FILTER CONTROL SYSTEM

Roa, Laura
E.T.S.I.I., Universidad de Sevilla.

Cantero, A.
Becario de la C.A.I.C.Y.T.

Solis Galera, A.
Becario adscrito al Dpto de Cirujia Plastica y Quemados. Ciudad Sanitaria Virgen del Rocio. Sevilla

Franco, A.
Dpto de Cirujia Plastica y Quemados. Ciudad Sanitaria Virgen del Rocio.Sevilla.

SUMMARY

A mathematical model and digital computer simulation of the human renal filtration controls are herein developed.The purpose of the model is to provide a method of analysing renal filtration control hypotheses which cannot easily be tested in an animal or human.

The method used in the construction of the model was system dynamics.

We propose an original formulation for the numerous different variables, eg. Bowman capsule pressure, glomerular absorption, net filtration and other considered variables in the model.

This model can simulate the dynamic functions of variables such as colloidal osmotic pressure, glomerular capillaries, tubular filter,along with other variables of difficult clinical determinants.

The model simulates disparate situations, such as the effects of renal filtration variations of arterial pressure, concentration of plasma proteins...

The results presented coincide with those of other authors.

INTRODUCTION

As is well known, the renal system regulates the longterm distribution of the human bodily liquids. The importance of the study of this regulatory mechanism is due as much to the number of pathological causes which can give rise to a kidney failure as to the critical clinical situations which are thus created, both of acute or chronic nature. Just as well- known is the importance of renal filtration as one of the determinant variables of diuresis, as is demonstrated in the ample bibliography which exists on the subjet.

Amongst others, we can highlight the physiological study carried out by Guyton (1976) giving an overall vision of the regulating mechanisms which participate in renal filtration, and also the exhaustive analysis carried out by Rose (1985) from a physiopathological point of view. In all these studies, the importance of two variables in the establishment of renal filtration is emphasized : arterial pressure and the concentration of plasma proteins, irrespective of whether normal or pathological situations are being considered.

It is in this line of research into renal filtration which the present study is included, but attempting to give a macroscopic and dynamic vision of the different mechanisms which take part in the regulation and interactions of renal filtration.

CONSTRUCTION OF THE MODEL

The techniques used in the construction of the model were those of Dynamics of Systems (Forrester,1968; Goodman, 1974; Aracil, 1984...).

The model was developed in two stages. The first stage dealt with the control mechanisms which regulate the net renal filtration. For this purpose the functioning of the renal system has been considered as that of a nephrom. Figure 1 shows the causal diagram corresponding to this stage.

To quantify the relations established in this first stage of the model, the experimental data determined by other authors has been used (Guyton,1976; Ganong,1982..). The conclusions reached were the following:

1- The pressure in the Bowman's Capsule is considered as a function of the net glomerular filtration at the afferent arterial level, and the reabsorption at the efferent arterial level.
2- The interstitial glomerular pressures are not taken into account.

With this first version of the model, it is possible to analyse the behaviour of the net glomerular filtration (GNF) when the variables of arterial pressure (AP) and the concentration of plasma proteins (PPC) are disturbed in isolation.

However this type of alteration would not have a great physiological significance since isolated alterations in the PPC and AP variables are going to produce certain reactions in the regulatory mechanisms of AP which do not permit an alteration in one of them whilst the other remains constant, given the relations between these variables. For this same reason, neither would we be able to disturb simultaneously both variables fixing a priori certain percentage variations.

In the second phase of the model the regulatory mechanisms of the variable AP are added to the existing structure.

At this stage, the exchange of fluids between the different compartments (extra and intracellular) are studied when some disturbance modifies the variables that we have named "net liquid input", defined as the difference between the input and output liquids by the mouth and the remaining vias (except the kidneys) respectively, and the "filled factor", which permits us to evaluate the alteration in the body fluids after an infusion of any solution into the circulating fluid.

The regulatory mechanics which have been considered in this stage are the following: the kidney's long-term regulation of arterial pressure, transcapillary fluid exchange, circulatory adaptability, the limphatic system and the regulation of the cardiac output by peripheral resistence.

In addition, the baroreceptor reflex system must be included to show the influence of sympathetic tone on the cardiac output, peripheral resistences, and the kidneys to alter urinary output and mean circulatory pressure.

Figure 2 show the causal diagram of the transcapillary fluid exchange. Similar causal diagrams have been elaborated for the remaining control mechanisms.

The state variables which determine the behaviour of the model are the plasma, free interstitial and intracellular volume, the interstitial and plasma protein, the extracellular and the intracellular electrolytes.

Figure 3 show the Forrester diagram of the interstitial compartment , similar Forrester diagrams have been elaborated for the remaining causal diagrams.

The considered supositions for the variables quantification wich takes places in this stage have similarity with the most of the macroscopic hemodinamic studyes (Rudinger, 1966; Warner, 1969 ; Leonard, 1973 ; Thain, 1967 ; Tanaka, 1979 ; Abbrecht, 1980 ; Kakinchi, 1981 ; Roa , 1982 ; Venkatachalam , 1978...).

In this form, a new version model can be perfomed which show the evolution of renal filtred under the influence of the long-intermediate and short-term control variables.

The function CVI have been incorporated to the program for the simulation of the model. This function is an interpolacion function used to determine the pressure of the right auricle from the values of cardiac output (Pickering, 1969). The control variables were incorporated into the model by CLIP function which facilitates the accesibility of the model to experts in the renal system even if they are not experts in system dynamics or computer.

ANALYSIS OF SENSIBILITY

The singular perturbations methods has been used to analyse the sensibility of the more significative state variables when

the following parameters are perturbed: Initial frecuency of baroreceptor pulse (IFBP) and mean circulatory normal pressure (MCNP).

The results of this analysis show that the model is not practically altered by perturbations of the parameter IFBP. The effects of varying the parameter MCNP are negligible for perturbations less that 10 per cent of the normal values of this parameter and when the simulation time is short (less 10 minutes).

This method show that the more significative state variables return to near normal values at the end of the simulation when a changes occurs in the interstitial or intracellular volume within physiological limits.

A more detailed analysis of model sensibility is made by Montecarlo's procedure.

The effect of change in the two parameters MCNP (mean circulatory normal pressure) and initial values of the most significant stated variables (plasma interstitial and intracellular volume) have been analysed. Variations of 5% in both, MCNP and initial values were produced in the model for various simulated times, TS, (TS=10, 180, and 360 minutes). The results have shown that interstitial and intercellular volume return to near normal values for TS= 180 minutes, while the plasma volume returns for TS= 360 minutes.

In conclusion, these results show that the model depends on its own structure but is not practically altered by the particular values of the initial conditions and model parameters when physiological conditions are considered.

SIMULATION RESULTS

In order to prove the validity and use of the constructed model different experiences have been simulated. The results are presented of simulating the known experience of increasing the net liquid intake from its normal value of 1 ml/min. to 3.5 ml/min. in an isotonic solution with the body fluids during a period of six days.

Figure 4 shows the behaviour of the variable AP As can be observed, this variable increases during the first two days and later decreases and establishes itself at a value of approximately 106 mmHg which allows it to eliminate by diuresis the excess liquid administered.

Figure 5 represents the behaviour of PPC,showing how while the variable AP increases, the concentration of plasma pro- teins decreases, and, after the second day, begins to recover establishing it self a value lower than the normal.

The behaviour of these variables is justified if one observes the evolution of the variables plasma volume (PV) Fig 6, and interstitial volume (IV) Fig 7. Very noticeable is the sharp

increase of PV during the first day which later decreases very slowly in spite of the fact that the disturbance is maintained. On the contrary, the increase of IV is slower due to the fact that the regulatory system of transference of liquids between the plasma and interstitial compartments is a short-term mechanism.

Figure 8 represents the behaviour of the cardiac output variable (CG) highlighting the fact that in the first two days its evolution is parallel to that of the AP, and that after the second day it decreases until approximately the fourth day on which it reaches practically its normal value in spite of the increase in the plasma volume. These results are in agreement with other reports in the references (Guyton et al., 1973, Guyton 1976).

Figure 9 shows the dynamic evolution of the net filtration variable (NGF). The parallel between the behaviour of this variable and that of the arterial pressure is noticeable, a result coinciding with those of other researchers which demonstrates the importance of the arterial pressure variable in the establishment of the net filtration and the favorable effect which the behaviour of the PPC exercises on the behaviour of the NGF.

CONCLUSIONS

Using the system dynamic approach a model has been constructed which is capable of predicting an integrated response from all the elements involved in the renal filtration.

The development of this model means, in our opinion, that it is possible to make the following contributions:

A contribution to the physiopathological study of renal filtration, from a macroscopic perspective which allows analysis of the interactions between the different regulatory mechanisms considered.

The knowledge through simulations of the qualitative and quantitative behaviour of different variables difficult to determine in daily clinical practice.

The possibilty of analysing the effects of different solutions on filtration.

The beginning of a line of research that will enable us, on adding to the present model the mechanisms of tubular control to make new contributios to the study of renal physiopathology.

Also worthy of emphasis is the general accessibilty of the model to experts in the renal system, even if they are not expert in system dynamics or computer.

REFERENCES

Abbrecht, P.H. (1980). "Regulation of extracellular fluid volume and osmolality" Annals of Biomedical Eng.,vol.8 pp 461-472.

Aracil,J (1984)."Introduction à la dynamique des systèmes" Presses Universitaires de Lyon.

Forrester,J W (1968). "Principles of Systems", Wringt-Allen Press.

Ganong, F.W. (1982). "Fisiologia Medica", 8 Edicción. El Manual Moderno S.A., Mexico D.F.

Guyton, A.C.,Jones, C.E.,Coleman, T.G. (1973). "Circulatory Physiology: Cardiac output and its regulation " , W.B. Sanders Co, pp. 298-300.

Guyton, A.C. (1976). "Textbook of medical physiology", W.B. Sanders Co.

Goodman, M.P. (1974). "Study notes in system dynamics" Wringt Allen Press.

Kakiuchi,Y.; Nakajima,S.; Arai, T.; Horimoto,M.; Kikuchi,Y.; Koyama, T. (1981)."Transvascular osmotic flow reflected by changes in plasma oncotic pressure of anasthetized dog". Japanesse journal of physiology. vol. 31,pp. 67-82.

Leonard, J.I.; Abbrecht,P.H. (1973)."Dynamics of plasma-interstitial fluid distribution following intravenous fusifusion in dogs". Circulation research,vol XXXIII pp.735-748.

Madden, A., De Deen, W. and Breener, B.M. (1974)"Dynamics of glomerular ultrafiltration, V I: Studies in the primate", Kidney Int., 5:271.

Pickering, W.D.; Nikiforuk, P.N. and Merriman, J.E. (1969). "Analoge computer model of the human cardiovascular control system", Med. Biol. Eng., Vol. 7 pp. 401-410.

Relman, A.S,and Levinsky, N.G.(1971)."Clinical examination of renal function",M.B. Straus and L.G.Welt (eds.) Diseases of the Kidney,Little,Brown,Boston.

Roa, L. (1982). "A model of the transport and distribution of the body fluids using the system dinamic approach". Procd. IEEE Computer Society International Conference on Medical Computer Science/Computational Medicine, pp. 393-401.

Rose,B.D. (1985)."Fisiopatologia de las enfermedades renales". McGRAW-HILL de Mexico, S.A. de C.V.

Rudinger, G. (1966). "Review of current mathematical methods for the analysis of blood flow", Biomedical Fluid Mechanics Symposium, ASME, pp. 1-33.

Scher, A.(1974). "Control of arterial blood pressure, in TC" Ruch and H.D. Patton (eds.),Physiology and Biophysics,vol 2, Saunders, Philadelphia.

Tanaka, Y., (1979). "Whole body transvascular filtration coefficient and interstitial space capacitance", Japanesse Journal of Physiologie, 29, pp. 181-193.

Thain, J.F., (1967). "Principles of osmotic phenomena: osmotic phenomena in animals", The Royal Inst. of Chem., monographs for teachers, London.

Venkatachalam, M.A. and Renuke, H.G . (1978). "The structure and molecular basis of glomerular filtration ".Cir. Res., 43:337.

Warner, H.R. and Russell, R.O., (1969). "Effect of combined sympathetic and vagal stimulation on heart rate in the dog", Circulation Research, vol. XXIV, pp. 567-573.

THIS MATERIAL IS BASED ON WORK SUPPORTED BY THE C.A.I.C.Y.T. UNDER GRANT 1078/84.

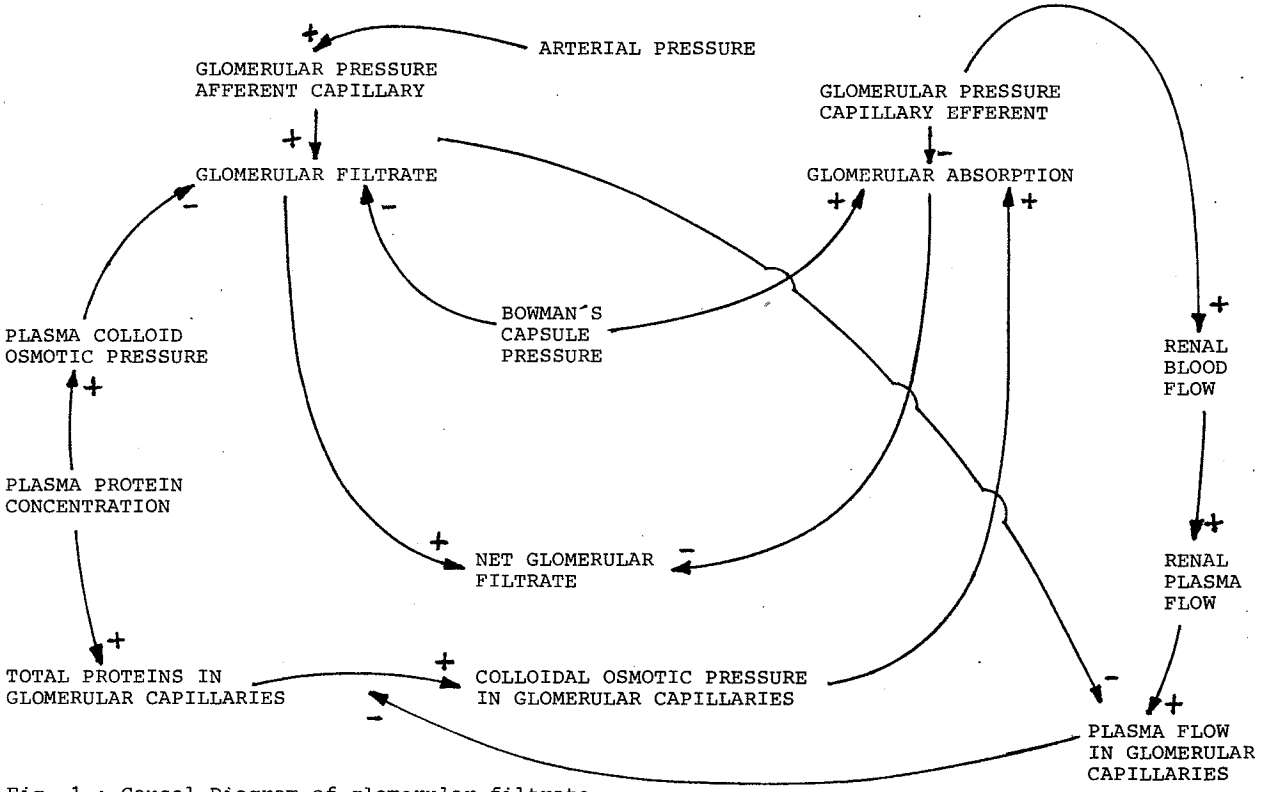

Fig. 1 : Causal Diagram of glomerular filtrate

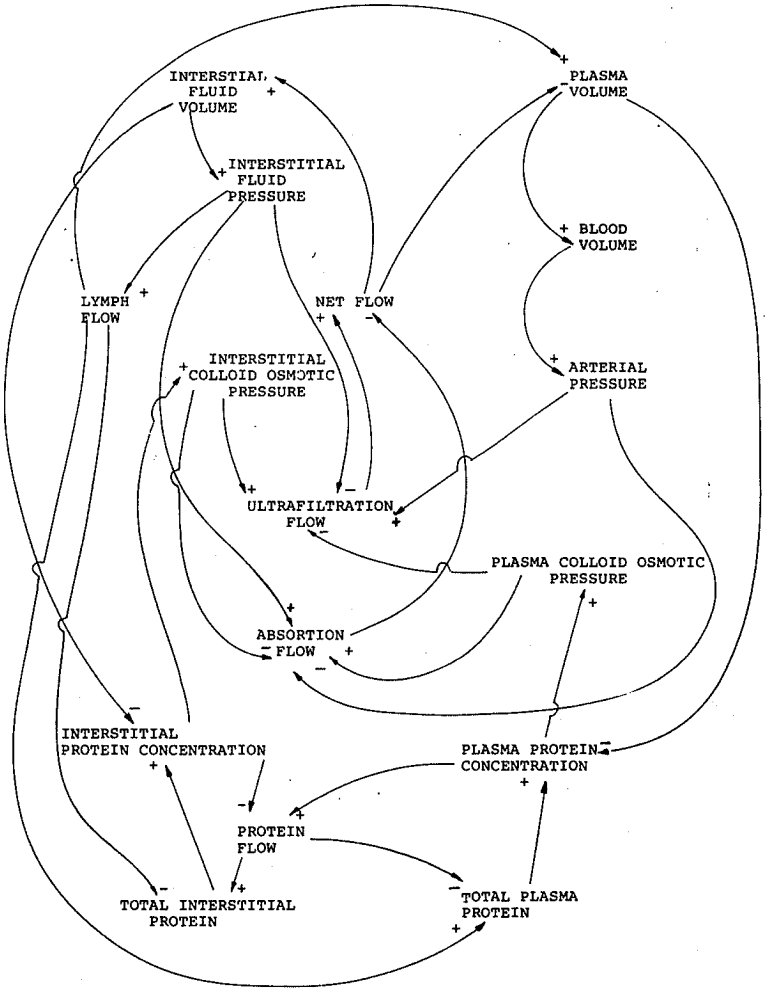

Figure 2 : Causal diagram of transcapillary fluids exchange.

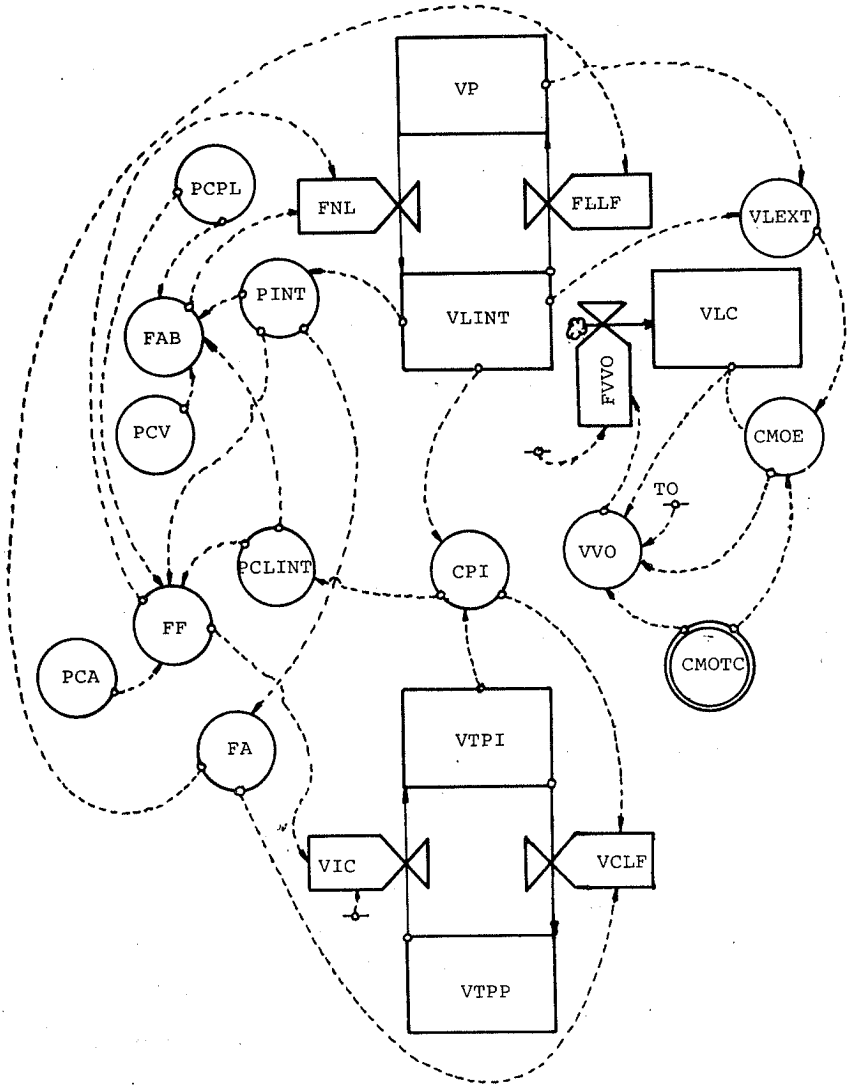

Figure 3. Forrester diagram of interstitial compartment

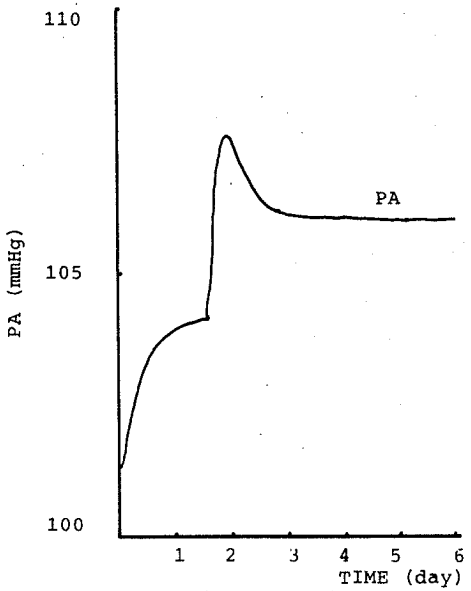

Figure 4. Simulation results for mean arterial pressure (PA)

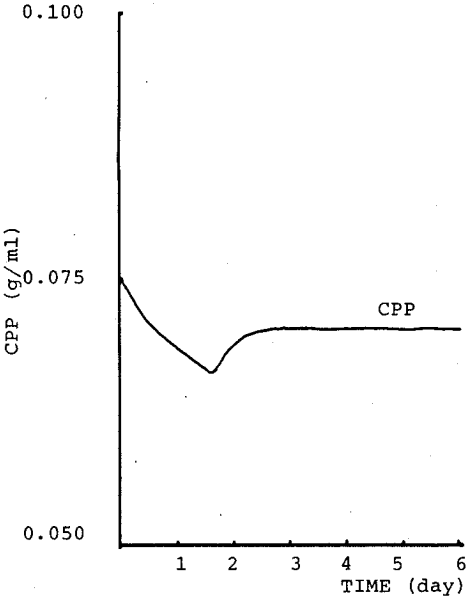

Figure 5. Simulation results for plasmatic proteins concentration (CPP)

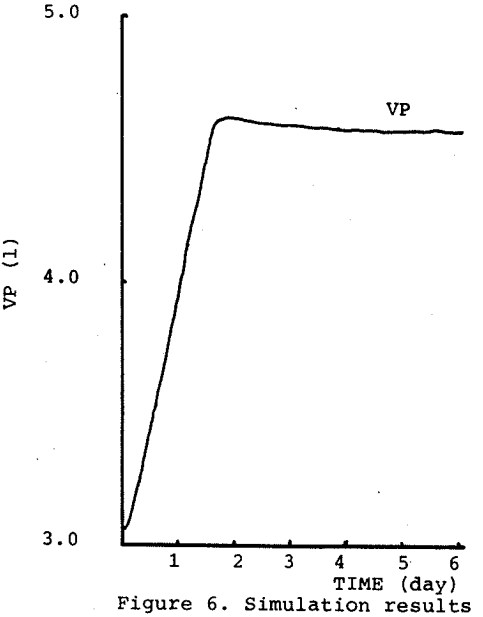

Figure 6. Simulation results for plasmatic volume (VP)

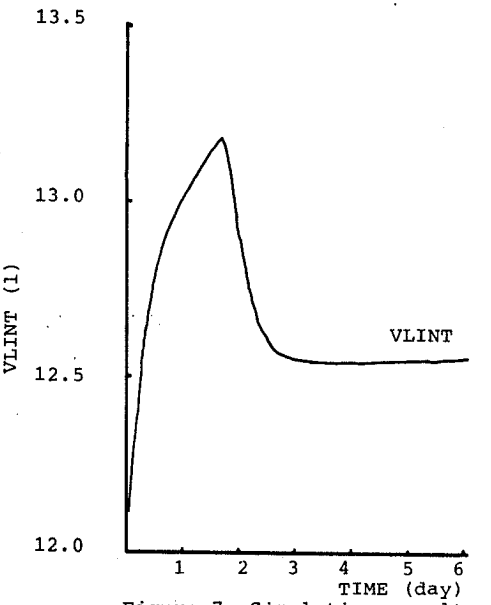

Figure 7. Simulation results for interstitial fluid volume (VLINT)

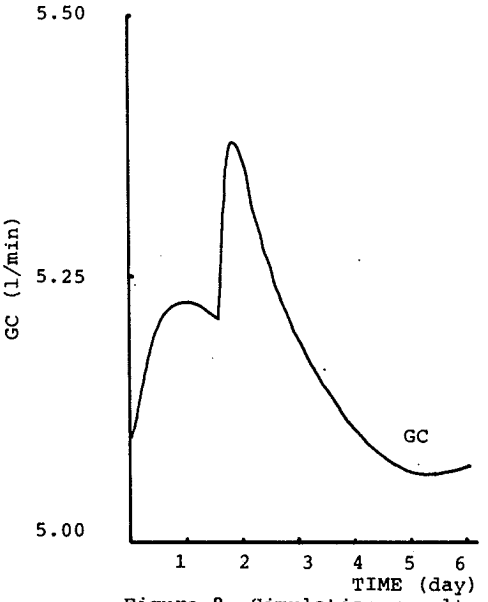

Figure 8. Simulation results for cardiac output (GC)

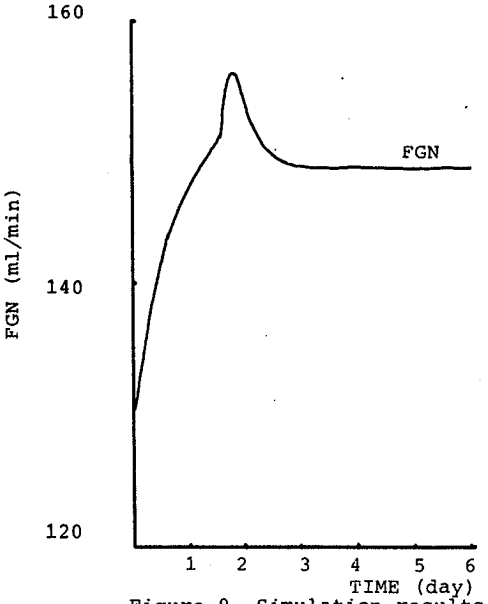

Figure 9. Simulation results for net glomerular filtrate (FGN)