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BLEEDING AND COAGULATION STUDIES IN SMALLPOX AND CHICKEN-POX MADRAS, INDIA, 1962-63

by

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A total of 71 patients were studied with various bleeding and coagulation tests during this period. Sixty patients in the group had smallpox, 29 with haemorrhagic smallpox and 41 without haemorrhage. Twelve patients with chicken-pox were also studied. The following studies were undertaken:

A. VASCULAR AND PLATELET FUNCTION

1. Bleeding time. Bleeding time was prolonged in 17 out of 17 patients with haemorrhagic smallpox, but was prolonged in only one out of nine patients with non-haemorrhagic smallpox; it was normal in all varicella patients.

2. Clot retraction. Clot retraction was abnormal in 16 out of 16 patients with haemorrhagic smallpox and in two of eight patients with non-haemorrhagic smallpox. It was normal in 12 patients with chicken-pox.

3. The tourniquet test was positive in seven of 18 patients with haemorrhagic smallpox and abnormal in only one of nine with non-haemorrhagic smallpox. It was normal in one patient studied with chicken-pox.

4. Blood smear for platelets revealed a deficiency in all with haemorrhagic smallpox in whom this observation was made. Platelet counts were not done routinely in this study.

The consistently prolonged bleeding time and abnormal clot retraction along with the deficiency of platelets on the blood smear support the previous observations that thrombocytopaenia is an important factor in the majority of cases with haemorrhagic smallpox.

B. COAGULATION STUDIES

Clotting time. A lee white coagulation time was performed in 15 haemorrhagic cases and was significantly abnormal in only four. It was normal in three of four non-haemorrhagic cases. The following coagulation studies were performed in 29 haemorrhagic cases, 41 patients with non-haemorrhagic smallpox, nine with chicken-pox and 69 controls.

1. One-stage prothrombin (quick test). This measures all of the second stage factors. The results (Figure 1) revealed a marked prolongation in all six cases of early haemorrhagic smallpox and only slight abnormality in a few of the other haemorrhagic cases and in non-haemorrhagic smallpox. It was within the range of the normal controls in all chicken-pox cases.

2. Specific prothrombin activity. Specific prothrombin was evaluated in the same patients (Figure 2). There was a significant decrease of prothrombin in the early haemorrhagic cases and in those classified as "early-late". In the late haemorrhagic patients and the non-haemorrhagic smallpox cases there were slightly decreased levels in a few, but not sufficient to be responsible for bleeding in the majority.

3. Thrombin time. The thrombin time, which is a test for antithrombin, was performed in the same group of patients. The results (Figure 3a) show a marked abnormality in all six patients with early haemorrhagic smallpox. There was no significant abnormality in those classified as "early-late" haemorrhagic or late haemorrhagic. A few patients with non-haemorrhagic smallpox showed prolongation of the thrombin time.

4. Serum prothrombin time (prothrombin consumption test). A serum prothrombin time was performed in the same group of patients. This determination evaluates the activity of platelets as well as all first stage factors. It will be noted (Figure 4a) that essentially all patients with haemorrhagic smallpox showed a significant abnormality. The early haemorrhagic patients had the most marked defect. A few patients with non-haemorrhagic smallpox showed a slight abnormality of serum prothrombin time, but the median for this group was comparable to that of the control.

The abnormal serum prothrombin time (prothrombin consumption test) occurred in all haemorrhagic cases and may be related to the thrombocytopaenia since deficiency of platelets will produce an abnormal consumption of prothrombin. This finding could also reflect other first stage coagulation defects. A definite second stage abnormality was noted in the early haemorrhagic cases which was much more marked than in any other patients. They showed a prolongation of the quick prothrombin time and a marked depression of the specific prothrombin itself. In addition, all early haemorrhagic cases showed a great increase in antithrombin activity. This was not observed in the other haemorrhagic cases or in most of the non-haemorrhagic smallpox patients.

SUMMARY OF RESULTS

Bleeding and coagulation studies were carried out in patients with haemorrhagic smallpox, non-haemorrhagic smallpox and chicken-pox as well as a comparable number of controls. A total of 60 patients with smallpox and 12 with chicken-pox were studied. The majority of these patients were investigated with the following coagulation studies: the quick prothrombin time, plasma specific prothrombin, thrombin time, prothrombin consumption (serum prothrombin time). The lee white coagulation time was performed in a small group. In a significant number of patients the bleeding time, clot retraction and tourniquet test were also studied.

Results of these determinations revealed that all haemorrhagic patients showed a prolonged bleeding time, abnormal clot retraction and many had a positive tourniquet test. Observation of the blood smear in many of these patients revealed decreased platelets. These findings are all compatible with thrombocytopaenia which has been previously described in haemorrhagic smallpox. These abnormalities were not found in the non-haemorrhagic smallpox or chicken-pox patients studied by these techniques.

The coagulation studies revealed an abnormal serum prothrombin time (prothrombin consumption test) in all haemorrhagic cases; this test was normal in almost all of the non-haemorrhagic smallpox patients and was normal in all of the chicken-pox patients.

This finding would be present in thrombocytopaenia, but could represent additional first stage clotting defects. Further evidence of a coagulation defect not been previously described in smallpox patients was found in all cases with the early haemorrhagic form of the disease. This group showed a markedly abnormal quick (one stage) prothrombin time, a very low level of specific prothrombin and a marked increase in antithrombin activity. Patients with the "early-late" and with "late" haemorrhagic disease did not show this marked abnormality and in particular did not have significant antithrombin activity. However, some of the "early-late" haemorrhagic patients did show a decrease in specific prothrombin indicating a coagulation defect that would be sufficient to produce haemorrhage.

FIG. I a

QUICK PROTHROMBIN TIMES
(RANGES OF VALUES)

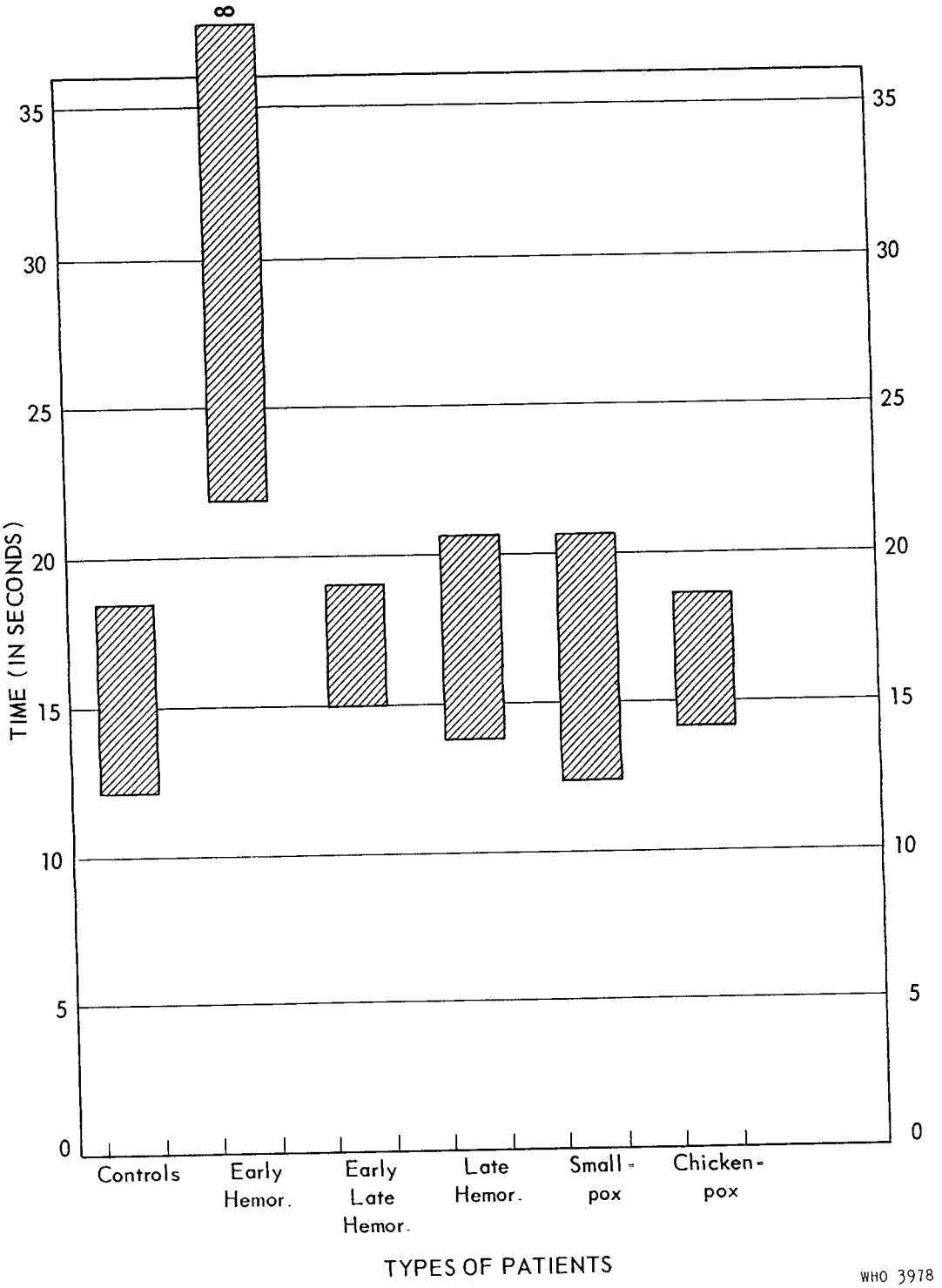

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FIG. II a

PLASMA SPECIFIC PROTHROMBIN ACTIVITY
(AS % OF CONTROL PLASMA ACTIVITY)
(RANGES OF VALUES)

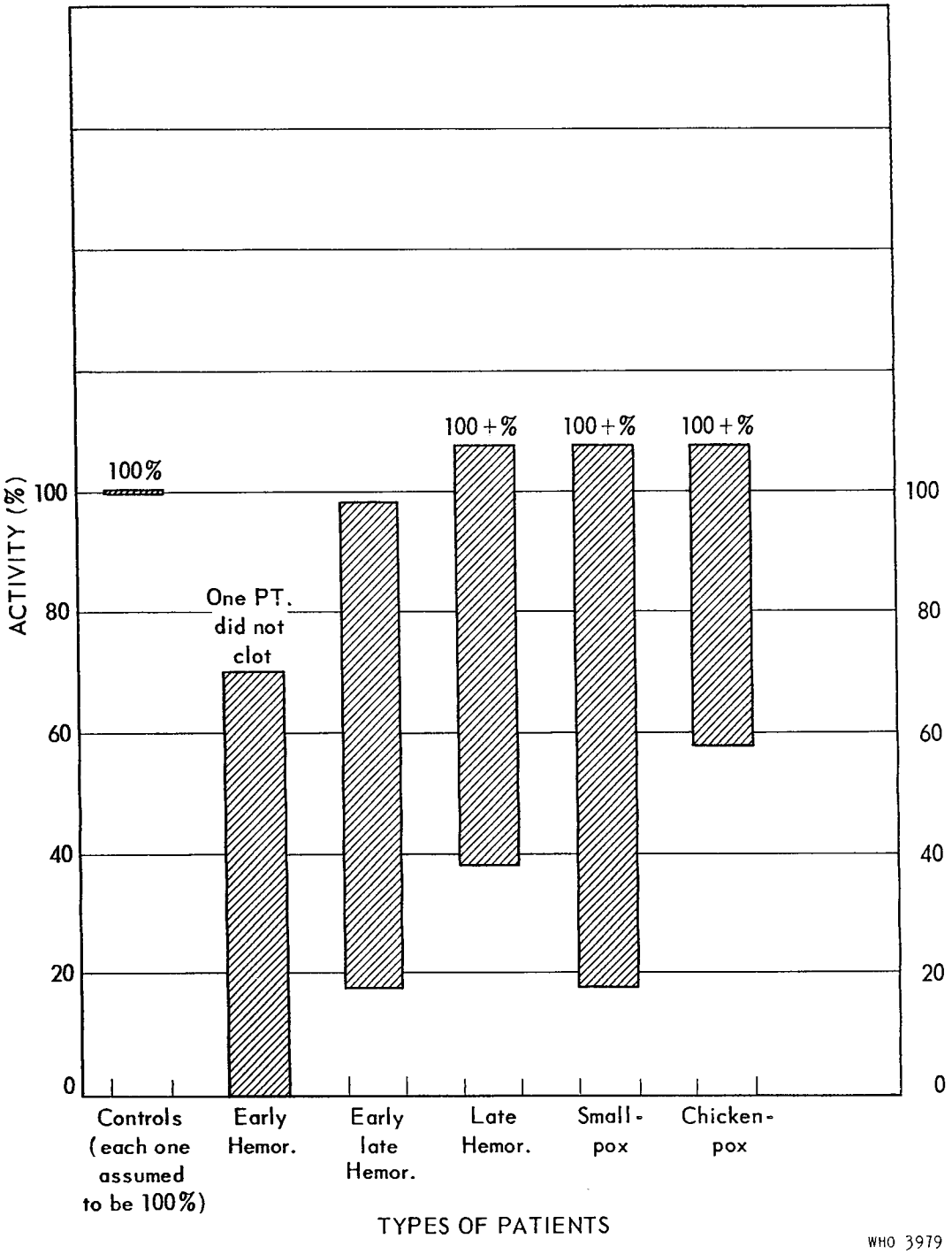

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FIG. III a

THROMBIN TIME
(RANGES OF VALUES)

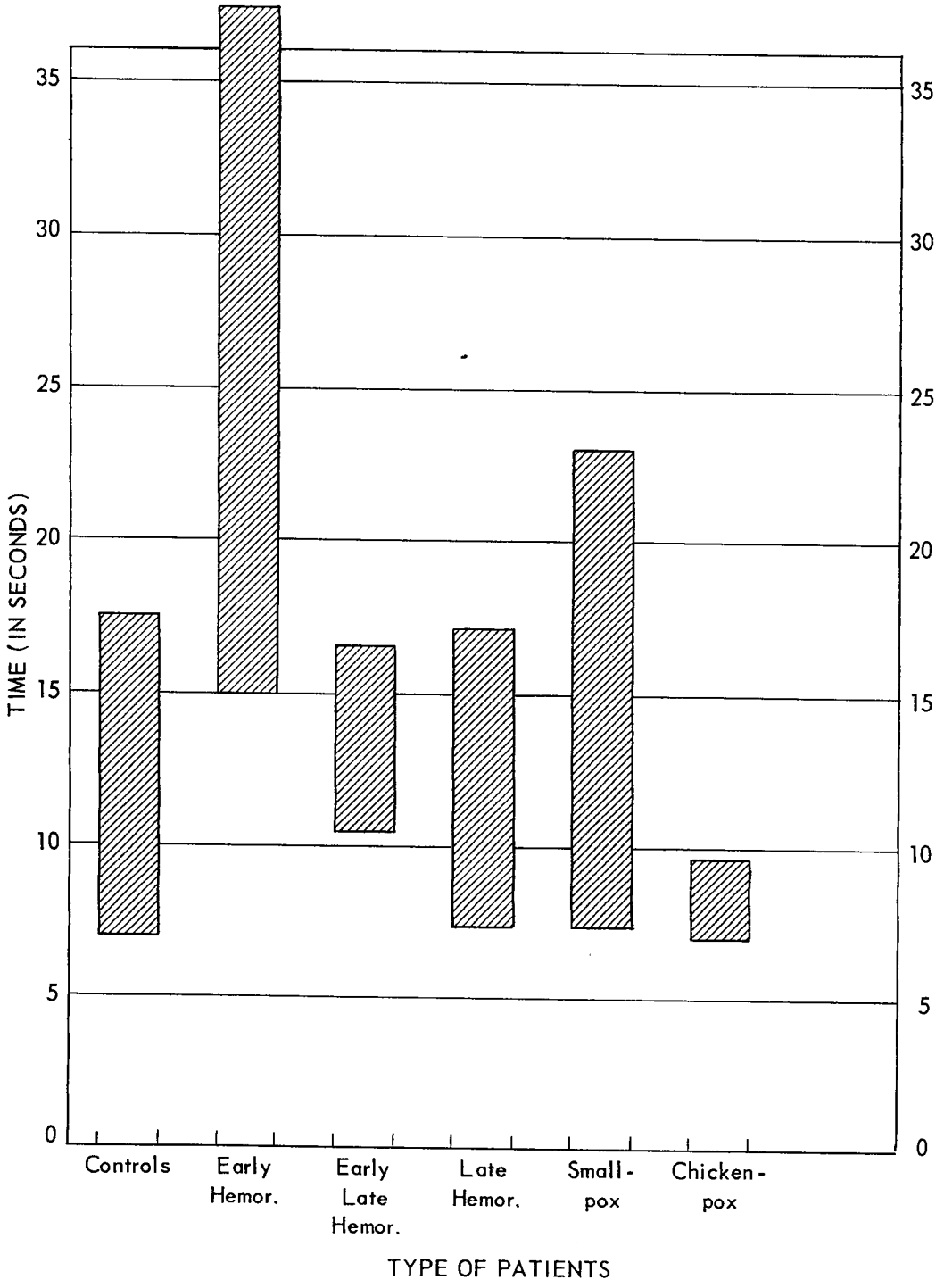

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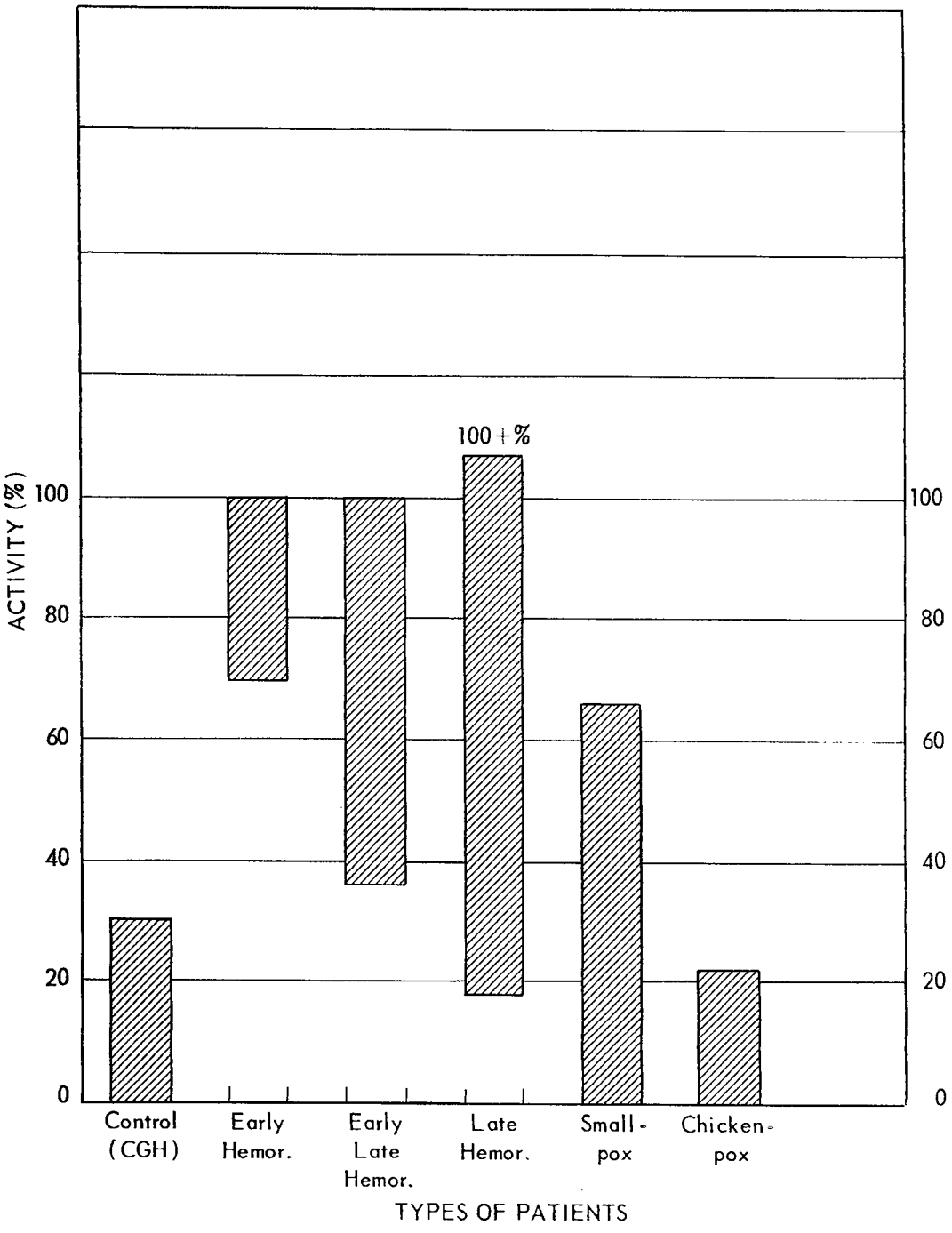
FIG. IV a

SERUM PROTHROMBIN ACTIVITY REMAINING
(AS % PATIENT'S PLASMA ACTIVITY)
(RANGES OF VALUES)



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