and sixth days of life and coincided with the peak bilirubin levels in the serum.

Diarrhoea may aggravate the jaundice.

There is no correlation between serum bilirubin and haemoglobin levels, and this suggests that "physiological" hyperbilirubinaemia is not attributable to haemolysis alone. This series provides confirmatory evidence that jaundice occurring during the first 36 hours of life is not necessarily haemolytic in origin. Hepatic immaturity and dysfunction are major factors in the production of high circulating levels of "indirect" serum bilirubin.

It is shown that serum bilirubin levels can be used as an indication for exchange transfusion only if taken in conjunction with the birth weight. A recurrence of hyperbilirubinaemia may occur after blood exchange. This "rebound" phenomenon may necessitate repeat exchange transfusions.

We thank Dr. I. Frack, superintendent of Baragwanath Hospital, for permission to publish this paper, and Drs. D. Lavery and W. Evans, of the obstetrics department, for referring the patients to us. We are indebted to Dr. R. Cassel, Dr. J. Metz, and their laboratory staff for the biochemical investigations; to the registrars of the paediatric department for technical assistance; to Dr. I. Simson for performing the necropsies; and to Dr. M. Shapiro and Dr. B. Ellis, of the South African Blood Transfusion Service, for carrying out the exchange transfusions, the blood grouping, and the serology. Last, but by no means least, we thank Dr. E. Kahn, senior paediatrician, for his encouragement, help, and criticism in the preparation of this paper.

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Infrared Absorption Spectra of Steroids: An Atlas, Volume II, by G. Roberts, B. S. Gallagher, and R. N. Jones, contains 98 pages of text matter and 452 charts of absorption spectra. Volume I (1953) dealt with 308 steroids, and the indexes included in Volume II cover both volumes. The book is published by Interscience Publishers Ltd., New York and London, price \$20.

PERIPHERAL EFFECTS OF "VASCULIT"

BY

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The search for an answer to the problem of degenerative arterial diseases has in recent years produced a bewildering variety of drugs with more or less of a vasodilator activity. Unfortunately, only a small proportion are found to have any clinical application, for, despite extensive animal studies, most are issued with insufficient appraisal of their effect on the human beings for whom they are intended. It is of considerable interest that slight alterations in the structure of substances chemically and pharmacologically related to noradrenaline may lead to a reversal of the vasoconstrictor effect. One of these, the butyl derivative of the para-oxy homologue of phenylephrine, was synthesized in the Boehringer Laboratories before the war, and has been used in Germany under the trade name of "vasculat" ("vasculit" in U.K.) in the treatment of peripheral ischaemic disorders (Becker and Kaiser, 1951; Beiglböck and Odenthal, 1954). The following is a report of some studies of the vascular effects of intra-arterial vasculit in a group of hospital patients of various ages and conditions.

Subjects and Methods

Patients of both sexes between the ages of 24 and 67 were studied during their convalescence from acute and chronic respiratory infections, pneumonia, or peptic ulcer, and one subject was suffering from malignant hypertension. None of them had clinical evidence of ischaemic disturbances of the extremities. Throughout each experiment the blood flow in both hands was measured plethysmographically under controlled conditions, while a continuous saline (0.9% w.v. NaCl) solution was infused into the right brachial artery (Duff, 1952). At regular intervals known amounts of the laevorotatory isomers of adrenaline and noradrenaline, and of vasculit, separately or in combination, were added to one of the infusion syringes for periods of four or six minutes. From the differences in blood flow between the two hands, the effect of each dose (of drug or hormone) on the volume of blood flowing through the infused right hand was calculated by a method that made due allowance for incidental fluctuations unrelated to the infusion (Ginsburg and Duff, 1956). The results provide a quantitative estimate of the net effect of each on the vascular bed (the hand) supplied by the right brachial artery.

The general procedure was to give a series of separate infusions of one or more doses of adrenaline and noradrenaline (0.125 µg./min. and 0.5 µg./min. for four minutes), each preceded by a saline control period of at least four minutes. Then vasculit was given during a four- or six-minute period, after the completion of which the adrenaline and noradrenaline infusions were repeated. In another series vasculit was instead given *along with* the second adrenaline and noradrenaline infusions. To begin with, pilot experiments were done to find a suitable concentration

of vasculit, sufficient to cause measurable changes in the blood flow in the right hand, but insufficient to alter systemic blood pressure or heart rate. It was found that doses of 100 $\mu\text{g./min.}$ were suitable, but in some experiments the effects of larger doses were tried. No subject complained of any systemic effect, nor were there any adverse local or general effects subsequently.

Results

Effect of Various Doses of Vasculit Alone on Blood Flow.—While some effect was detected with the concentration of 25 $\mu\text{g./min.}$ (total dose $6 \times 25 = 150 \mu\text{g.}$) the most conspicuous changes were those seen with doses of 100 $\mu\text{g./min.}$ or 200 or 500 $\mu\text{g./min.}$ Data relating to 10 experiments are given in Table I. In six

TABLE I.—Effect of Intra-arterial Vasculit on Hand Blood Flow in Different Individuals

No.	Dose of Drug $\mu\text{g./min.}$	Control Blood-flow Level ml./100 ml./min.	Mean Percentage Change in Flow
1	25	6.1	+15
2	100	5.5	+47
3	200	2.8	+132
4	500	5.2	+38
5	200	4.0	+90
6	100	3.1	+81
7	100	3.1	+112
8	100	5.6	+30
9	100	18.1	+31
10	100	6.7	-02
Average	150	6.0	+57

the dose was 100 $\mu\text{g./min.}$; the average for the group was 150 $\mu\text{g./min.}$ for four minutes—that is, 600 $\mu\text{g.}$ In all but one subject there was definite vasodilatation ranging from +15% to +132% of the control blood-flow level. The mean increase in blood flow for the entire group was +57%. The average control level of flow was 6 ml./100 ml. hand volume/minute, a value close to that found in healthy subjects under identical conditions (Duff, 1952; Ginsburg and Duff, 1956). The results are summarized in Table I.

Effect of Vasculit on the Response to Adrenaline.—When the effect of adrenaline alone was compared with that obtained with the same dose of adrenaline given along with an infusion of vasculit, the latter was generally associated with a vasodilatation that more than counteracted the constrictor effect of the adrenaline. In a dose of 0.125 $\mu\text{g./min.}$ (total amount $4 \times 0.125 \mu\text{g.} = 0.5 \mu\text{g.}$) the adrenaline itself caused an

TABLE II.—Response to Adrenaline and Noradrenaline Before, During, and After Vasculit Infusions

Hormone Concentration	Percentage Change in Flow	
(a) <i>Adrenaline Before and During Vasculit Infusions</i>		
Adrenaline 0.125 $\mu\text{g./min.}$	-54	+30
" " " " " "	-25	+27
" " " " " "	-34	-22
Average	-38	+12
(b) <i>Adrenaline and Noradrenaline Before and After Vasculit Infusions</i>		
Adrenaline 0.5 $\mu\text{g./min.}$	-72	-77
" " " " " "	-88	-79
" " " " " "	-86	-83
Average	-82	-80
Noradrenaline 0.5 $\mu\text{g./min.}$	-12	-09
" " " " " "	-84	-87
" " " " " "	-75	-86
" " " " " "	-78	-50
" " " " " "	-86	-94
Average	-67	-65

average reduction in flow of 38%. When the infusion was repeated with vasculit (in a concentration of 100 $\mu\text{g./min.}$) the blood flow showed an average increase in flow of 12%, the net effect therefore being about 50% increase (Table IIa).

Effect of Separate Doses of Adrenaline and Noradrenaline Before and After Completing Vasculit Infusions.—In eight tests the initial infusions of adrenaline and noradrenaline, in concentrations of 0.5 $\mu\text{g./min.}$ (total dose 2 $\mu\text{g.}$), caused an average reduction in blood flow of 82% and 67%, respectively. When these doses were repeated within half an hour of completing the infusion of vasculit, the reduction in flow with each was substantially unchanged, being 80% and 65%, respectively. There was thus no evidence of a persistence of the anti-adrenergic effect of vasculit, nor was the vasodilatation due to the latter present at this time (Table IIb).

Discussion

The experiments have demonstrated that when given intra-arterially vasculit causes an immediate increase in blood flow in the perfused hand. This effect is a peripheral one and not due to any systemic effect of the drug, which was given in a total dose (well under 1 mg.) that is too small to influence the heart or general circulation. The increased flow was observed in 9 out of 10 patients, in whom it ranged between 15% and 132%, averaging, for the entire group, 57%. In the tenth patient the arterioles were presumably unreactive. The control blood-flow level, before vasculit was given, varied between 2.8 and 18.1 ml./100 ml. hand volume/minute, averaging 6 ml. These values are in the normal range. There did not appear (see Chart) to be

Relationship between control blood-flow level and response to vasculit.

any consistent relationship between the initial blood-flow level and the response to vasculit. For this reason, and because of the peripheral site of action of this drug, it may be anticipated that vasculit will be capable of producing vasodilatation even in patients in whom therapeutic sympathectomy has been carried out. The vasodilator effect of the drug was sufficient to counteract the constrictor effect of concurrently administered adrenaline, at the concentration of 0.125 $\mu\text{g./min.}$ (total dose 0.5 $\mu\text{g./adrenaline}$), but was not associated with any increase in flow greater than that

expected from the direct relaxing action on the arteriolar smooth muscle. Thus there was no evidence of a specific chemical reversal of the adrenaline effect.

Although sufficient studies have not been made of the action of vasculit in counteracting the effect of noradrenaline, the drug may be expected to have this property. There may therefore be a place for vasculit in the diagnosis of phaeochromocytoma. Patients with a considerable rise in the level of circulating adrenergic hormones would, on the evidence of the present study, be expected to respond to intra-arterial vasculit (in a total dose of 0.5 mg.) with a smaller increase in flow than the normally expected average increase of 50–60%, but because of individual variations in the response to the drug the significance of any such test would probably become apparent only when a series of patients are studied under conditions comparable with those of the present investigation. The hypertensive patient in this series behaved no differently from the others.

The effect of vasculit was seen to persist only so long as the drug was being infused, for the dilator effects passed off soon after the infusions were completed. However, it seems likely that in the concentration of 100 $\mu\text{g.}/\text{min.}$ the increase in flow is maximal, and higher doses do not have any greater effect. It would therefore be reasonable to administer vasculit intra-arterially in this concentration over longer periods of time to patients suffering from ischaemic disorders, fundamentally of one or other extremity—for example, from arterial embolization. The absence of any systemic effect in increasing heart rate or lowering blood pressure is a further advantage of using vasculit in this way.

Summary

The effects of infusing vasculit into the brachial artery have been measured with plethysmographs in a group of hospital patients under controlled conditions.

With amounts totalling between 0.1 and 2 mg. (average 0.6 mg.) vasculit caused an increase in blood flow in the infused hand which averaged 57%.

The dilator effect was at the periphery, and was sufficient to counteract the constrictor effect of simultaneously infused adrenaline (in the total dose of 0.5 $\mu\text{g.}$).

The effect of the vasculit did not appear to depend on the initial level of blood flow in the infused hand.

The effect of vasculit persisted for only the duration of the infusions, but, on the other hand, was not associated with any detectable systemic effects.

Some clinical and pharmacological implications of these findings are discussed.

I am grateful to Dr. W. A. Bullen, medical director, Boehringer Division of Pfizer Ltd., for supplies of vasculit and for kindly providing information about the drug, for access to the relevant German literature, and for arranging clerical assistance. I am indebted to Dr. J. J. Daly for valuable help in some of the studies, and to Mr. Bryan Sellars for efficient technical assistance.

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EMOTIONAL DISTURBANCES OF BURNED CHILDREN

BY

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For some years the staff of the Burns Unit at the Birmingham Accident Hospital were becoming increasingly aware of the social and emotional problems of their child patients. Many of these children came from "broken homes," and the almoners found that much more time was needed for patients with burns than other accident cases. This led to the question: Do emotionally disturbed children tend to get burned, or do severe burns tend to produce disturbed children?

This present study was based on 198 children aged under 15 years on admission, who sustained burns of 10% or more surface area and who were in-patients during 1952–5. These children were the survivors from the more severe burn cases, and represented about half of the total child admissions. The mothers of these children were asked to give an opinion about the emotional state of their child at the time of the investigation (1957–8). This was compared with the state of the child prior to the burn, so far as the mothers could recall it.

Similar investigations were made of the 608 siblings of the patients, about whom the mothers also gave an opinion. A further independent control group of 50 children was selected at random from the same districts in the city as the patients.

The purpose of the investigation was to try to find out (a) whether emotional disturbance really existed, and if it preceded or followed the accident; (b) if it did exist, the forms it took; and (c) whether disturbance was related to any particular factors involved in the accident or hospitalization. The sample of 198 patients was taken from a possible 208. The 10 cases excluded were untraceable, or living over 50 miles (80 km.) from the hospital.

A letter was sent asking each mother if she was willing to help. This was followed in nearly every case by a home visit. Three mothers were seen in the hospital. Answers were obtained to the same 10 questions, either by the mother providing them spontaneously or, if this did not happen, by putting the questions directly. Notes were made after each interview and the data tabulated later for analysis.

Existence of Emotional Disturbance

The mother's opinion was chosen as the main criterion of disturbance, as she knew the child intimately both before and after the accident, and could probably assess any changes that might have occurred. However, estimates by the investigator were also made, and are discussed later.

Disturbances in the children were classified according to severity. "Severe" cases were those where the mother was sufficiently concerned to seek outside help—for example, child guidance, G.P., etc. Cases were classified as "slight" if the mother considered the child only a little affected. Of the 198 cases investigated, 81% showed signs of emotional disturbance according