ing" property, *i.e.*, desoxycorticosterone, resulted in the formation of a compound with relatively low "sodium and chloride-retaining" potency, the addition of a hydroxyl group on C_{17} to a compound which initially possessed moderate "sodium and chloride-retaining" potency, *i.e.*, corticosterone, resulted in the formation of a compound in which all "sodium and chloride-retaining" effect had disappeared. In this latter instance, the new compound actually facilitated sodium and chloride excretion (Fig. 1).

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CHILDREN'S SPEECH

IN a recent note about my studies (SCIENCE, December 26, 1941) John B. Carroll stated that he had tried without success to study mathematically the distribution of words in children's speech. The readers of SCIENCE may therefore be interested in the nature of the results of a fairly extensive mathematical investigation that I have been conducting on this subject.[1]

In Fig. 1 is presented the Rank-Frequency distribution of the different ranked words (X) with their respective frequencies (Y), with straight lines connecting successive points, of an aggregate of approximately 24,000 words dictated into an Ediphone by a girl during the six weeks preceding her fifth birthday, as reported by R. S. Uhrbrock.[2]

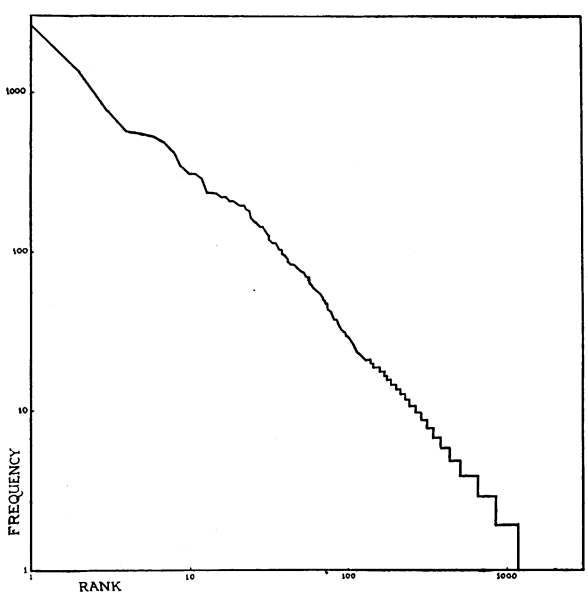

FIG. 1. The rank-frequency distribution of *ca.* 24,000 running words of a five-year-old girl recorded by R. S. Uhrbrock.

Dr. Uhrbrock put at my disposal the manuscript not only of the above material, but also of the dictations of the same girl made on or about her 6th, 6½th and 7th birthdays. The results of five samples of 2,000 words each from the 5-, 6½- and 7-year material, and of two samples of the same length from the less extensive 6-year material are presented in Table I, where the closeness of the calculated values to the theoretical slope, −1, is apparent. The best lines of X's and of Y's were calculated by least squares, and the error is the root-mean-square error of the deviations from the best line of Y's.

TABLE I

RANK-FREQUENCY DISTRIBUTION OF THE UHRBROCK RECORDINGS OF THE SPEECH OF A GIRL

Sample number	Age	Length of sample (words)	No. ranks (X)	Best X-slope (negative)	Best Y-slope (negative)	Error (Y)
5 yrs.	1	2,002	513	.97	.92	.086
	2	2,000	501	.95	.93	.055
	3	2,003	496	.96	.92	.077
	4	2,000	484	.97	.94	.078
	5	2,000	475	1.00	.95	.091
6 yrs.	1	2,000	466	1.00	.96	.080
	2	2,000	459	.99	.96	.081
6½ yrs.	1	2,000	467	.99	.95	.082
	2	2,000	500	.97	.93	.077
	3	2,000	413	1.02	.99	.074
	4	2,000	404	1.02	.99	.074
	5	2,000	476	.96	.93	.069
7 yrs.	1	2,000	437	1.02	.99	.074
	2	2,000	440	1.01	.98	.074
	3	2,000	398	1.04	1.01	.076
	4	2,000	457	.98	.95	.070
	5	2,000	487	.95	.92	.073

In addition to the above Uhrbrock material I have similarly analyzed the words of the extensive speech-material ranging from 22 through 59 months as collected and reported by M. S. Fisher[3] and as generously made available to me for the above purposes by Dr. L. H. Meek, director of the Child Development Institute of Teachers College, Columbia University. Though the 72 samples examined vary considerably in size and in best Y-slope, nevertheless the median slope is −1.02. In discussing the above material in greater detail in a future publication,[4] I shall present quantitative information on the general relationship between the size of sample and slope[5] and also the positive correlation

[3] John D. Archbold fellow in medicine.

[1] This investigation was made possible by grants from the Milton fund and from the Committee on Research in the Social Sciences at Harvard University. I here acknowledge the help of my wife and of my research assistants, Miss Inez Randall and Dr. Sydney Fairbanks.

[2] R. S. Uhrbrock, *Ed. Research Bull.*, 14: 85–97; also *Jour. Ed. Psychol.*, 27: 155–158.

[3] M. S. Fisher, *Child Development Monograph* No. 15, New York, 1934.

[4] Chap. III of "The Principle of Least Effort" now in preparation.

[5] G. K. Zipf, "The Psycho-Biology of Language," p. 44, Boston, 1935; *Jour. Psychol.*, 4: 239–244; *Psychol. Record*, 2: 347–367.

between age of child and size of the constant, C (in terms of R F = C), together with an analysis of its possible bearing upon the problem of intelligence and of the general meaning of bends from the straight line.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

HYPO-PROTHROMBINEMIA PRODUCED BY 3,3[1]-METHYLENEBIS (4-HYDROXYCOUMARIN) AND ITS USE IN THE TREATMENT OF THROMBOSIS

PROTHROMBIN is formed in the liver, and it can be assumed that one or more enzymes are responsible for its formation. The activity of the enzymes is dependent on the presence of vitamin K, which may possibly be a prosthetic group attached to an active protein. On this assumption, the administration of a compound that could displace vitamin K and thus inactivate the enzymes would produce a hypo-prothrombinemia and thus could be used to reduce the incidence of post-operative thrombosis and thrombosis from other causes. Several naphthoquinone derivatives were tried first but without success.

The work of Quick,[1] Schoefield[2] and Campbell *et al.*[3] showed that the ingestion of spoiled sweet clover (*melilotus albus*) by cattle and rabbits caused a hypoprothrombinemia. The active agent was isolated by Stahmann *et al.*[4] and shown to be 3,3,[1]-methylenebis (4-hydroxycoumarin). This compound, called · AP (antiprothrombin), was supplied by the Ferrosan Company of Malmö, Sweden, and used in the following experiments.

When AP is given per os to rabbits in a dose of 3–4 mg/kg the prothrombin index (Quick) was lowered for 1–2 days to between 10–20. (Similar effects have recently been reported by Overman *et al.*[5]). This effect was reproducible and reversible. Fig. 1 shows that the prothrombin index rapidly returns to normal even after almost daily administration of the drug for a month. No toxic effects were seen on the circulation, respiration, intestines, liver, kidney, heart and the composition of the blood. The lethal dose is 250 mg/kg for rabbits, almost ten times the effective dose. The cause of death was not determined but is probably the result of kidney damage. Fig. 2 shows that the simultaneous administration of 5 mg of vitamin K has no effect on the action of AP. Blood transfusion can raise the prothrombin level for 3–5 hours in the animal receiving the drug.

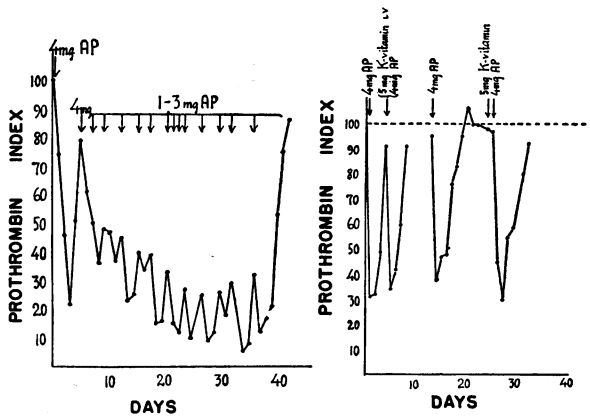

FIG. 1. The restoration of the normal prothrombin index in the rabbit after administration of AP for one month. FIG. 2. The inability of 5.0 mg of vitamin K to antagonize the effect of AP on the prothrombin index of the rabbit.

When 0.25–1.0 gm of AP is given by mouth to normal human subjects a similar fall of the prothrombin index occurs. Seventeen cases of thrombosis of the extremities were treated. When the initial fall in prothrombin index occurred there was a concomitant improvement as indicated by the fall in temperature, and diminished turgor of the leg. Cases of thrombosis cruris (*phlegmasia alba dolens*) were more resistant to the drug and required larger doses. In all cases the course of the disease was shortened and no further thrombosis occurred after the fall in the prothrombin index. Administration of AP is contraindicated in kidney, heart and liver diseases. In actual or suspected vitamin C deficiency, ascorbic acid should be given along with the drug to prevent hemorrhages. The use of AP in the prevention of post-operative thrombosis is under investigation.

In man mild toxic symptoms, such as vomiting and diarrhea, were observed in a few cases after the first administration of the drug, but seldom after subsequent ones. Liver and kidney function tests after treatment with the drug were normal. In two cases minor hemorrhages occurred. These were controlled by the administration of 100–200 mg of 2-methyl-1,4-naphthaquinone disulfate which increased the pro-

[1] A. J. Quick, *Am. Jour. Physiol.*, 118: 260, 1937.
[2] F. S. Schoefield, *Canadian Vet. Rec.*, 3: 74, 1922; *Jour. Am. Vet. Med. Asn.*, 64: 553, 1924.
[3] H. A. Campbell, W. K. Smith, W. L. Roberts and K. P. Link, *Jour. Biol. Chem.*, 136: 47, 1940; 1938: 1, 1941.
[4] M. A. Stahmann, C. F. Huebner and K. P. Link, *Jour. Biol. Chem.*, 138: 513, 1941.
[5] R. S. Overman, M. A. Stahmann, W. R. Sullivan, C. F. Huebner, H. A. Campbell and K. P. Link, *Jour. Biol. Chem.*, 142: 941, 1942.