Serotonin Levels in Acute Experimental Ascariasis

Keyphrases ☐ Serotonin levels—acute ascariasis ☐ Ascariasis, effect—serotonin toxicity

Sir:

The effects of acute human ascariasis (irritability, low-grade fever, bronchial asthma, dyspnea, diarrhea, cyanosis, psychoses, convulsions, and mental regression) have often been thought to involve mobilization of histamine in the body. However, Borella *et al.* (1) noted a decrease in the histamine content of lung and brain of 6-day ascariasis-infected guinea pigs with no changes seen for the content of blood, liver, kidney, and intestine. Infected animals were more resistant to histamine administered either by aerosol or intracardiac injection, and the diamineoxidase-like activity of liver appeared enhanced. The release of both histamine and serotonin has been implicated in the anaphylactoid process (2), as well as a number of other endogenous substances. Systemically released serotonin as produced by certain carcinoid tumors (argentaffinomas) will produce flushing and tachycardia followed by asthma and cyanosis as well as pulmonary and tricuspid stenosis (3, 4). These effects could be related to the syndrome seen in acute ascariasis; therefore, it was considered of value to determine whether blood and tissue levels would change during experimentally induced ascariasis, and whether such changes would parallel those reported for histamine (1).

Using the same methods of infection, same sources of guinea pigs, and *Ascaris suum* as Borella *et al.* (1), the infected guinea pigs were sacrificed 2 and 6 days after administration of 20,000 infective eggs orally. The times of sacrifice correspond to peak infections of the liver and lung, respectively (1). A minimum of 3 ml. of blood was drawn from each animal by cardiac puncture, and the serotonin level determined by the Method 2 technique of Waalkes (5). The entire liver, lungs, and brain were collected, along with the kidneys and random samples of intestine, and the serotonin content estimated by the method of Bogdanski *et al.* (6). Tissue larval counts were made in the manner of Borella *et al.* (1). Data were treated by analysis of variance methods (7), and the mean results and degree of infection are summarized in Table I. No significant changes from the normal were documented for either blood or the other tissues studied. The nonsignificant increases seen for brain (2- and 6-day infected) and intestine (6-day infected) do not parallel the significant decrease in histamine content of brain and lung documented by Borella *et al.* (1).

Using the same source of guinea pigs and the methods of Borella *et al.* (1), nonfasted guinea pigs were injected with serotonin *via* the intracardiac route or exposed in a closed chamber to a 2% serotonin aerosol to determine whether the infection would increase or decrease their susceptibility to serotonin. No significant differences in toxicity were noted between the noninfected and the 6-day infected animals.

It would appear from these studies that serotonin does not play a major role in producing the symptomatology of acute ascariasis.

Table I—Blood and Tissue Levels of Serotonin in Normal and Ascariasis-Infected Adult Guinea Pigs[a]

	Mean Serotonin mcg./ml. or mcg./g. Wet Tissue (*SD*)[b]					
	Blood	Liver	Lung	Brain	Intestine	Kidney
Uninfected	0.05(0.05)	0.10(0.04)	0.11(0.08)	0.32(0.09)	4.17(1.62)	0.10(0.04)
2-Day infected[c]	0.07(0.06)	0.11(0.04)	0.08(0.06)	0.41(0.10)	4.46(1.76)	0.12(0.05)
Calculated *F*	0.78	0.31	0.49	3.77	0.41	1.61
Observed *p*	>0.25	>0.50	>0.25	>0.05	>0.50	>0.20
6-Day infected[d]	0.06(0.04)	0.10(0.06)	0.06(0.04)[e]	0.40(0.09)	6.42(3.48)[e]	0.12(0.07)
Calculated *F*	0.12	0.11	2.72	3.58	3.13	0.82
Observed *p*	>0.50	>0.50	>0.10	>0.05	>0.05	>0.25

[a] Ten animals per test group. Uninfected were isolated from infected, with all autopsied to determine presence or absence of infection. [b] Recoveries of serotonin added to tissue homogenates had mean percent values ranging from 92–106. Standard serotonin solutions (serotonin creatinine sulfate, Calbiochem lot 502871) were prepared fresh daily (0.125, 0.25, 0.50, 1.0, and 2.0 mcg./ml. as base) and run concurrent with tissue and blood samples. Infection dates were scheduled so that the controls and the two infected test groups were sacrificed at the same time. The Aminco-Bowman spectrophotofluorometer was used. [c] Mean larval count/g. for liver and lung were 94 and 61, respectively. [d] Mean larval count/g. for liver and lung were 38 and 320, respectively. [e] Variance of the infected was significantly different from that of the controls (observed $p < 0.05$). The larger variance was placed in the numerator, and the resultant quotient (*F* test) exceeded the tabular value at $p = 0.025$(8).

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Received September 16, 1968.
Accepted for publication October 8, 1968.

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This work was sponsored in part by contract DA-49-193-MD-2338 of the U. S. Army Medical Research and Development Command, Dept. of the Army.

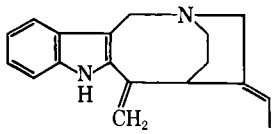
The authors wish to thank Drs. Luis E. Borella and Harry W. Huizinga for their assistance in carrying out certain phases of this work and Drs. Nicholas J. Giarman, Donald Fairburn, Lawrence R. Penner, and Richard E. Shope for their helpful advice.

Identity of Pericalline, Tabernoschizine, Apparicine, and Gomezine

Keyphrases ☐ Pericalline—identity confirmation ☐ IR spectrophotometry—identity ☐ Optical rotation—identity

Sir:

The alkaloid pericalline was first reported by Svoboda from the roots of *Catharanthus roseus* (1).[1] This was followed shortly thereafter by a report on an alkaloid with similar composition, tabernoschizine, from *Schizozygia caffaeoides* (2).[1] A year later, we isolated pericalline from the roots of *Catharanthus lanceus* (3). Subsequently, (−)-apparicine was isolated from *Aspidosperma olivaceum*, *A. eburneum*, *A. multiflorum*, and *A. gomezianum* by Gilbert *et al.* (4), and (+)-apparicine from *Aspidosperma dasycarpon* (4). The structure for (−)-apparicine was subsequently elucidated by Joule *et al.* (5) as I. Finally, an alkaloid named gomezine was isolated from *Aspidosperma gomezianum* by Owellen (6).



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An inspection of the physical data reported for all of these alkaloids (see Table I) shows them to be very similar, if not identical. Samples of pericalline from *Catharanthus roseus* and *C. lanceus* were available as were samples of tabernoschizine from *Schizozygia caffaeoides*[2] and (−)-apparicine from *Aspidosperma* sp.,[3] and IR spectra (KBr) of all four alkaloids were superimposable.

Since the report announcing the discovery of pericalline (1) predates those for the other alkaloids in question, *i.e.*, tabernoschizine (2), gomezine (6), and apparicine (4), the name pericalline for this alkaloid should have priority.

Table I—Comparison of Physical Data for Alkaloids

Name	Source	Formula	M.p., °C.	pKa	$[\alpha]_D$	λ_{max}, mμ	Ref.
Pericalline	*Catharanthus roseus*	—	196–202	8.05	−183°[a]	304	1
Tabernoschizine	*Schizozygia caffaeoides*	$C_{18}H_{20}N_2$	198–199	7.26	−138°	303	2
Pericalline	*Catharanthus lanceus*	—	196–202	8.02	−186°[a]	304	3
(−)-Apparicine	*Aspidosperma olivaceum*	—	188–191	—	−179°	—	4
(−)-Apparicine	*Aspidosperma eburneum*	—	195–198	—	—	—	4
(−)-Apparicine	*Aspidosperma multiflorum*	—	188–192	—	−126°	—	4
(−)-Apparicine	*Aspidosperma gomezianum*	—	188–191	—	—	—	4
(−)-Apparicine	*Aspidosperma* sp.	$C_{18}H_{20}N_2$	192–194	—	±177°	303	5
(+)-Apparicine	*Aspidosperma dasycarpon*	—	192–194	—	+176°	303	4
Gomezine	*Aspidosperma gomezianum*	$C_{18}H_{20}N_2$	195–198	—	—	304	6

[a] Data not given in original reference, but determined subsequently in our laboratory.

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Received October 16, 1968.
Accepted for publication October 31, 1968.

[1] The date of receipt of the manuscript describing pericalline was Jan. 30, 1963 (1), and that for tabernoschizine was Feb. 6, 1963 (2).

[2] Generously provided by Dr. U. Renner.
[3] Generously provided by Dr. C. Djerassi.