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AN ATTEMPT AT NOSOLOGICAL AND ETIOLOGICAL DIARRHEA SYNDROME DECODING IN PATIENTS WITH PRESUMED ENTERAL INFECTION

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The clinical multiformity of the most widespread bacterial enteroinfections — shigelloses and salmonelloses — and the ever increasing role as a contributory cause of a variety of other pathogenic and conditionally pathogenic "old" and rather new bacteria, as well as clarification of the etiological significance for the diarrhea syndrome of a number of viruses, helminths, protozoa and fungi make mandatory the undertaking of concrete clinical and laboratory researches into the diagnosis of this large and polymorphic group of infectious diseases (1—23).

A comprehensive observation was carried out on 521 sucklings, children and adults with pathological phenomena (chiefly diarrhea) in the gastrointestinal tract, undergoing treatment during 1974 and 1975. According to diagnosis on admission, the patients were distributed in the following fashion: Obs. Dysentery — 24, clinical dysentery — 64, Toxiinfectio alimentaris — 86, Enterocolitis acuta — 40, Obs. Salmonellosis — 24, Gastroenterocolitis — 16 and miscellaneous — ten.

In the course of hospitalization, apart from the routine blood picture and urine tests, the patients were subjected in addition to the following investigations: bacteriologic study for *Shigella*, *Salmonella*, *Escherichia coli* and *Vibrio cholerae*, repeated (twice) serologic study with viral antigens (Influenza, Parainfluenza, Adeno, Coxsackie A and B, ECHO and Mycoplasma), virological investigations, parasitologic tests and determination of serum immunoglobulin concentrations (IgG, IgA and IgM).

Thus the case material was distributed into groups according to definitive diagnosis, namely: clinical dysentery — 138 cases, bacteriologically confirmed dysentery — 95, acute enterocolitis — 89, alimentary toxicoinfection — 71, salmonellosis — 41, acute gastroenterocolitis (NAG-vibrios, group II) — 1, influenza — 37, influenza and parainfluenza — 3, ECHO-viral infection — 3, Coxsackie-viral infection — 3, RS-viral infection — 2, adenoviral infection — 1 and others — 37.

Diagnoses with viral etiology were retrogradely established — after dismissal of the patients — insofar as the results of virological and serological investigations were unavailable during the hospitalization period. On establishing the listed above definitive diagnoses we endeavoured to exert maximum circumspection and objectivity, and avoid the absolute and unconditional interpretation of virological and serological findings.

In the above group we ventured to assign those of the cases where equally virological (agent isolation), serological (at least quadruple rise of titer) and bacteriologic (negative coproculture) studies, as well as clinical data supported the diagnosis with viral genesis. Certainly, such criteria could hardly be present in all the patients of the group. In the latter instance a more differentiated interpretation of each individual result was necessary.

Bacteriologic confirmation of the definitive diagnosis "dysentery" was made in 49.48 per cent of the patients. Shigellae isolated from 95 patients were distributed in percentages by serological types as follows: *Sh. flexneri* — 68.93, *Sh. sonnei* — 25.23, *Sh. boydii* — 3.72 and *Sh. shmitzi* — 2.12. The 41 salmonellae isolated are classified with the following types (in percentages): *S. heidelbergi* — 34.14, *S. typhimurium* — 14.65, *S. derby* — 2.44, *S. glostrup* — 2.44, group B — 9.75 and group C — 2.44.

The parasitologic study in the 531 patients under review shows the following results: protozoa: *Lamblia intestinalis* — 18, *Entamoeba coli* — 19, *Endolimax nana* — 1, *Jodamoeba bütschli* — 1. Large tapeworms-*Hymenolepis nana* — 1, dwarf tapeworms-*Enterobius vermicularis* — 1.

In 17 cases with isolated lamblia it was a matter of demonstrating cysts, and in one — vegetative forms. Positive coprocultures for *Sh. flexneri* were obtained in three patients of the series, and for *S. heidelbergi* — in one. In the 18 patients in question (aged 6 months to 34 years) the clinical picture observed was consistent with the basic nosological groups under consideration. No variations were recorded in the pattern and course of the diarrhea syndrome, nor in the other morbid signs and laboratory data.

Proceeding from the above data and from the fact that all the 18 patients referred to above lent themselves readily to clinical and bacteriological cure (except for those with coproculture positive for *Sh. heidelbergi*) through antibiotic therapy without resorting to antilambiasis means, there was no reason to consider the lamblia found as a basic etiological agent and accordingly, the listed below definitive diagnoses were established: bacteriologically confirmed dysentery — 3, clinical dysentery — 3, salmonellosis — 1, enterocolitis — 8, alimentary toxicoinfection — 2 and dyspepsia — one.

Analogically — lack of proofs for a concrete etiological role played by the diarrhea syndrome — the same holds true for the rest of the positive parasitic findings.

What does the comparison between primary (on admission) and final diagnosis in our series show?

Insofar as two of the basic diagnoses are concerned — dysentery and alimentary toxicoinfection — a reduction of the number of cases was noted at the final working out of the diagnosis, i. e. it was a matter of hyperdiagnostics upon admission of the patients; the presence of shigellosis and toxicoinfection was accepted more frequently than actually established after performing the respective observation and investigations.

In "alimentary toxicoinfection" the final diagnosing likewise imposed a reduction with 15 cases, i. e. from 86 to 71 cases. In fact the number of patients referred to us with the above diagnosis, established by the physician who made the primary examination, was much higher since in the health network practice there is a marked proneness toward hyperdiagnosing alimentary toxicoinfection, and not infrequently a great variety of foodstuffs are being inated off hand.

The number of cases with diagnosis "enterocolitis" was likewise increased — from 40 to 89 cases — mainly at the expense of patients with enterocolitis manifestations. On the one hand, no infectious causing agents which would explain such manifestations were discovered, and on the other, the clinical data were insufficiently conclusive to allow the assignment of these patients to the groups of differentiated nosological entities, e. g. clinical dysentery. Hence, without rejecting the infectious nature in this particular group of patients, we had to be content with the etiologically uncommitted diagnosis "enterocolitis".

The influenza (and parainfluenza) group, numbering 40 cases, is of particular interest. Here the phenomena pointing to digestive tract involvement on admission were quite different. This explains the diversity of primary diagnosis, namely: Obs. Dysentery — 15, Enterocolitis acuta — 11, Toxiinfectio alimentaris — 10, Gastroenterocolitis — four.

In two patients the marked catarrhal phenomena in the upper airways made mandatory to supplement the admission diagnosis with: Angina and Tracheobronchitis acuta under the heading "concomitant diseases".

After analysis of clinical and paraclinical data, the listed below more important conclusions were reached:

The acute onset of the affection in more than $\frac{3}{4}$ of the patients from all groups is impressive. It was particularly pronounced in "alimentary toxicoinfection" diagnosis where the disease begins acutely in 98.59 per cent of the cases, and in 70.42 per cent of them — on the last day (prior to admission). The onset in the latter group was markedly acute in 94.59 per cent.

Temperature did not prove a characteristic sign. On admission, more than half of the patients, influenza cases inclusive, were without fever. In none of the groups was febrility unduely high and sustained — most frequently, a subfebrile temperature for several days was recorded in about one third of the patients. In 67.52 per cent of influenza patients febrility which is one of the characteristic symptoms of the disease, was absent on admission to the clinic. As a matter of fact, in the same group another basic sign of influenza — catarrhal phenomena of the upper airways — was rarely established (only in 18.91 per cent). Anamnestically, however, there was evidence of such phenomena in 64.86 per cent, which led to the inference that the influenza affection really began with the usual respiratory mucosa catarrh. Anyway, it was obviously a matter of slight and rapidly subsiding phenomenon, promptly replaced by catarrhal gastrointestinal mucosa manifestations which led the patients to seek medical advice in the infectious enteral department. It is worth noting that on admission, catarrhal nasopharynx manifestations were also observed in part of the other patients, particularly in those with evidence of salmonella infection (in 32.50 per cent).

General intoxication symptoms such as vertigo, articular and muscular pains and poor appetite were most frequently found in influenza patients, in 51.35 and 83.78 per cent respectively. Rather often, the first two of the signs listed above were also present in the patients with toxicoinfection. In intestinal infections appetite was most frequently diminished in case of bacteriologically proved dysentery — 82.48 per cent.

According to expectations, nausea proved a rather frequent symptom (in 77.46 per cent) in the group with pronounced gastric phenomena — alimentary toxicoinfections. It is interesting to note, however, that by incidence of the

latter syndrome next ranks the group of influenza patients (51.35 per cent). Most likely, here the general intoxication was more strongly manifested.

Vomiting according to past history data was most frequently observed in alimentary toxicoinfections (in 100 per cent), followed by the enterocolitis group (93.96 per cent). Among the patients of the two dysentery groups (summed up) alone vomiting was absent in slightly more than half of them. Influenza patients occupied an intermediate position between the two extremes (59.42 per cent). However, vomiting was quite often in nearly one fourth of them (24.32 per cent) — more than five times daily. Therefore, by the latter indicator they closely resemble toxicoinfection patients where it amounts to 25.37 per cent. Vomiting proved a short-lasting symptom in the overwhelming number of patients in all groups. In influenza patients it ceased as early as the first hospitalization day, whilst in the remainder it lasted for two and more days after admission in sporadic cases only (0.05 to 5.00 per cent).

Subjective and palpatory abdominal pains were most frequently noted in toxicoinfection (81.65 and 77.46 per cent respectively), and most rarely — in bacterially confirmed dysentery (53.68 and 45.26 per cent). These symptoms were often met with in influenza patients also (72.97 and 45.94 per cent).

Spastic sigmoid flexure of colon was palpated on admission in about one fourth of the patients except for those with toxicoinfection where it was never detected. This sign was present equally often in patients with clinical dysentery and salmonellosis (27.00 and 27.50 per cent). This is in keeping with the impression had from the practice concerning the increased incidence of salmonellosis cases with colitis phenomena. It was furthermore supported by the practically equal incidence of tenesmus among the patients with bacteriologically proved dysentery and salmonellosis, established in the present study (16.84 and 15.00 per cent). It is noteworthy that tenesmus in patients with clinical dysentery and influenza had virtually equal incidence (27.00 and 27.02 per cent). Tenesmus phenomena were the rarest among cases with alimentary toxicoinfection.

In most of the patients the illness ran a slight and moderately heavy course. Severe clinical forms were observed in isolated cases, most frequently in toxicoinfections (11.26 per cent). No grave cases whatsoever were recorded in the salmonellosis group.

The basic syndrome in the clinical case material under study — diarrhea — was present in absolutely all patients with shigellosis, salmonellosis and enterocolitis, and virtually in all patients with toxicoinfection (96.57 per cent). Among influenza patients diarrhea was less frequent — it was absent in 32.93 per cent. The impression is that whenever diarrhea was present it was characterized by a rather high frequency of defecations — in 45.94 per cent exceeding the rate of five times daily. Such a frequency was very rarely recorded among toxicoinfection patients (9.85 per cent).

Pathological admixtures in the stools such as blood and mucus were usually established in dysentery patients — blood up to 78.10 per cent and mucus 88.32 per cent. The latter finding was by no means characteristic of the patients with alimentary toxicoinfection — here blood was detected only in 9.85 per cent, and mucus — in 15.17 per cent. However, analogical findings were present in more than one third of the influenza cases (37.83 and 43.24 per cent respectively).

ESR was speeded up in most of the patients — rather often in dysentery (80.00 and 80.28 per cent for either group), and rather seldom in toxicoinfection (53.74 per cent). An analogical finding was established in terms of the indicator “strongly (exceeding 30 mm after Westergren) speeded up ESR” — in 40.00 per cent of bacteriologically proved dysentery, and in 8.45 per cent of alimentary toxicoinfections.

The overall increase in leukocytes (exceeding 9000) was most frequently recorded among the patients with clinical dysentery (60.56 per cent), and most rarely in those with enterocolitis (40.43 per cent). A rather considerable leukocytosis (above 12 000) was present in the patients with bacterially proved dysentery. Leukocytes were often increased (in 43.64 per cent) in influenza patients too, but usually displayed insignificant values; leukocytes above the 12 000 level were recorded only in 3.10 per cent. Leukopenia (below 4000) was absent, or else it was detected in an insignificant percentage in the various groups of patients.

A shift to the left of white blood cells was recorded in a great number of patients, particularly in those affected with influenza (59.45 per cent). The latter phenomenon is most rarely observed in alimentary toxicoinfection — 36.61 per cent.

Leukocytosis (above 40 per cent lymphocytes in the differential blood count) was a rather seldom encountered sign. Its frequency ranged from 13.68 per cent (in bacterially confirmed dysentery) to 35.00 per cent (in salmonellosis). In influenza patients it amounted to 27.02 per cent which, no doubt, is comparatively rare phenomenon for a viral disease, uncomplicated by bacterial infection. However the viral character of this group of patients was evidently manifested with the frequent presence of virocytes. Thus, in the latter group the percentage of virocytes established in the peripheral blood amounted to 51.35 per cent, whilst in the other groups it was much lower, e. g. 12.63 per cent in bacterially confirmed dysentery and alimentary toxicoinfection.

IgA and IgG as compared to control healthy individuals (accordingly 199 ± 84 mg % and 1582 ± 423 mg %) showed an appreciable increase in all groups of patients, especially in salmonellosis (446 ± 61 mg % and 216 ± 423 mg %) and alimentary toxicoinfection (452 ± 121 mg % and 2455 ± 261 mg %). IgG was likewise considerably increased among the influenza patients (2497 ± 344 mg %). IgM proved to be with slightly reduced values in the patients with salmonellosis (78 ± 24 mg %) and in either group of shigellosis (95 ± 34 mg % and 106 ± 28 mg %), as compared to controls (129 ± 61 mg %). In the other groups of patients the serum IgM concentration was within normal limits.

The comparative study of the clinical symptoms in shigellosis and salmonellosis demonstrates a noticeable similarity (practically equal or close incidence percentages) between the two conditions in terms of a number of signs, the presence of tenesmus inclusive. Nevertheless, differences were likewise established. While in salmonellosis catarrhal phenomena involving the upper airways, headache, vomiting and frequent defecations (more than five times daily) were more frequent than in shigellosis patients, in the latter group a higher incidence was recorded of cases in heavy general condition, anorexia and mucous-bloody stools. It is well known that mucous-bloody diarrhea is a manifestation of hemorrhagic colitis characteristic of shigellosis, but the same phenomenon was also established in about half of the salmonellosis patients.

The so-called "dysentery-like" clinical form of salmonellosis is likewise familiar. Not infrequently, in patients admitted with diagnosis "observatio dysenteria" salmonellosis was demonstrated. These facts in conjunction with the already mentioned virtually equal incidence of spastic sigmoid flexure and tenesmus in patients with shigellosis and salmonellosis furthermore support our impression about the rise in clinical "dysentery equivalents" among salmonellosis patients. Certainly, this by all means leads to an increasing difficulty, eventually rendering impossible the differential diagnosis between the two diseases.

Among the observed influenza patients three distinct syndromes emerge: general-intoxication, catarrhal and gastrointestinal. While the first is well and often manifested with adequate morbid symptoms (except for febrility which is comparatively low), the catarrhal phenomena of the upper always are insignificant and of short duration. Catarrhs are very often recorded in the past history of patients, but on admission they are seldom present. Gastrointestinal phenomena are more strongly pronounced but, nevertheless, they are not as much frequent as in the other groups of patients. Diarrhea, for instance, is by no means a mandatory sign. The frequently established presence of virocytes in the peripheral blood corroborates the viral diagnosis and the viral mono-infection. On the other hand, leukocytosis and accelerated ESR, found not infrequently, hardly point to the same effect.

Conclusions

1 Out of the total number of 521 patients with diarrhea syndrome observed and studied, etiological agents were demonstrated in 186 cases with 137 of them being of bacterial nature, and 49 — of viral.

2. The bacterial stimulating agents were assigned to the group of shigellosis, salmonellosis and nonagglutinating vibrios, whilst the viral ones were influenza, parainfluenza, ECHO, Coxsackie, RS and adeno.

3. On the basis of clinical and laboratory data the following definitive diagnoses were established: dysentery — 233 cases, acute enterocolitis — 89, alimentary toxicoinfection — 71, salmonellosis — 41, acute gastroenterocolitis from NAG-vibrios — 1, influenza — 37, other viral infections — 11, and other diagnoses — 37.

4. The numerous clinical and laboratory points in common of the disease under study render difficult their clinical diagnostics, and lay emphasis on the necessity to carry out updated and precise microbiologic (bacteriologic, serologic and virologic) control.

5. A certain degree of hyperdiagnostics was established relative to "dysentery" and "alimentary toxicoinfection".

6. A reliable and exact diagnosis of dysentery can be also made without resorting to bacteriologic confirmation.

7. The incidence of dysentery-like salmonellosis shows an increase.

8. The laboratory data (ESR, white blood count, serum immunoglobulins) in constellation with other findings facilitate somewhat the diagnosing of diarrhea conditions.

9. Viral diseases did not show characteristic symptomatics allowing a timely diagnosis, and that is why the latter was necessarily retrospective.

10. Maximum circumspection, objectiveness and comprehensiveness are mandatory in the interpretation of the results of virological and serological study.

11. The gastrointestinal phenomena in the viral etiology cases observed may be due to a secondary bacterial infection — e. g. activation of conditionally pathogenic enterobacteria.

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**ОПЫТ НОЗОЛОГИЧЕСКОГО И ЭТИОЛОГИЧЕСКОГО РАСШИФРОВЫВАНИЯ
ДИАРРИЧЕСКОГО СИНДРОМА С ПРЕДПОЛАГАЕМОЙ
КИШЕЧНОЙ ИНФЕКЦИЕЙ**

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РЕЗЮМЕ

Проведены комплексные исследования 521 больных с диаррическим синдромом, принятых и лечившихся в клинике инфекционных болезней — Варна, в 1974—1975 году. У 186 наблюдаемых случаев доказаны этиологические агенты: у 137 бактериального естества и у 49 — вирусного. Бактериологические возбудители группы Шигелла, Сальмонелла и неаглотинирующие виброны, а вирусные — грипп, парагрипп, ЕСНО-, Коксакки, RS и Адено. На основании клинических и бактериологических данных поставлены следующие окончательные диагнозы: дизентерия — в 233 случаев, острый гастроэнтероколит — 89, пищевая токсикоинфекция 71, сальмонеллез — 51, острый гастроэнтероколит от НАГ-вибрионов — 1, грипп-

37, другие вирусные инфекции — II, другие диагнозы — 37. Авторы находят, что многочисленные клинические и лабораторные точки соприкосновения рассматриваемых заболеваний крайне затрудняют их клиническую диагностику и увеличивают необходимость современного и тщательного микробиологического (бактериологического, серологического и вирусологического) контроля. Устанавливается известная гипердиагностика в отношении диагнозов «дизентерия» и «пищевая токсикоинфекция», norостаёт частота дизентериеподобного сальмонелоза. Вирусные заболевания не показали характерной симптоматики, позволяющей их своевременный диагноз, поэтому он по необходимости поставлен ретроспективно. Лабораторные данные при исследовании больных — РОЭ, картина крови, уровень иммуноглобулинов в сыворотке крови, в сочетании с другими находками имели известную пользу в диагностике диаррических заболеваний. Авторы находят, что необходима известная осторожность, объективность и компетентность в интерпретации результатов вирусологических и серологических исследований у больных с диаррическим синдромом.