

Isolation of *N. meningitidis* from Patients in a Gonorrhea Screening Program: A Four-Year Survey in New York City

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Abstract: In the course of the screening program for gonorrhea in New York City, a total of 964 *N. meningitidis* strains were recovered from the genitourinary tract and/or anal canal over a four-year period (April 1975–April 1979), the rate of such recoveries having tripled during this time.

The majority of strains were isolated from anal canal cultures of male patients most of whom were seen in a clinic treating homosexuals. *N. meningitidis* and *N. gonorrhoeae* were cultured together from 41 patients: in 24 cases from different sites and in 17 instances from the same specimen. Evidence of clinical-

ly significant *N. meningitidis* involvement of genitourinary sites was obtained in a number of cases of urethritis and proctitis as well as in three instances of epidemiologically linked cases.

The rising frequency of *N. meningitidis* isolations from these sites, with its potential clinical implications, should alert microbiologists, clinicians, and epidemiologists to the need for careful distinction of meningococcal from gonorrheal infection, particularly among homosexual men. (*Am J Public Health* 1981; 71:53–58.)

Introduction

During the first trimester of 1975, an increase was noted in the incidence of *N. meningitidis* in cultures from the genitourinary tract and anal canal of patients screened for gonorrhea in New York City.¹ At that time, there were very few documented instances in which meningococci had been isolated from the genitourinary tract and only one report of its recovery from the anal canal could be found in the literature.

Over the ensuing years such reports have become more numerous,^{2–11} and the presence of *N. meningitidis* in these sites has been associated with various clinical syndromes, such as salpingitis,^{5, 11} fatal neonatal meningococcal meningitis,⁶ postpartum infection,⁸ pelvic inflammatory disease,^{5, 10} urethritis,^{5, 7, 9, 10} epididymitis,¹⁰ and proctitis.⁵

This paper describes the results of a continuous survey, conducted in New York City over a four-year period, from April 1975 through April 1979, of *N. meningitidis* isolation from the genitourinary tract and anal canal. Results are also presented for a large number of throat cultures, as well as genitourinary and anal cultures, collected at one clinic for homosexual men ("test clinic").

The surveillance has been facilitated by the ease of differentiating *N. meningitidis* from *N. gonorrhoeae* on NYC medium in primary isolation plates. Correlation of meningococcal colonization of these sites with clinical symptomatology and epidemiology was limited, however, to a few documented cases, briefly cited here.

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Materials and Methods

Two groups of patients were included in the survey: the first group consisted of all patients, male and female, cultured in the gonorrhea screening program conducted by the Bureau of Venereal Disease Control of the Department of Health, City of New York; the second group included only homosexual males attending one clinic referred to hereafter as the "test clinic." The culturing routines were the same for all patients in the two groups.

NYC medium was used throughout the survey period. The medium was prepared as previously described^{12, 13} with the following modifications in the concentration of the antibiotics: vancomycin 2 ug/ml;¹⁴ colistin 6 ug/ml; amphotericin B, 1.2 ug/ml; and trimethoprim lactate 3 ug/ml.

Specimens were streaked directly on to isolation plates at clinic sites. After 40 hours of incubation in candle extinction jars, at 35 C, plates were examined for the presence of oxidase positive, Gram negative diplococci. Strains presenting the characteristic colonial morphology of *N. meningitidis*¹ were further identified by sugar fermentation reactions on NYC fermentation media¹⁵ with dextrose, maltose, sucrose, and fructose.* O-nitrophenyl- β -D-galactopyranoside medium prepared according to the formulation of Lowe¹⁶ was used to test the strains for the presence of β -D-galactosidase.

*The characteristic macroscopic colonial morphology of *N. meningitidis* and *N. gonorrhoeae* on NYC medium, with confirmation on NYC fermentation media, provides accurate speciation in all instances. For quality control, serological confirmation is used routinely for all referred *Neisseria* isolates identified as *N. meningitidis* by fermentation tests. There is consistent agreement between the two types of tests. This reliability has been described in detail in our previous publications.^{1, 15}

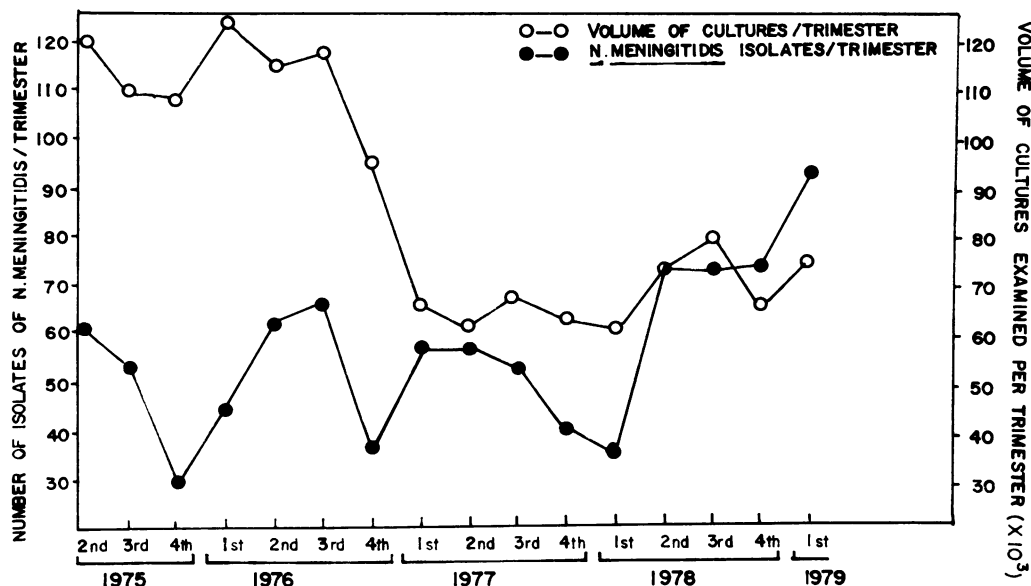


FIGURE 1—Frequency of Recovery of *N. Meningitidis* from the Genito-Urinary Tract and Anal Canal, from the Second Trimester of 1975 through the First Trimester of 1979

A total of 118 *N. meningitidis* strains were grouped serologically by the slide agglutination test using antisera obtained from Difco Laboratories, and from the National Center for Disease Control, Atlanta, GA.

Isolated *N. meningitidis* strains were cultured overnight on NYC medium prepared without the addition of VCAT antibiotics. A penicillin susceptibility test was performed on plates containing the same medium following the technique described by Bennett, *et al.*¹⁷ Strains were tested with 10-unit penicillin discs, and zone sizes were interpreted as recommended by Wiggins, *et al.*¹⁸

Beginning in 1977, all *N. meningitidis* strains isolated from the genitourinary tract and anal canal were tested for the presence of cephalosporinase using cephalosporin 87/312,** prepared as recommended by CDC.¹⁹ The test was performed on Whatman #2 filter paper to which a drop of the cephalosporin reagent had been applied. Several colonies were touched with a loop and the growth rubbed in a circular fashion over the moistened zone of the filter paper. The color change was read within one minute.

Isolation of meningococci and gonococci from the same patient from two different anatomic sites, or from the same specimen, has also been recorded. When growth of both *N. meningitidis* and *N. gonorrhoeae* occurred on a plate, the number of colonies of each was noted.

Results

The volume of cultures from the genitourinary tract and anal canal received for *N. gonorrhoeae* screening during the survey period is shown in Figure 1, together with the frequency of *N. meningitidis* recovery from these cultures.

**Supplied by Glaxo Laboratories, Greenford, Middlesex, England

There was a sharp decrease in the total volume of cultures in the second half of 1976, after which it remained fairly constant at the new level established by early 1977.

During the first three years of the survey period, the frequency of *N. meningitidis* recovery displayed a pattern of seasonal fluctuation, with peaks during the summer months and fewer isolations in the cold season. This pattern changed as isolation of *N. meningitidis* rose in the 2nd trimester of 1978, reaching a new high in the early part of 1979.***

The majority of meningococcal isolates were recovered from male patients, 84 per cent in the first two years of observation, 92 per cent and 95 per cent respectively in the last two years. In the male, the largest number of strains, 62 per cent to 71 per cent, was isolated from the anal canal (Figure 2).

In females, from whom only a small number of *N. meningitidis* strains were isolated, the cervix was the most common site involved (Figure 3). Colonization of the female anal canal with *N. meningitidis* was seen much more frequently during the last three years than in the first year. Urethral colonization remained at a relatively low level throughout.

In Figures 4 through 6 data are presented on *N. meningitidis* isolation from homosexual male patients attending the "test clinic." These data include throat culture results as well as those from other sites. *N. meningitidis* isolations from this patient group have also been compared with gonococcal recoveries.

The rate of *N. meningitidis* isolation from throat cultures taken from patients at the "test clinic" for homosexual men is shown in Figure 4 and compared with the rate for all

***Since the completion of Figure 1 (and compilation of the data on which subsequent analyses are based) *N. meningitidis* recovery rates have remained at a high level: 95 in the second trimester of 1979, 81 and 84 in the third and fourth trimesters of that year, and 70 and 77 in the first and second trimesters of 1980, while the total volume of cultures continues virtually unchanged.

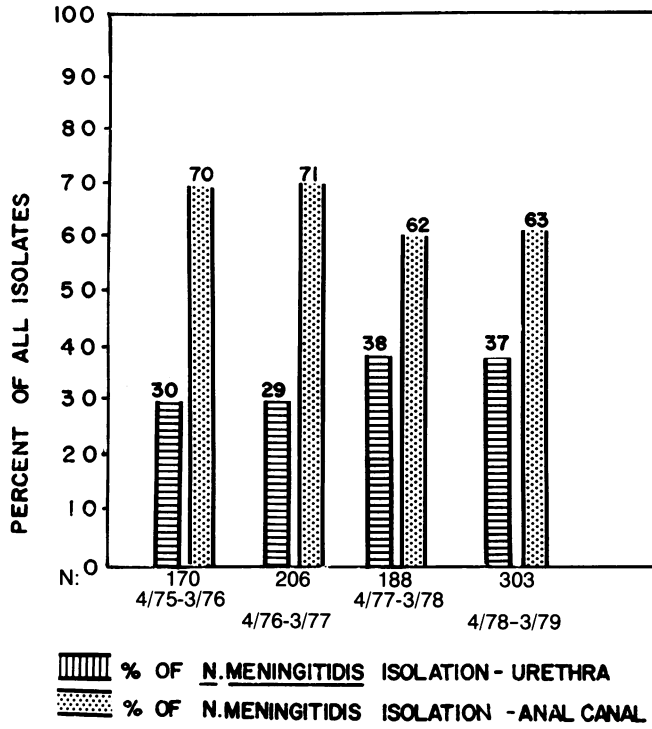


FIGURE 2—Sites of *N. meningitidis* Isolation from All Males

other patients from whom throat cultures were taken for gonorrhea screening. The total group of throat cultures from all clinics showed no significant monthly differences in the rate of meningococcal recoveries, and the percentages of isolates (29 per cent-36 per cent) were within the range reported for the general population in studies done some years ago.²⁰ Among the "test clinic" patients, however, the percentages were much higher, often nearly double those of the

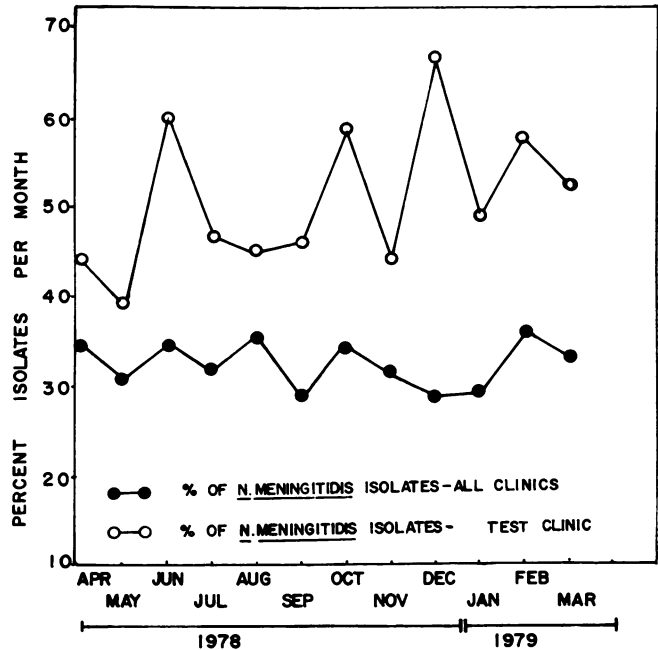


FIGURE 4—Per cent of *N. meningitidis* Isolates from the Throats of All Patients and Test Clinic Patients, from April 1978 through April 1979

whole group, with peaks up to 60 per cent and 67 per cent in some months.

Figures 5 and 6 compare the frequency of isolation of *N. meningitidis* with that of *N. gonorrhoeae* from the throats of patients seen in the "test clinic" (Figure 5) or from their genitourinary and anal cultures (Figure 6). It can be seen that the relationship between meningococcal and gonococcal recoveries from this patient group is reversed for these culture sites, meningococci being isolated more frequently from the throat, gonococci in larger numbers of genitourinary and anal cultures. When the percentages of isolation of both organisms from all sites were reviewed, it was found that *N. meningitidis* rates were higher among the "test clinic" patients than among the total group of patients screened, whereas the rate of *N. gonorrhoeae* colonization was lower in the "test clinic" than in the total group.

Simultaneous isolation of *N. meningitidis* and *N. gonorrhoeae*

N. meningitidis and *N. gonorrhoeae* were cultured together from 41 patients. In 17 of these patients both organisms were recovered from the same specimen, while in 24 cases organisms were isolated from different sites.

Among male patients, simultaneous recoveries were made 10 times from anal cultures and in three cases from urethral specimens. From female patients, there were three mixed cultures taken from the cervix and one from the anal canal. In each of these instances, the number of *N. gonorrhoeae* colonies outnumbered those of meningococci.

When the two organisms were recovered from different sites of the same male patient, we more commonly found *N. gonorrhoeae* in anal cultures with meningococci in the urethra (12 patients) than the reverse (6 patients). There were five female patients with *N. gonorrhoeae* in the cervix and

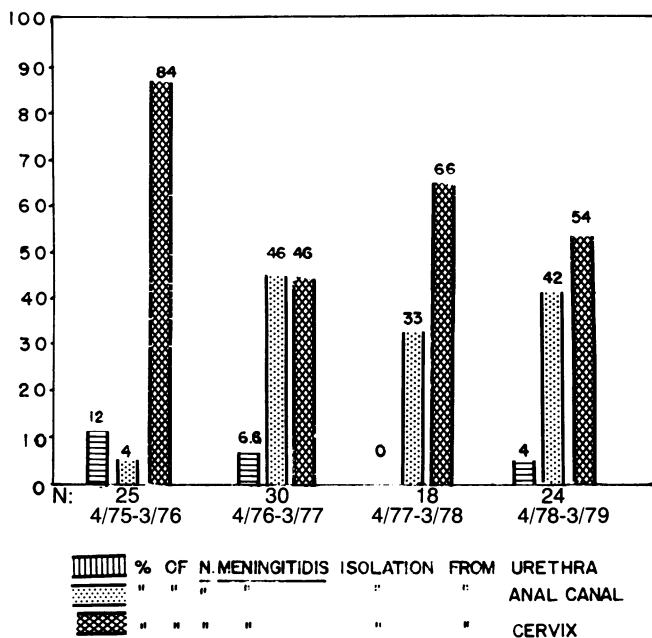


FIGURE 3—Sites of *N. meningitidis* Isolation from All Females

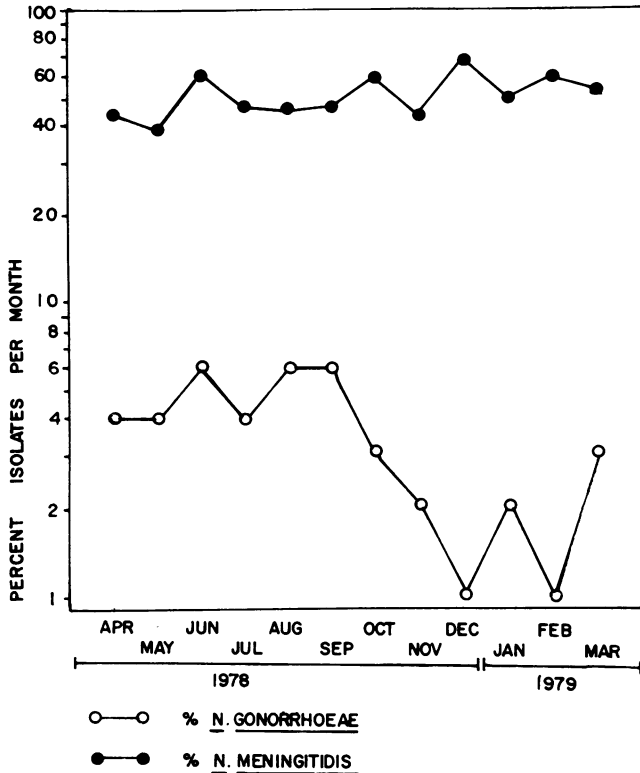


FIGURE 5—Per Cent of *N. Meningitidis* and *N. Gonorrhoeae* Isolates from the Throats of Test Clinic Patients from April 1978 through April 1979

N. meningitidis in the anal canal, and one with opposite findings.

A total of 118 *N. meningitidis* strains were serotyped; 97 of these being typable. The distribution of serogroups was not significantly different from that currently prevalent in the community. Group B was the most common serogroup, accounting for 48 per cent of the isolates. Group C was second in frequency (22 per cent), and Group Y third (13 per cent). The rest of the strains were distributed among all other serogroups except Group D.

None of the *N. meningitidis* strains was found to produce cephalosporinase and all were susceptible to penicillin when tested with 10 u penicillin discs.

Clinical Correlations

Information regarding the clinical history was available for 44 patients with meningococcal colonization. Among these, 30 were asymptomatic (26 with positive anal, four with positive urethral cultures), while 14 displayed clinically apparent infection. Seven patients of the symptomatic group presented with urethral symptoms, described as "urethritis-like gonorrhea"; the other seven with anal canal infection, their symptoms including slight discharge, pain, and local burning.

There were three instances in which it was possible to document epidemiologically linked cases of meningococcal colonization in sex partners. In one such instance,¹⁰ both

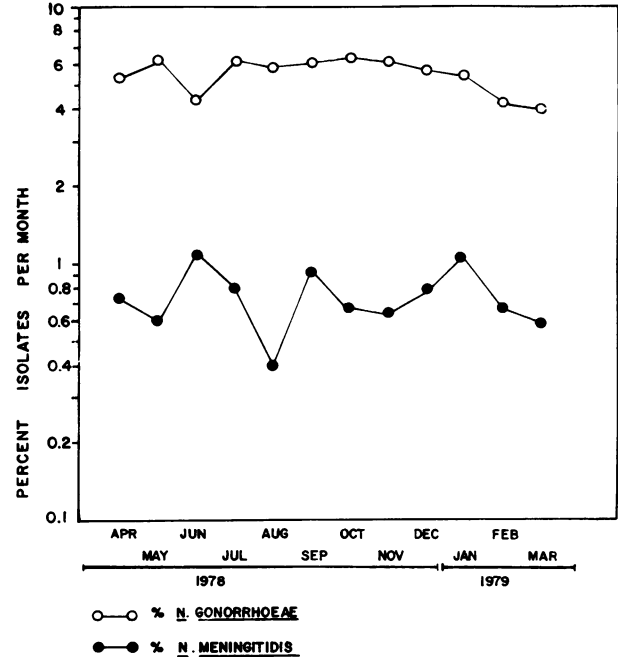


FIGURE 6—Per cent of *N. Meningitidis* and *N. Gonorrhoeae* Isolates from the Genito-Urinary Tract and Anal Canal of Test Clinic Patients, from April 1978 through April 1979

patients developed symptomatic, localized infection, the male partner presenting with symptomatic urethritis unresponsive to ampicillin-probenicid therapy. He subsequently developed epididymitis. His female contact developed pelvic inflammatory disease. *N. meningitidis*, serotype 29E, was isolated from the original genital specimens of both patients as well as from subsequent exudates.

Discussion

During the course of the gonorrhea screening program in New York City, a total of 964 strains of *N. meningitidis* was recovered from urogenital sites and the anal canal in the four-year period from April 1975 to April 1979. To date (August, 1980), the total of meningococcal recoveries made in our laboratory from such sites has increased to 1,390 strains. Although the occurrence of meningococci in the genitourinary tract and anal canal has been noted previously,^{1-5, 7, 10, 21-23} to our knowledge this report presents the largest survey of meningococcal colonization of this type yet described in the literature.

Since the beginning of our survey in 1975, the rate of *N. meningitidis* isolations from these sites has tripled, whereas the overall number of specimens collected for the screening program has diminished. The majority of strains were cultured from the anal canal of male patients, most of whom were seen in the "test clinic" for homosexual men. It is possible that similar colonization with *N. meningitidis* also occurs among other male patients routinely tested for gonor-

rhea only by smear. Information regarding four contacts of such patients who were cultured and found to be infected with *N. meningitidis* substantiates such a possibility.

A survey of the meningococcal carrier rate in the throats of patients attending the "test clinic" revealed it to be substantially higher than has ever been reported for the population at large in non-epidemic times. This high rate of throat carriers, together with the rising incidence of *N. meningitidis* isolations from the genitourinary tract and anal canal, although mostly confined to homosexual men, poses the question of its clinical and epidemiological import. Although the full significance of meningococcal colonization of these sites is not yet known, there is increasing documentation of the association of *N. meningitidis* with symptomatic urogenital infection in males, e.g., urethritis,^{5, 21-23} epididymitis,¹⁰ and proctitis.^{5, 21} In females, *N. meningitidis* has been implicated in a number of cases of salpingitis^{5, 7, 11} and of pelvic inflammatory disease.^{5, 10} In addition, two fatal cases of meningococcal meningitis in neonates, both related to maternal cervicovaginal colonization, have been presented, one by Sunderland, *et al*,²⁴ the other by Jones, *et al*.⁶

Evidence of clinically significant *N. meningitidis* involvement of genitourinary sites was obtained in our own survey in a number of isolated cases of urethritis and proctitis, as well as in three instances of epidemiologically linked cases. In one such instance, *N. meningitidis* strains of the same serotype were isolated from each of two sexual partners, both of whom developed symptomatic local infection.¹⁰ Such evidence that *N. meningitidis* is transmitted by sexual routes, that it has a pathogenic potential at sites involved in sexual activity, and that there is an increasing frequency of meningococcal colonization at these sites should alert microbiologists, clinicians, and epidemiologists to the need for careful distinction of meningococcal from gonorrheal infection, particularly among homosexual men. Improved recognition of meningococcal carriers as well as those with overt disease may contribute answers to the question of clinical management.

Finally, it is worth noting that our survey revealed a relatively sparse incidence of double infection with *N. meningitidis* and *N. gonorrhoeae*. In this context it is of interest that Volk, *et al*,⁹ have described a bacteriocin with antigenococcal activity produced by a meningococcal strain isolated from the urethra. Inhibition of the growth of *N. gonorrhoeae* due to meningococcal interference was also reported by Kraus, *et al*,²⁵ and by Shtibel.²⁶ In a study of bacteriocinogeny in *N. gonorrhoeae*, Knapp, *et al*,²⁷ employed a strain of *N. meningitidis* that actively inhibited gonococci. The possible occurrence of such interactions among strains of *N. meningitidis* and *N. gonorrhoeae* encountered in our continuing surveillance may explain the infrequency of double infections and is under consideration for further study.

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A 'Delicate' Rejection

‘ ‘ *D*ear Doctor, I have read your play,
Which is a good one in its way—
Purges the eyes and moves the bowels,
And drenches handkerchiefs like towels.
I like your moral and machinery;
Your plot, too, has such scope for scenery;
Your dialogue is apt and smart;
The play's concoction full of art;
Your hero raves, your heroine cries,
All stab, and everybody dies.
In short, your tragedy would be
The very thing to hear and see;
And for a piece of publication,
If I decline on this occasion,
It is not that I am not sensible
To merits in themselves ostensible,
But—and I grieve to speak it—plays
Are drugs—mere drugs sir—nowadays.
My hands are full, my head so busy,
I'm almost dead, and always dizzy;
And so, with endless truth and hurry
Dear Doctor, I am yours, John Murray.’ ’

—The above, written in 1817 by Lord Byron, was in response to an appeal from his publisher, John Murray, who wrote to Lord Byron, saying that his physician, John William Polidori “has sent me his tragedy. Do me the kindness to send by return post a delicate decision of it, which I engage faithfully to copy.”