All plasmids in bacteria are units which replicate independently of the bacterial chromosome, are generally less than 1/20 the size of the bacterial chromosome, and contain the information for self-replication. The 2.6-megadalton (MDa) cryptic gonococcal plasmids were first identified in the genus Neisseria in 1972 (13). Since cryptic plasmids had no measurable phenotype, they attracted little attention. The importance of plasmids in Neisseria spp. changed with the identification of β-lactamase plasmids in N. gonorrhoeae in 1976 (12). These plasmids encoded a β-lactamase which rendered the strains resistant to penicillin, the drug of choice for the therapy of gonorrhea at that time. As a result, β-lactamase plasmids had a great influence on the antibiotic treatment of gonorrhea. Since then, the indigenous 24.5-MDa conjugative gonococcal plasmids have been described and were shown to code for their own conjugal transfer, as well as mobilize the small gonococcal β-lactamase plasmids to other N. gonorrhoeae strains and Neisseria species (10, 16, 17, 21, 27, 32, 33). More recently, plasmids containing resistance determinants for tetracycline, sulfonamide, and other antibiotics have been described for various Neisseria species (14, 23–25, 28, 29, 37, 38).

Antibiotic resistance plasmids found in the genus Neisseria appear to be created either by direct acquisition of plasmids from other gram-negative bacteria or by the transposition of antibiotic resistance genes into indigenous neisserial plasmids. The β-lactamase and Rsf1010-like plasmids are examples of direct acquisition of plasmids from other species (14, 38), whereas the 25.2 MDa TetM-containing plasmid is an example of a composite plasmid (28).

The presence of genetically related β-lactamase plasmids in both N. gonorrhoeae and Haemophilus spp. strongly suggested that plasmid exchange between these two genera had occurred in nature (4–6). Similarly, the presence of the Rsf1010-like plasmids in Neisseria spp. indicated that plasmid exchange also occurred between the genus Neisseria and enteric bacteria (14, 37, 38). The 25.2-MDa plasmid has been transferred from N. gonorrhoeae, where it appears to have been created (28), into clinical strains of N. meningitidis, Eikenella corrodens, and Kingella denitrificans (22, 24, 35). Experimental studies have confirmed that the 25.2-MDa plasmid can be transferred to these species by conjugation under laboratory conditions.

In this review, I will describe the different types of plasmids currently found in the genus Neisseria and will indicate whether related plasmids are found in other genera as well. A summary of the plasmids discussed in this review is given in Table 1. Finding genetically related plasmids in both Neisseria spp. and other genera has helped to define the origin of many of the neisserial plasmids and has illustrated that the plasmids found in Neisseria spp. are directly related to the plasmid load carried by other bacteria which inhabit humans. On the basis of studies of the plasmids in Neisseria spp., one may conclude that gene and plasmid exchange is an ongoing process in nature and predict that the number of different plasmids and associated antibiotic resistance genes will increase in the genus over time.

NEISSERIA PLASMIDS

Cryptic Plasmids

The cryptic 2.6-MDa plasmids from N. gonorrhoeae were first described in 1972 (13). In an initial survey, we found that 96% of clinical isolates of N. gonorrhoeae carried this plasmid (34). However, more recently, it has been determined that all isolates of the proline-, citrulline-, and uracil-requiring auxotype are plasmid free (8). The reason for this is unclear; however, other auxotypes can also be plasmid free, although these are rare.

The 2.6-MDa cryptic plasmid is not correlated with the virulence of the gonococcal strains, pilus production, or the pilin protein, nor is it associated with the gonococcal outer membrane proteins PI, PII, or PIII, the immunoglobulin A1 proteases, the 37-kDa iron-regulated protein, or the receptor protein for the iron-retrieving siderophores (1, 2, 19). Thus, to date, this plasmid has no known function, even though the complete nucleotide sequence has been determined (26). Korch et al. (26) proposed a model for the genetic organization of the plasmid that predicted two transcriptional units, each composed of five compactly spaced genes. The promoter of one of the transcriptional units was shown to function in Escherichia coli. The products of three of the five genes in this operon were identified in minicell systems. Two genes in the other transcriptional unit were expressed in minicells when transcribed from an E. coli promoter.

It has been suggested that large segments of the 2.6-MDa plasmid can be integrated into the gonococcal chromosome in both plasmid-bearing and plasmid-free strains (19). In a few strains the entire 2.6-MDa plasmid may be integrated into the chromosome. A deletable region that contains repeated sequences has been identified in the plasmid. It is hypothesized that these repeats are involved in site-specific recombination with the chromosome and may explain why about 20% of the clinical isolates examined by Hagblom et al. carried a deleted variant of the cryptic plasmid (19).

Other Neisseria spp. also carry cryptic plasmids (11, 22, 30, 42). In one study, 69% of the plasmid-containing N. meningitidis strains, 33% of the plasmid-containing N. lactamica strains, 9% of the plasmid-containing N. mucosa strains, and 14% of the plasmid-containing N. cinerea strains were shown to carry plasmids of various sizes that hybridize with probes made from the 2.6-MDa plasmids (22). A few cryptic plasmids which do not share deoxyribonucleic acid (DNA) sequences with the 2.6-MDa plasmid have also been identified in strains of N. meningitidis (30, 42) and other commensal Neisseria spp. (10, 16). The cryptic plasmids, found in other Neisseria spp., do not occur as frequently as the 2.6-MDa gonococcal plasmid, and in general they have not been as well characterized as the 2.6-MDa gonococcal plasmid (11).

Gonococcal β-Lactamase Plasmids

The β-lactamase plasmids were first isolated in 1976 and were associated with strains from Africa and the Far East...
TABLE 1. Plasmid classes found in the genus Neisseria

<table>
<thead>
<tr>
<th>Plasmid class</th>
<th>Species</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptic (2.6 MDa)</td>
<td>N. gonorrhoeae</td>
<td>13, 19, 26, 34</td>
</tr>
<tr>
<td></td>
<td>N. cinerea</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>N. lactamia</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>N. meningitidis</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>N. mucosa</td>
<td>22</td>
</tr>
<tr>
<td>β-Lactamaseb (2.9, 3.05, 3.2, and 4.4 MDa)</td>
<td>N. gonorrhoeae</td>
<td>4-13, 33, 39, 41, 43</td>
</tr>
<tr>
<td></td>
<td>N. meningitidis</td>
<td>14, 28</td>
</tr>
<tr>
<td>24.5-MDa conjugative</td>
<td>N. gonorrhoeae</td>
<td>11, 16, 17, 32-34</td>
</tr>
<tr>
<td>25.2-MDa conjugative</td>
<td>N. gonorrhoeae</td>
<td>23, 25, 28</td>
</tr>
<tr>
<td></td>
<td>N. meningitidis</td>
<td>24</td>
</tr>
<tr>
<td>RSFI1010-likeb (4.9, 7.0, 8.5, and 9.4 kb)</td>
<td>N. meningitidis</td>
<td>14, 38</td>
</tr>
<tr>
<td></td>
<td>N. mucosa</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>N. subflava</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>N. sicca</td>
<td>29</td>
</tr>
<tr>
<td>Other (29 MDa)</td>
<td>N. sicca</td>
<td>Robledano et al., abstract</td>
</tr>
</tbody>
</table>

a These species were shown to carry plasmids of various sizes which hybridized with probes made from the 2.6-MDa plasmid.
b Related plasmids are found in the genus Haemophilus (4).c Identical plasmids are found in clinical isolates of K. denitrificans and Eikenella corrodens (24).d Related plasmids are found in enteric bacteria and Eikenella corrodens (37).

(12, 31). However, these plasmids are now endemic in isolates from North America, the Caribbean, and Europe, as well as Africa and Asia. They carry a TEM β-lactamase which hydrolyzes the cyclic amide bond in the β-lactam molecule and inactivates benzylpenicillin, ampicillin, and cephaloridine substrates but has low activity against isoxazolyl penicillins such as oxacillin and methicillin (20). Originally, two plasmids were recognized at 4.4 and 3.2 MDa; each carried the TEM β-lactamase gene and 40% of TnA transposon, which is the most frequent β-lactamase-encoding transposon in enteric bacteria (12, 20, 31). Recently, 2.9- and 3.05-MDa β-lactamase plasmids have been described; these appear to have been created by independent deletions of the 4.4-MDa plasmid (Fig. 1) (41, 43). The 2.9- and 3.05-MDa plasmids are not as common as the 4.4- or the 3.2-MDa plasmid.

The gonococcal β-lactamase plasmids are genetically related to small β-lactamase plasmids in various Haemophilus spp. (4-6, 31). These small β-lactamase plasmids from both genera are highly related and appear to represent a family of plasmids; they differ from each other by small deletions or insertions in either the TnA region, which encodes the TEM β-lactamase, or the non-TnA region (Fig. 1). The data indicate that these plasmids evolved from a single ancestral plasmid (4, 6, 7, 31). The small β-lactamase plasmids commonly found in Haemophilus ducreyi and N. gonorrhoeae contain 40 to 100% of the TnA transposon sequences. These plasmids are less common in both H. influenzae and H. parainfluenzae (4-6, 31). The β-lactamase gene, which contains less than 100% of the TnA transposon, is not transposable but gives rise to a functional transposon when linked to the left 2.4-kilobase (kb) BamHI fragment from a complete TnA transposon (15). These reconstructed transposons behaved like complete TnA transposons because of their transposition frequencies. This suggested that the partial transposons contained the inverted repeats on the right side (IR-R) of the flanking sequence and must contain an intact fragment or a transposase (tnpR)-like gene. This supports the hypothesis that all the TEM β-lactamase genes originated from an intact TnA-like transposon. DNA sequence analysis of the various plasmids has confirmed this hypothesis and is illustrated in Fig. 1 (5).

Gonococcal β-lactamase plasmids may be mobilized experimentally to E. coli or Haemophilus spp. by a variety of conjugative plasmids, including those from E. coli, N. gonorrhoeae, or H. ducreyi (4, 10, 16, 27, 32, 33). However, initial attempts to transfer these β-lactamase plasmids into other Neisseria spp. met with only limited success (17). When introduced into the commensal Neisseria spp., the β-lactamase plasmids were very unstable and were quickly lost from most of the recipient strains. In a later study, Ikeda et al. (21) used the indigenous 24.5-MDa plasmid to transfer the 4.4-MDa β-lactamase plasmids from N. gonorrhoeae to strains of N. meningitidis.

Recently, using strains containing both the β-lactamase plasmid and the 25.2-MDa tetracycline resistance conjugative plasmid, we mobilized the 4.4- and 3.2-MDa β-lactamase plasmids into a variety of Neisseria spp., including N. meningitidis (36). A number of the transconjugants maintained the β-lactamase plasmids in the absence of selective antibiotic pressure. In all cases, the β-lactamase plasmid was associated with the 25.2-MDa plasmids in the transconjugants. We found that the N. cinerea transconjugants were exceptions to this generalization because when they were used as recipients, the β-lactamase plasmids were found without the 25.2-MDa plasmids (36). Recently, β-lactamase-producing N. meningitidis strains have been described (3, 9). In one case, the strain was isolated from a mixed culture with N. gonorrhoeae (9), and in the second case, it was not clear whether the β-lactamase enzyme was located on a plasmid or in the chromosome (3).

The small TEM β-lactamase plasmids have been transferred into N. gonorrhoeae and E. coli by transformation (31, 39). Sox et al. (39) showed that 25% of the plasmids in the gonococcal transformants had deletions, the most common of which was a 3.2-MDa plasmid. It is possible that the various gonococcal β-lactamase plasmids were created by deletions following transformation (39).

The DNA sequences of the gonococcal 4.4- and 3.2-MDa β-lactamase plasmids and the H. ducreyi 5.7- and 7.0-MDa β-lactamase plasmids have been determined (5). On the basis of these data and those of Yeung et al. (43) and Van Embden et al. (41), a model has been devised to account for the evolution of the small TEM β-lactamase plasmids (Fig. 1). The sequence of events hypothesized for this model is shown by the numbers 1 to 9 in Fig. 1 and explained in detail in the legend. Dickgiesser et al. (6) have suggested that the 1.8-kb insertion found in the 4.4- and 7.0-MDa plasmids, but not in the 5.7- or 3.4-MDa plasmids, is bounded by a short (200-base-pairs) terminal inverted repeat sequence and may be a bona fide insertion element.

GONOCOCCAL CONJUGATIVE PLASMIDS

24.5-MDa Conjugative Plasmids

The 24.5-MDa conjugative plasmid was first described in 1974 (11). It has been found in clinical strains of non-penicillinase-producing N. gonorrhoeae as well as in penicillinase-producing N. gonorrhoeae (11, 34), but not in any other clinical species. The prevalence of this plasmid varies geographically and temporally (34). In a recent survey of five geographical locations within the United States, the number of strains carrying the 24.5-MDa plasmid varied from 10 to

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FIG. 1. Model for the creation of the small β-lactamase plasmids in *Neisseria* and *Haemophilus* spp. The events numbered in the figure are as follows. 1: Transposition of a Tn2-like transposon from an enteric plasmid onto an ancestral *Haemophilus* plasmid; 2: mutation in Tn2 to replace a cytosine with a thymidine at base pair 3773 from the IR-L terminus of Tn2 (*†*); 3: insertion of a 1.8-kb insertion sequence distal to IR-L; 4: deletion in the plasmid created in step 2 to produce the 3.2-MDa *N. gonorrhoeae* plasmid; 5: mutation from cytosine to thymidine (*‡*) in the noninsert plasmid made in step 2, to form the 5.7-MDa *H. ducreyi* plasmid; 6: independent deletion from the plasmid created in step 3, to produce the 4.4-MDa *N. gonorrhoeae* plasmid; 7: deletion of most of the 1.8-kb insert and a portion of the flanking sequences to create the 3.05-MDa *N. gonorrhoeae* "Toronto" plasmid; 8: another, separate, deletion in the same region of the plasmid to create the 2.9-MDa *N. gonorrhoeae* "Rio" plasmid; 9: mutation from guanosine to adenosine at position 3771 3' (+) of the IR-L terminus to form the 7.0-MDa *H. ducreyi* plasmid. The 4.4-, 3.05-, 2.9-, and 3.2-MDa plasmids have been isolated from strains of *N. gonorrhoeae*, whereas the 7.0- and 5.7-MDa plasmid have been isolated from strains of *H. ducreyi*. The other plasmids have not been isolated and are hypothetical. Data are summarized from references 5, 6, and 43.

53% (J. S. Knapp, J. M. Zenilman, R. Rice, M. C. Roberts, S. McIntire, and S. A. Morse, Sex. Transm. Dis., in press). In some cases, the 24.5-MDa plasmid is the only plasmid species present; however, it can coexist with the 2.6-MDa and the gonococcal β-lactamase plasmids (34).

The 24.5-MDa plasmid carries no detectable markers for antibiotic resistance, heavy metal, or ultraviolet resistance. However, it efficiently mobilizes itself and the smaller β-lactamase plasmids between strains of *N. gonorrhoeae* (10, 32, 33). When short mating times are used, only the β-lactamase plasmids are transferred to the recipient, whereas after overnight matings, many of the *N. gonorrhoeae* transconjugants carry both the β-lactamase and 24.5-MDa plasmids and can transfer both plasmids to other *Neisseria* spp. and *E. coli* (17, 21); however, it is not transferred to these other species. Its host range is very limited even under laboratory conditions, and other than *N. gonorrhoeae*, only certain strains of *N. cinnerea* maintain it (17).

The structures of a limited number of 24.5-MDa plasmids have been determined; all had similar restriction patterns and shared 69 to 100% of their DNA sequences with two reference 24.5-MDa plasmids (34).

25.2-MDa TetM Conjugative Plasmids

The 25.2-MDa plasmid was first identified in a strain of *N. gonorrhoeae* isolated in 1982 (25). By 1985, a number of clinical isolates in North America and Europe carried this plasmid (23, 35, 28; M. C. Roberts, J. H. T. Wagenvoort, B. van Klinger, and J. S. Knapp, Letter, Antimicrob. Agents Chemother. 32:158, 1988). At present, the 25.2-MDa plasmid appears to be endemic in North America and has been found...
in Great Britain and The Netherlands. Most of the strains in The Netherlands and a few from North America carry the 3.2-MDa β-lactamase plasmid in addition to the 25.5- and 2.6-MDa plasmids (25; Roberts et al., letter). Recently, the 24.5-MDa conjugative gonococcal plasmids have been shown to share >60% of their DNA sequences with the 25.2-MDa plasmids (28). These data have led to the hypothesis that the 25.2-MDa plasmid was formed by the transposition of the TetM determinant, encoding tetracycline resistance, onto the 24.5-MDa plasmid. The 25.2-MDa plasmids have characteristics which differ from those of the 24.5-MDa ancestral plasmids, but they have maintained the ability to move themselves and the β-lactamase plasmids to recipient strains (36). The 25.2-MDa plasmid has been associated only with the 3.2-MDa plasmid; therefore, it can be hypothesized that the 25.2-MDa plasmid was created in an N. gonorrhoeae with the 3.2-MDa plasmid; therefore, it can be hypothesized that the 25.2-MDa plasmid was created in an N. gonorrhoeae population which carries the 3.2-MDa plasmid, such as in North America, Europe, Africa, or the Caribbean.

Naturally occurring strains of N. meningitidis, K. denitrificans, and Eikenella corrodens that carry the 25.2-MDa plasmid have been identified in both North America and Great Britain (24, 40); these species do not normally harbor the indigenous 24.5-MDa plasmid, and attempts to introduce this plasmid into strains of N. meningitidis and other Neisseria spp. have generally been unsuccessful (17). However, it has been shown experimentally that the 25.2-MDa plasmids can be transferred by conjugation, maintained, and transferred back to N. gonorrhoeae from N. meningitidis, as well as to the other Neisseria spp. tested (35).

Both the 24.5- and the 25.2-MDa plasmids can mobilize the gonococcal 4.4- and 3.2-MDa β-lactamase plasmids to a variety of bacterial species. However, when the 24.5-MDa plasmid is used to mobilize the β-lactamase plasmids, only N. gonorrhoeae and some of the N. cinerea transconjugants receive or maintain the 24.5-MDa plasmid (17). When the 25.2-MDa plasmid was used to mobilize the β-lactamase plasmids, all transconjugants, with the exception of some N. cinerea recipients, acquired and maintained the 25.2-MDa plasmid, whereas fewer transconjugants acquired the β-lactamase plasmid (36). Thus, the 25.2-MDa plasmid differs from the ancestral 24.5-MDa plasmid by its wide natural host range, while retaining its ability to mobilize the β-lactamase plasmids between strains. It is not known whether the ability of the 25.2-MDa plasmid to transfer to many bacterial species is due to the direct influence of the TetM genes, or whether the TetM determinant was inserted into the 24.5-MDa plasmid in such a way that it has altered or deleted DNA sequences that previously restricted the ability of the 24.5-MDa plasmid to be accepted or maintained in other bacterial species.

**Rsf1010-Like Plasmids**

Recently, a new group of plasmids ranging in size from 4.9 to 9.4 MDA has been described for N. meningitidis, N. mucosa, N. subflava, and N. sicca (14, 29, 38). These plasmids are genetically related to the enteric plasmid Rsf1010 which is an IncQ(P-4) plasmid that encodes streptomycin and sulfonamide resistance owing to the production of a streptomycin phosphotransferase and sulfonamide-resistant dihydropterotate synthetase (14, 38). A related plasmid has also been found in Eikenella corrodens (37). Some of these plasmids specify resistance to sulfonamide alone, whereas others specify resistance to penicillin, streptomycin, and sulfonamide (14, 29, 37, 38). In some cases, the relationship of the Neisseria plasmids to the ancestral Rsf1010 plasmid has been based on DNA homology with the Rsf1010 plasmid, including the antibiotic resistance region as well as regions outside the antibiotic resistance genes (29, 37, 38). In other cases, the relationship between the Neisseria plasmids has been based on more circumstantial data, such as similarities between the proteins encoded by the antibiotic resistance genes (14).

Plasmids encoding streptomycin, sulfonamide, and TEM-type β-lactamase resistance have been isolated from N. mucosa, N. subflava, N. sicca, and Eikenella corrodens (29, 37, 38), whereas plasmids specifying resistance to sulfonamide alone have been found in N. meningitidis strains (14). All of the multiresistance plasmids can be transferred by transformation and maintained in E. coli (29, 37, 38). The N. meningitidis sulfonamide resistance plasmid has been transferred by transformation and maintained in N. gonorrhoeae (14). This sulfonamide resistance plasmid may have been created (by the deletion of the streptomyacin gene) from Rsf1010 and then introduced into N. meningitidis. However, the N. meningitidis plasmid is larger than the Rsf1010 ancestral plasmid, suggesting that the Rsf1010 ancestral plasmid did not exist before the Rsf1010 plasmid was introduced into N. meningitidis by transformation and maintained in E. coli (29, 37, 38). The fact that the transposition of Tn10 onto Rsf1010 occurred following the insertion of other sequences or by the duplication of existing sequences (14).

The data obtained by several investigators suggest that the multiresistance plasmids carrying streptomycin, sulfonamide, and TEM β-lactamase (14, 38) were created by the transposition of Tn4 onto Rsf1010. These plasmids were subsequently spread, by mobilization or transformation, to other bacterial strains. The fact that the transposition of Tn4 onto Rsf1010-related plasmids occurs under laboratory conditions would support this hypothesis (20). However, there are differences between the naturally occurring plasmids and those created in the laboratory. The laboratory-created plasmids carry the whole Tn4 transposon, whereas the naturally occurring plasmids do not (20). The possession of an incomplete Tn4-like segment by the multiresistance plasmids found in commensal Neisseria species is the only similarity between them and the gonococcal β-lactamase plasmids.

**Other Plasmids**

Robledano et al. (L. Robledano, M. J. Rivera, P. Madero, M. A. Marco, I. Otal, M. C. Aquido and R. Gomez-Lus, Abstr. 5th Int. Congr. Chemother. 1987) reported the presence of a 29-MDa plasmid coding for ampicillin, tetracycline, streptomycin, kanamycin, neomycin and lividomycin resistance in a strain of N. sicca. The plasmid coded for two aminoglycoside-modifying enzymes, APH3' and APH3'. This plasmid was conjugally transferred to an N. sicca but not to an E. coli recipient strain, suggesting that it was not of enteric origin. The genetic relationship of this plasmid to other Neisseria plasmids has not been determined, and, as a result, the origin of this plasmid is unclear.

**CONCLUSIONS**

The 2.6- and 24.5-MDa plasmids have been found in isolates of N. gonorrhoeae preserved since the 1940s (34). In contrast, plasmids carrying antibiotic resistance genes are relatively new; the β-lactamase plasmids appeared in the 1970s (12) and the TetM-containing plasmids in the 1980s (25). Most of the antibiotic resistance genes that have spread into Neisseria spp. are associated with transposons. These determinants can either be introduced into new species on
plasmids capable of being maintained in the host, such as the 

-<br> broad-host-range enteric RSF1010-like plasmid or the 

-<br> Haemophilus β-lactamase plasmid, or be integrated into indige-

nous host plasmids as seen with the 25.2-MDa plasmid. In 

either case, once the R factor is created or introduced, it can 

then be spread by conjugation or mobilization to other 

strains, other species within the same genus, and other 

genera of bacteria. Transformation may play a role in 

plasmid spread between strains, because many of the plas-

mids discussed above have been experimentally transferred 

to various hosts by transformation (39). However, deletions 

often appear in these plasmids during transformation, and 

the frequency of transfer by transformation is usually signif-

icantly lower than the frequency of transfer by conjugation 

(39).

Gene spread has also occurred in the genus Neisseria as a 

result of the transfer of antibiotic resistance genes associated 

with the conjugative transposon, TetM (24). Clinical isolates 

of commensal Neisseria species have been isolated that have 

the TetM determinant integrated into their chromosome (24). 

The fact that commensal Neisseria spp can acquire and 

maintain the 25.2-MDa plasmid if given the opportunity (35) 
suggests that the commensal Neisseria strains have not 

acquired the TetM determinant from N. gonorrhoeae but 

rather from other bacterial species. This would explain why 

in the laboratory the 25.2-MDa plasmid is stable in the 

commensal Neisseria spp. but all the natural clinical isolates 

carry the TetM determinant in the chromosome.

The RSF1010-like plasmids, in general, appear to be rather 

limited in their geographical distribution; this may be be-

cause very few investigators have examined commensal 

Neisseria spp. for antibiotic resistance genes. The recent 

observation that the RSF1010-like plasmids can carry not 

only the sulfonamide-resistant dihydropteroate synthetase 

and streptomycin phosphotransferase (normally associated 

with this plasmid) but also the TEM β-lactamase is of 

interest. The RSF1010-like plasmids are the first multiresis-

tance plasmid group found in Neisseria spp. The versatility 

in the number of antibiotic resistance genes which the 

RSF1010-like plasmid can carry is unique among the neisse-

rial plasmids. In addition, these plasmids are found in a 

number of different species. Since the RSF1010-like plasmid 

has already been found in N. meningitidis, it is very possible 

that this plasmid group will be disseminated to N. gonor-

rhoeae; therefore, more work to characterize this plasmid 

family should be done.

The number of plasmids carrying antibiotic resistance 

genes has increased in the genus Neisseria over the past 10 

years. This increase is due not only to an increase in the 

number of strains carrying the previously described plas-

mids, but also to the identification of new plasmids carrying 

a number of different antibiotic resistance determinants in 

various commensal Neisseria spp. The antibiotic resistance 

genes currently found have all been identified in other 

bacterial genera, usually enteric species, and, with the 

exception of the TetM determinant, all plasmids carrying 

antibiotic resistance genes appear to have originated in other 

gram-negative bacteria. The TetM determinant appears to 

have originated in gram-positive streptococci (28). It might 

be anticipated that when the prevalence of plasmids and 

antibiotic resistance genes increases in other bacteria, espe-

cially the enteric species, it may lead to the transfer of these 

plasmids and antibiotic resistance genes to Neisseria spp. It 

is important, therefore, to continue screening isolates of 

both pathogenic and nonpathogenic Neisseria spp. for anti-

bacterial resistance and then to determine whether the resis-

tance is due to the acquisition of new genetic material or to 

chromosomal mutation. The commensal species have been 

shown to carry multiresistance plasmids and may act as 

reservoirs for plasmids and antibiotic resistance genes that 

might be transferred to the pathogenic Neisseria species at a 

later date. Antimicrobial therapy for gonorrhea and menin-
gitis may be more complicated in the future if these multire-

sistance plasmids become established in the pathogenic 

Neisseria spp.

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